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TITIO

# **Book Release**

Synopsis by Faroque A Khan



Prof.Faroque A Khan (New York)

This book is about the lives and achievements of one hundred Kashmiri doctors who have done outstanding work in Kashmir or outside Kashmir. The book focuses on prominent doctors who served in Kashmir in the postmissionary era. It covers nearly a century of health care in Kashmir through the profiles of Kashmiri doctors of various eras who served there. Published by Partridge Publishing India (September 12, 2023)

# Authors:

# Dr. Rumana Makdoomi

Professor ,Department of Pathology at SKIMS ,Soura Srinagar. Her earlier book "WHITE MAN in DARK' is an account of the work done by the healthcare professions during the Turmoil in Kashmir

#### **Dr.Faroque A Khan**

Dr Khan has served as Regent of the American College of Physicians, as President of Nargis Dutt Memorial Foundation, as President of Islamic Medical Association of North America (IMANA), as President of Islamic Center of Long Island and has served on the Majlis Shura of the Islamic Society of North America .Dr Khan has received many awards for his interfaith work.He is is one of the founding members of ICLI, involved in interfaith outreach since 1992 and serves on ICLI board of trustees..

# Warriors and Falcons

Available amazon.in Kindle Edition Rs.140 Paperback Rs.594 Hardcover. Rs.1231



#### Dr. Farqoue A Khan

Kashmiri doctors have done a remarkable job, everywhere in the world. We are filled with pride when we hear the tales of their accomplishment. Back home in Kashmir, they have braved the odds fighting illiteracy, poverty and conflict. They have kept the candle of medicine burning through Govt. Medical College Srinagar, which in spite constraints continued to train doctors, who were truly world class. Government Medical College Srinagar has become a mother institution that leads from the front to supply doctors to all the regions of Jammu &Kashmir and many prestigious institutions of the world.

Kashmir has produced too many heroes in medicine who have contributed here and abroad. While all else could close in an atmosphere of tension and turmoilthe hospitals in Kashmir could not afford to shut their doors to the people. For a doctor working in Kashmir turmoil has been almost a constant companion. The doctors in Kashmir had to deal with injuries caused by bullets, pellets, and blasts besides dealing with the whole epidemic of psychiatric diseases consequent to mental trauma. Thankfully! The doctors working here did not fail their population. Every crisis was managed effectively though no doctor working during peak years of turmoil had ever been trained for what he was treating...Doctors sacrificed their time and comfort, compromised their own security and worked hard. They restored man's faith in humanity and medicine. Most doctors suffered braving the challenging times that would collapse the best healthcare systems of the world. All doctors working in those times need to be complimented for how theyworked under pressure and pain. There are stories of exemplary work; exceptional courage and tortuous suffering that went unheard and unpublished. No gallantry awards were given and no certificates of appreciation were distributed. In such a scenario every doctor is a hero, how can I quantify his work? When your outside is burning and inside is in pain-how do you practice medicine? When in the line of your duty you have to declare your own son dead, what code will you follow? When you have to remove bullets from a professors eye with whom out of respect you could never maintain an eye contact, which ethics will you follow? What when you intubate your life partner who received a bullet injury on his way to the hospital? What when before declaring unfortunate news of death to the old and weak parents of a boy who received a stray bullet- you are yourself inconsolable? What when you cannot decide whose life to save first- a man with three tiny daughters or a young man gasping for breath? I know we need to credit each one for what one did. We will need a lifetime to put into limelight those stories of compassion and valor that doctors of Kashmir exhibited amidst crises -and let the world learn from them.

The book is the first of its kind and is thoroughly researched. It goes back in time and brings to limelight the era when Kashmir hardly had any doctors. The book has five sections –first three sections deal with the doctors who served in Kashmir whereas one section deals with the Kashmiri doctors who worked abroad and made some phenomenal contributions to medicine. It is followed by Tribute section based on tribute to the non-Kashmiri doctors who made significant contributions to healthcare. The sections are as under:

Section I: The Legends Section II: The Pioneers Section III: The Innovators Section IV: The Path –breakers Section V: Tribute Section I: The Legends

This section includes 25 doctors who greatly influenced the healthcare landscape in Kashmir. Prominent among them are Dr.Ali Jan, Dr.Gwash Lal Kaul, Dr.Vashnavi, Dr.Ghulam Rasool, Dr.Allaqaband, Dr.Syed Naseer Ahmad Shah,

Dr.GirjaDhar,Dr.Bilqees Jamila, Dr.MS Khuroo, etc. who were the founding fathers of medicine,

surgery and gyne and helped to establish GMC Srinagar as the prime medical college of the state.

## **Section II: The Pioneers**

This section includes 25 doctors who established themselves as clinicians and surgeons of repute and contributed to GMC Srinagar as excellent teachers and trendsetters. They helped to develop specialties and sub-specialty departments. Prominent among them areDr. Abdul Ahad Beig,Dr. Abdul Ahad Guru,Dr. Abdul Hamid Fazili, Dr. Abdul Hamid Zargar ,Dr. Abdul Rashid Khan Dr.Amarjeet Singh Sethi etc.

## Section III: The Innovators

This section includes 25 doctors who did outstanding work in spite of the constraints in Kashmir and held the institutions of Kashmir together braving the odds. Turmoil and challenging times did not hold them back from delivering their best in the most trying times. Prominent among them are Dr.Showkat Ali Zargar, Dr.Khurshid Iqbal, Dr.Shabir Iqbal, Dr.ParvaizKoul,Dr.OmarJaved etc.

#### Section IV: The Path –breakers

This includes Non resident Kashmiri doctors who went to far off lands like Europe and America and made a name for themselves by doing extraordinary work and establishing themselves as world leaders. Prominent among them are Dr.fayaz Shawl the interventional cardiologist of international repute, Dr.Mian Mohammad Ashraf cardiothoracic surgeon, Dr.PK Shah an expert cardiologist and researcher, Dr.Arfa Khan a renowned pulmonary radiologist, Dr.Ghulam Jeelani Mufti a hematologist of repute and Dr.Owase Jeelani an expert neurosurgeon and others who did an outstanding work. This part of the book is authored and introduced by Prof.Faroque A Khan the eminent pulmonologist from New York who is involved in community work and has helped to launch the Interfaith Institute of Long Island.

#### **Section V: Tribute**

This sections deals with the tribute to some of the prominent non Kashmiri doctors who did a remarkable job for the development and improvement of healthcare in Kashmir.Dr.ErnaHoch,Dr.Jagat Mohini, Dr.Nagpal etc. have been included in this section.

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#### **Review**

# Euthanasia: Universal Human Concern- An Analytical Study in Jurisdictions of Netherlands, Canada and India

Ishita Saboo, Fakkiresh S. Sakkarnaikar

#### Abstract:

The recent inventions in the Information Technology (IT) have transformed the world into a global village wherein the geographical boundaries have vanished significantly. The recent pandemic Covid-19 has again proved the affiliation of the world. IT coupled with the Artificial Intelligence has revolutionized the medical science. It has demystified various terminal diseases; however, the "man is still mortal". A good number of diseases are still terminal and cause incurable, unbearable pain, mental and financial trauma for the victims and their family. The surety of death in near-term originated the thought of Euthanasia or mercy killing. *Euthanasia* in simple words refers to a voluntary/consent as given by the patient to terminate the life in a dignified manner to get relieved from sufferings. Different countries have different variation of Euthanasia. This Article aims to study the euthanasia practice in Netherlands, Canada, and India. India is a country where recently Supreme Court has recognized passive Euthanasia and Living Will.

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**Keywords:** Active and passive Euthanasia, LivingWill,MAID.

### Introduction

Euthanasia refers to a voluntary/consent as given by the patient who is suffering from incurable diseases with no prospect of cure to end or terminate the sufferings [1] in a dignified manner. Euthanasia has been legalized in different geographies of Europe and Western countries but still many countries are in the discussion mode while their citizens are very vocal in favor of Euthanasia. Among the Asian countries, Supreme Court of India has given the approval for passive Euthanasia [2] in recent decisions. India is one such progressive country which is working proactively towards giving a green signal for the act of Euthanasia. The proactive and liberal approach on Euthanasia by a few countries is encouraging "Euthanasia tourism" among Euthanasia restricted countries [3].

This Article reviews and analytically studies the legal accreditation of Euthanasia by Netherlands, being the first European country approving Euthanasia, Canada very recent country (March'21) issued detail guidelines under "Medical Assistance in DyingAct" (MAID) [4] and India where Supreme Court has recognized Passive Euthanasia and the execution of "Living Will". India is the only one among SARRC countries where positive thoughts on Euthanasia has gained momentum India is experiencing the similar to

psyturve in legal decisions like that in Canada. The study of Euthanasia changeover in Netherlands, Canada may be helpful to India which is in still in nascent stage of set up the legal system in the country. In terms of the jurisprudential argument in terms of the theory as given by Thomas Acquinas, "the principle of double effect" wherein "it may be permissible to bring about as a foreseeable side effect a harmful event that would be impermissible to cause intentionally, particularly when the potential benefit outweighs the side effect's harm" [5]. Hence, it holds the view that terminating or shortening the process of dying in order to relieve the sufferings is justifiable by the Physicians [6].

Indian philosophy and culture have not been in complete favor of the practice of Euthanasia in its entirety and hold a conservative approach. The legal professionals or the medical fraternity in India are also not comfortable with the idea of Euthanasia or self-killing by the individuals [7]. India's journey shares a close association with the path as followed by Canada. The origin of Right to Die with respect to Right to Life and subsequently passing law on Passive Euthanasia and Living Will has been analyzed and traced in detail via the judicial pronouncements.

The Netherlands legal system on Euthanasia: Netherlands is one such country, which holds the

feather in its cap for passing a law/Act on Euthanasia, **"Dutch Termination of Life on Request and Assisted Suicide (Review Procedures) Act**[8]"in April 2001which came into force on 1<sup>st</sup> April2002. Although, the enactment of law was an active outcome of the brainstorming as done by the stakeholders for more than two decades, the issue gained momentum later in nineteens. Netherlands has formulated a structured legislation on Euthanasia serving as a skeleton role model for the other nations to follow.

The distinguishing feature of the Act is that it has clearly laid down the criteria with respect to Euthanasia as christened as "Assisted Suicide". The Act has also imposed the legal duty of due diligence on the medical professionals/physicians who shall ensure meticulous compliance of the Act to avoid any criminal action and get full protection for assisting in suicide of the patient who voluntarily wishes to terminate the sufferings. In other words, according to the provision of this Act, "Euthanasia and physicianassisted-suicide" are not a punishable offence if the physician administering Euthanasia, acts in accordance with the doctrine of "due care" [9].

As explained above, Euthanasia is essentially the active/passive termination of the life of the patient who is suffering from terminal disease and bearing incurable and unbearable pain and mental trauma. In Netherlands[11], the Physicians can assist in life termination only after obtaining the voluntary and the well-informed request of the patient. Only physicians are allowed to perform Euthanasia or terminate the sufferings of the patient. It should be discussed with the patient and his family, and it can be initiated when there is no any other alternative is available for a dying patient.

The physician who is providing medical treatment should take an independent opinion from other physician who is not related with the treatment to avoid any malpractice/ or motives, the "Royal Dutch Medical Association (KNMG)" has prepared a panel of independent, expert doctors known as SCEN physicians (SCEN: Support and Consultation on Euthanasia in the Netherlands). SCEN physicians are available for support, information and formal consultation [8].

According to the Act [8], there is a provision of "Review Committee" wherein the Physicians are under the legal obligation to report the Euthanasia cases. There has been established a five regional Review Committee who are given the task of dealing with the cases of Euthanasia or that of the Assisted Suicide. Each Committee consists of three members, the usual one and the three alternate members who are legal expert, physician and one expert on the ethical issues. The Physician who is going to assist the patient must inform and make a report of the Euthanasia to one out of the five Regional Review Committees as established for carrying out Euthanasia. The committee acts as a checks and balance mechanism and evaluates that whether the medical professional(s) who are assisting the Euthanasia are complying with the due care norms or not. Abiding by the same ensures greater consistency and the transparency in the manner the cases are reported and thereby assessed. Any casual approach or laxity on the part of physician may be prosecuted.

The most recent watershed news on Euthanasia in Netherlands is the case of Noa Pothoven, a Dutch Author and an eminent mental health activist [10]. She died at the age of seventeen that had led to a global controversy owing to the public statements made by her about her wish to die[11]. She wrote her autobiography, "Winnen of Leren" [10], wherein she described her own battle with PTSD as a result of the sexual assault, anorexia and her self-harm tendencies. Around May 2019, she had completely stopped eating and drinking. She subsequently expired on June 02, 2019 and media falsely and allegedly reported that she died of an assisted suicide, however she had stopped eating and drinking which eventually led to her death and not by administration of any lethal drug or assisted suicide [12]. This is one such instance of "passive euthanasia" done by her. AndriesPostma (1973) [13] is a landmark case which initiated the debate on Euthanasia in Netherlands. At that time Euthanasia was not permitted in Netherlands. Dr. Postma was a physician and found guilty of voluntarily euthanasia and was convicted. Mother of Dr. Postma was 78-year-old and undergoing the recovery treatment from a cerebral hemorrhage. She expressed her desire to die and be relived of all the sufferings to her daughter as well as the staff of the nursing home. Dr. Postma administered the Euthanasia on her mother to relive her of all the sufferings. This case initiated the legal arguments and discussion on euthanasia. Thirty years after of this case, Euthanasia got the legal approval and Netherlands became the first country for legal recognition to Euthanasia. Thisled to the formulation of Dutch Termination of Life on Request and Assisted Suicide (Review Procedures) Act as passed in 2002 [8] which absolves the physicians of criminal liabilities while administering euthanasia if they comply with the following guidelines strictly:

- If the suffering of the patient is unbearable and it shows no signs of improvement.
- The request should be made at the instance of the patient voluntarily and should persist over a period.
- There should be an awareness of the condition, prospects, and the options to the patient.
- There should be a consultation regarding the same with at least one independent doctor who confirms owing to the facts of the circumstances in the given case.
- The procedure of administering the death should be done in a medically appropriate

fashion by the doctor or that of the patient and the former must be mandatorily present.

The patient in question shall be at least 12 years old (patients who are between the age of 12 and 16 years required the valid consent from their parents).

Though in the above-mentioned case [13], the administration of lethal drug to end the sufferings of the patients was not accepted, subsequently over the years, a proper law has been formulated to accept such act of assisted suicide and criminal liability is not imposed on the physicians who are performing the same.

Therefore, the progress in the journey of Netherlands serves as a role model for other nations to follow. They are more liberal in supporting the Euthanasia [14].

# Legal battle on Euthanasian in Canada:

Canadian Parliament passed the Criminal Code [15] in 1892. When the code was introduced, the offence of "*suicide*" and "*attempted suicide*" was attracting the criminal punishment under "Section 241(b)", but it was repelled in 1972. However, abetment or assisting suicide continues to be a criminal offence under "Section241(a)" and an imprisonment up to 14 years may be imposed under the code. This law is still in existence [15].

Sue Rodriguez [16] was resident of Victoria, British Columbia. In 1991, she was diagnosed with "Amyotrophic Lateral Sclerosis (ALS), which is a rare neurological disease that primarily affects the nerve cells (neurons) responsible for controlling voluntary muscle movement (those muscles we choose to move). Voluntary muscles produce movements like chewing, walking, and talking. The disease is progressive and get worst over time". Rodriguez sought assisted suicide at her convenient time and challenged the constitutionality of "Section 241 (b) of the Criminal Code" in the Supreme Court of British Columbia in December 1992. She pleaded that it violates the section 7 of "the Canadian Charter of Rights and Freedoms" which guarantees the right to life, liberty and security to everyone. But Rodriguez lost the case and appealed on 8<sup>th</sup>March, 1993 in Supreme Court of Canada. Unfortunately, Supreme Court with 5-4 majority also ruled out her appeal on 30<sup>th</sup> September 1993, upholding that "Section 241(b) provision was constitutional and did not violate the Canadian Charter of Rights and Freedoms". Rodriguez died by assisted suicide in February 1994 with the help of anonymous physician. "Physician-Assisted Suicide Becomes Legal in Canada (2015)": The British Columbia Civil Liberties Association (BCCLA) again filed a case in 2011, challenging the law against assisted suicide on the same ground on which Rodriguez [16] fought. This time the case was on behalf of Kay Carter (died in 2010), who suffered from "degenerative spinal

stenosis", and Gloria Taylor (died in 2012), who was suffering from ALS. However, this time the Supreme Court of British Columbia ruled in favor of the plaintiffs. The decision came in June,2012and the federal government decided to appeal the ruling. The Court of Appeal for British Columbia reversed the decision in October, 2013 and then the BCCLA took up the matter to the Supreme Court of Canada. Considering contrary to the Canadian Charter of Rights and Freedom, The Supreme Court of Canada overruled the decision.

The Supreme Court in case of Carter vs. Canada [17] held that the infringing provisions of the Criminal Code void so far as they impose prohibition on the physician-assisted death for that of the competent adult person who:

- Clearly has given consent to the termination of his or life.
- The person is suffering from a grievous and irremediable medical condition which in turn causes the suffering which is intolerable as per the given circumstances of the conditions of the individual.

Hence, the Supreme Court allowed physician-assisted suicide for a person who is suffering from terminal painful disease with irremediable medical conditions and the patient has given his explicit consent for assisted suicide. The court recognized that the Criminal Code [15] prohibition was unconstitutional because it breached the rights to life, liberty and security of the person, as enshrined in Section 7 of the Charter[15]. The Supreme Court provided 12 months' time to frame a new law approving assisted suicide and further extension of four months was allowed uptoJune,2016.

Although no new law was framed but w.e.f. 6th June, 2016, Physician Assisted Suicide became legal in Canada just as the case of Netherlands [13]. House of Commons had passed "*Bill C-14*" and it became law. Hence, "*The Medical Assistance in Dying (MAID) Act*" [4] prescribed the procedure to ensure that it is used for genuine cases only. Assisted Suicide would be applicable on those patients who are above 18 years of age and suffering from terminal diseases and passing through "grievous and irremediable medical condition" that causes "enduring physical or psychological suffering that is intolerable" to the patient. Moreover, they must be in an "advanced state of irreversible decline," in which their "natural death has become reasonably foreseeable."

In February 2020, the Liberal government introduced a bill approving Euthanasia which is christened as "Bill C-7, which proposed to allow Medical Assistance in Dying (MAID) for those patients whose natural death was not reasonably foreseeable [18]. Pandemic delayed the discussion in parliament and thereafter, the federal government modified some of the amendments and presented a revised version the Bill. The same was therefore duly approved by the House of Commons and the Senate and became a validly existing law on 17 March 2021".**Euthanasia: An Indian Landscape:** 

Alike Canada, India also witnessed a stormy debate off the legal platform as well on the legal landscape. Indian society has witnessed a large amount of prevalence of self-immolation instances right from the Vedic era wherein Lord Ram and Lord Krishna accepted "dehtyag" (death) by renouncing the will to live more. This mythological origination depicts that the practice of "self-killing" has been in existence in the Indian context since ancient times and the clamor for the act of Euthanasia as existing now is not something that is novel.

In India, the trace of the origin of the Right to Dignified Death emancipates from that of Right to Life as laid down under Article 21 of the Indian Constitution. The same is silent on Right to Die with dignity or Euthanasia and explicit does not cover the ambit of Right to Die. Seven decades back at the time of independence of India, medical science was in evolving stage and many diseases were unknown. Constitution thinkers and makers could not envisage that one day society will seek for right to die with dignity also. But in a series of civil suits, the High Courts and Supreme Court have recognized the need of mercy killing or Euthanasia in case of terminally ill patients.

The case wherein the debate originated on the notion of Right to Diein India can be seen in the case of P. Rathinam v. Union of India & another [19], the writ petitions to challenge the constitutional validity of the Section 309 of the Indian Penal Code. This Section imposes punishment on anyone who attempts to commit suicide. The punishment which is imposed who attempts to commit suicide is of simple imprisonment up to one year. Supreme Court in this case, drew a parallel analogy with that of the other fundamental rights for instance; the "freedom of speech and expression as guaranteed under the Article 19 of the Constitution of India" gives not only the right to speak but also it includes under its ambit the right not to speak; the right to live as provided under the Article 21 of the Indian Constitution also gives the Right not to Live. Therefore, in the same manner, "Section 309 was held to be unconstitutional". This implies that Right to Life does include under its ambit the Right to Die.

In "Gian Kaur v. the State of Punjab[20]" case, Gian Kaur and her husband Mr. Harbans Singh were convicted by the trial code under the provisions of the Section 306 of the Indian Penal Code. They were being sentenced to the imprisonment of six years along with the fine of RS. 2,000/- for abetment of the suicide to Ms. Kulwant Kaur, "Section 306 of the Indian Penal Code punishes any person who abets the commission of suicide and that of Section 309 anyone who attempts to commit the suicide". This case argued that the preceding case (P. Rathinam v. Union of India) held that the Article 21 of the Indian

Constitution, which guarantees Right to Life, includes under its ambit the Right to Die. It argued that a person abetting the commission of suicide of another person is merely performing the act of assistance in the enforcement and the application of the Article 21 of the Indian Constitution. Therefore, the five-judge bench of the Supreme Court in this case overruled the P.Rathinam case. It held that the analogy stated in that case was wrong one and not applicable in all the circumstances. The other fundamental rights include the "the right not to…"; for instance, the analogy of right to speak is an omission, while on the other hand that of the taking a life is an act itself[21]. Hence, the court finally upheld the constitutional validity of the Section 306 and 309 of the Indian Penal Code.

In "Aruna Ramchandra Shanbaug v. Union of India & Others"[22], the "next friend" of MsAruna Shanbaug had filed the petition before Supreme Court of India, since she was in a persistent vegetative stage and not in a condition to express or give her consent. The petition was filed to direct the hospital to stop feeding her through mechanical or artificial means and allow her to die peacefully. She has been in the Persistent Vegetative State (PVS) since she had been sexually assaulted in the year 1973. The court in this case had formulated a team of three doctors in order to examine her condition and submit a report about both, her mental and physical condition. "The court though did not allow the removal or withdrawal of the medical treatment to Ms. Shanbaug, it did discuss the issue of Euthanasia in detail and permitted passive Euthanasia". The court in this case defined "Passive Euthanasia" as deliberate withdrawal of the treatment with deliberate intention in order to cause the death of the patient. It held that the same can be allowed or permitted only if the doctors work as per the notified medical opinion and withdraw the life supporting system only taking into consideration the "best interest" of the patient. The court also invoked the principle of "Parens Patriae" which means the parent of the nation and held that the court has the ultimate and absolute power to decide what factors constitute and fall as the "best interest" of the patient. This is one such instance in the Indian context wherein the courts have adopted and applied this doctrine. In the landmark decision in Common Cause v. Union of India [23], the Supreme Court of India under the "Article 32 of the Indian Constitution", briefed the following;

- The Right to Die with Dignity as a fundamental right as under Article 21 of the Indian Constitution.
- The Court to issue directions to the Union Government to allow or permit the terminally ill patients or that suffering from incurable diseases to execute living wills for conduction of the appropriate cause of action in case they have admitted to the hospitals.

As an Alternative Prayer, it sought guidelines form the Court of law on this issue and the appointment of that of an expert committee to be comprised of that of the doctors, lawyers and social scientists in order to determine concept of living within the Indian context".

On 9<sup>th</sup>March 2018; a five judge Bench was constituted that had held that the "Right to Die with dignity is a fundamental right". It also held that the individual's right of execution of the "advance medical directive" or that of the "Living Will" is itself am assertion which embodies within itself the right to "bodily integrity and self-determination" which thereby does not depend upon any of the recognition or enactment of any of the legislature by the state. Thus, as mentioned above, shows how the idea of Euthanasia has been interpreted and given recognition in the context of various jurisdictions at the international level with the help of the landmark cases in comparison to that of India. The timeline of India gives an insight as to how Right to Die evolved. It was recognized, overruled, and then again recognized. It shows that India has adopted a progressive attitude towards the concept of Euthanasia.

In India, the Constitution of India and the other statutes are dynamic in nature and change with the changing needs of the society. This approach ultimately led to the recognition of the right to die and subsequently passive Euthanasia. In view of the same, in January 2023, Supreme Court had agreed to hear the plea and simplify the process of Euthanasia and Living Will based upon the representations as given by the Petitioners, to be applicable throughout the country pursuant to the Order [24] is awaited [25]. However, this Order serves as a fruitful measure for framing the law on Living Will or Advanced Medical Directives in India. The need of improvising the guidelines for Living Will and Euthanasia in Indian context by Supreme Court [26]reflects the liberal and pro-active approach and in sync with the existing laws globally. This shows that India though started on a conventional approach but gradually shifted to a more liberal take on such issue and is working proactively.

# Conclusion:

In last decade, due to public pressure and judicial activism, a good number of countries have passed the law in favor of Euthanasia. Netherlands, Canada, India has seen a drastic and dynamic transition from their initial legislation on Euthanasia to that of the final law as passed. The common thread which binds these nations journey is that it all begins from a debate which finally gets crystalized into a judicial enactment. India for instance followed the foot-steps as that of Canada. It is passing via the similar phase and transition in terms of legalizing the practice of Euthanasia and can thereby learn and implement the same for positive results. Although Euthanasia is much talked in the developed and democratic countries but now it is becoming evident in developing countries like India also. Therefore, nations have been advocating in favor for the practice of Euthanasia, it has been a popular part of art, culture and media as well. However, the approach differs from the evolving needs of the society. Netherlands started off with this discussion much ahead of time and has a proper legalized legislation in place; Canada's journey though began more than two decades ago, the law could be formulated recently only and India's approach has been based on the jurisprudential aspect of the pronouncements, overruling previously passed judgments and then finally coming into a conclusion. These jurisdictions have witnessed their own ups and downs in achieving the milestone which they have now.

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# **Original Article**

# Feto maternal outcome in patients with peripartum cardiomyopathy in a tertiary care centre in Kashmir

Samina Ashraf, Asima Afzal, Zarnain Abid

### Abstract:

**Background:** Peripartum cardiomyopathy (PPCM) or postpartum cardiomyopathy is an uncommon form of heart failure that occurs during the last month of pregnancy or up to 5 months postpartum. The exact incidence is uncertain perhaps due to the misdiagnosis of this entity. The aim of the study was to understand the clinical profile, risk factors and management of the patients with PPCM and their fetomaternal outcome.

**Methods:** This prospective observational study was conducted in the Department of Obstetrics and Gyneacology Government Medical College Srinagar over a period of 30 months between October 2019 to April 2022. The study included women who had features of heart failure in the last 6 weeks of pregnancy or 5 months postpartum, with absence of other identifiable causes of heart failure or absence of features of heart failure prior to the last month of pregnancy and absence of left ventricular dysfunction prior to this.

**Results:** Most of our patients were multigravid as with a mean age of 31years.14 out of 22 cases presented with complaints of dyspnea. 63% of patients had ejection fraction between 26-35%. Hypertension was present as a risk factor in 45.4% cases. Maternal Mortality was 5out of 22 patients and Neonatal Mortality was 2 out of 22 cases.

**Conclusion:** Our prospective cohort study concluded that the maternal outcome was poor in cases with decreased ejection fraction and severe symptoms. Early identification and management of the disease is a crucial step for improvising the feto-maternal outcome. An integral slant comprising of the cardiologist, intensivist, obstetrician and perinatologist is required for a successful fetomaternal outcome.

### Introduction:

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Peripartum cardiomyopathy (PPCM) or postpartum cardiomyopathy is an uncommon form of heart failure that occur during the last month of pregnancy or upto 5months postpartum. The exact incidence is uncertain perhaps due to the misdiagnosis of this entity. The occurrences pectrum is likely to represent the diverse population dynamics, description and misrepresentation arising from its lack of understanding. It usually is a diagnosis of exclusion. PPCM has been postulated to be a multifactorial disease. To fully define PPCM, we should at least identify one of the following factors using echocardiography: left ventricular end diastolic area size greater than 2.7cm/m2 of BSA, ejection fraction <45% or a reduced fractional shortening of less than 30%.[1]

Risk factors include pre-eclampsia, eclampsia, diabetes mellitus, smoking, hypertension, multigestational pregnancy and older maternal age[2] PPCM is a disease with diverse manifestations and to someextent unexplored pathogenesis. The deleterious effects of this disease usually reverse within one year after delivery as compared to other forms of cardiomyopathy [3]. The outcome of PPCM has been shown to be strongly associated with race and ethinicity. The most feared complication is sudden cardiac arrest due to ventricular tachyarrythmia. Even when LVEF recovers, there is an elevated risk for recurrent PPCM in future pregnancies.

Despite increased awareness of the disease over last few years, there are still many stones unturned for the exact understanding of its epidemiology, risk factors, pathophysiology and management.

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Keywords

peripartum cardiomyopathy, heart failure, echocardiogram, pregnancy

#### **Material and Methods**

This prospective observational study was conducted in the Department of Obstetrics and Gynaecology, Lalla Ded hospital, associated hospital of Government Medical College Srinagar over a period of 30 months between October 2019 to April 2022. The study included women who had features of heart failure in the last 6 weeks of pregnancy or 5 months postpartum, with absence of other identifiable causes of heart failure or absence of features of heart failure prior to the last month of pregnancy and absence of left ventricular dysfunction prior to this. Features of peripartum cardiomyopathy on ECHO were defined as LVEF <45%, LV fractional shortening<30% or both and LV end diastolic dimension >2.7 cm/m2 BSA.

Baseline data recorded age, parity, gestational age, type of lesion on echocardiography, time and duration of disease, risk factors, presenting features, treatment received, maternal complications, mode of delivery and neonatal outcome. All echocardiograms were performed in the hospital by trained cardiologists. All the patients were under multidisciplinary care of obstetrician, intensive care specialist and cardiologists.

#### Results

Of the 55, 101 delivered patients during our study period, 22women met the criterion for the diagnosis of peripartum cardiomyopathy.

Mean age at the time of presentation was31 years.

8 out of 22 patients were primigravida (36.3%) and the rest were multigravida.

The time of onset of the symptoms of peripartum cardiomyopathy was between 37 to 40 weeks in 77.2 % patients followed by 22.7 % within a week. During our study period we did not received any patient with features of peripartum cardiomyopathy beyond 1st week of delivery.

#### TABLE1

Age	No. Of Patients(n=22)
26-28	5
29-32	13
>32	4
Mean Age	31Years

TABLE2

Parity	No.Of Patients(n=22)	Percentage
Primigravida	8	36.3
Multigravida	14	63.7

TABLE3

Onset	No. Of Patients (n=22)	Percentage
37-42Weeks	17	77.2
1WeekPost-Partum	5	22.8

The predominant symptoms at presentation were dyspnea, in 14 out of 22 cases (63.6%). Majority cases were of NYHA Grade III (57.14) followed by Grade II in 28.5%.

#### TABLE4

NYHA Grading	No. Of Patients(n=22)	Percentage
1	1	7.14
2	4	28.5
3	8	57.14
4	1	7.14

The associated risk factors present in our study for the development of PPCM were hypertensionduring pregnancy in 10cases, anemia in4 cases and GDM in1 patient.

#### TABLE5

Risk Factors	No.Of	Percentage
	Patients(n=22)	
Hypertension	10	45.4
Anaemia	4	18.18
GDM	1	4.54

Majority of the cases had EF between ejection fraction between 26 - 35% (14 cases). While 5 cases had ejection fraction below 25% and 3 cases had ejection fraction between 36 to 45%. All cases had varying degree of mitral regurgitation. 9cases had tricuspid regurgitation.

# TABLE6

Ejection Fraction	No. Of		Perce	entage
	Patients	(n=22)		
<25%	5		22.7	
26-35%	14		63.63	3
36-45%	3		13.6	
	1		1	
Mitral Regurgitation		22		100
Tricuspid Regurgitation		9		40.9

Women with PPCM were mostly delivered via caesarean section, 18 out of 22 in our study. The indication for caesarean section was often a maternal cardiovascular instability or pre- eclampsia.ICU admission was required in all the cases. Maternal mortality was 5 out of 22 patients.

TABLE7
IADLL/

	No. Of	Percentage
	Patients(n=22)	
VaginalDelivery	4	18.18
Caesarean Section	18	81.81
ICUAdmission	22	100
MaternalMortality	5	22.7

Neonatal mortality was 2 out of total 22 cases. **Discussion** 

Peripartum cardiomyopathy is a rare form of congestive heart failure of unknown etiology occurring between the last month of pregnancy and 5 months post delivery with no determinable cause. Its incidence and prevalence is highly variable across different geographical regions and is also race determinant. It has a wide clinical spectrum ranging from complete recovery to death. Peripartum cardiomyopathy is diagnosis of exclusion. Several unconfirmed etiologies have been proposed like viral myocarditis, nutritional deficiencies, autoimmunity, micro chimerism, hemodynamic stresses, vascular dysfunction, harmonal insults and underlying genetics[4]. PPCM has also been speculated to been mediated by a 16 kDa fragment of prolactin [5].

In the present study the incidence of PPC Min pregnant woman was 22 per 51,732 live births. Or 0.4 per 1000 live births

Elkayametal had previously reported a higher incidence of PPC Minwoman aged 30 years or more [6]. Our cohort showed showed similar results with the mean age of our patients being 31 years. Multigravida formed the majority of our patients, 63.7%. This was however in contrast to the study of Singh S et al [7] and Aruja et al[8]Reported a majority incidence in the primigravidas.

Most patients had onset of symptoms between 37 and 40 weeks of gestation. Similar observation was made by Singh et al [7].

The most common symptom at presentation was dyspnea (NYHA 3 >2) in 63.6% cases. Another similar Indian study by S Singh et al [7] also reported dyspnea to be the predominant symptom. The predominant risk factor identified in our study was hypertension. This is in accordance with the results of Singh S et al (7) but contrary to those of Aditya John Bimietal[9]who reported no significant relation.

Patients with PPCM should be dealt at multidisciplinary tertiary care centres for the better outcome of the mother and the baby. Pregnancy is usually terminated in maternal interest. Although vaginal delivery is the preferable mode of termination, in our study 81% cases were delivered via caesarean section. This was similar to the studies of Aditya John's Binuet al [9] and Singh S et al [7].

All the patients were managed in the ICU following the confirmation of diagnosis and were taken care by the intensive care specialist, cardiologist and obstetricians. In our study maternal mortality was 22.7%. Most studies have shown mortality ranging from 18 to 56% [10-12]. Neonatal mortality in our study was 2 out of 22 cases which show a favourable result with regard to the fetal outcome. Similar results with regards to the fetal outcome. Similar results were demonstrated by Singh S et al [7] Favourable fetal outcome can also be attributed to the departmental neonatology specialists and a well-equipped NICU.

The sign and symptoms of PPCM like dyspnea, orthopnea, pedal edema overlap with the expected physiological changes of pregnancy. As such a high index of suspicion is required while making the diagnosis of PPCM which is aided by the echocardiography findings.

Treatment usually is supportive and directed towards the management of the heart failure symptoms [13]. Standard heart failure therapy is used to optimize the patient's volume status. Beta blockers and ACE inhibitors are the most commonly used drugs [14]. Novel anti heart failure medications have been reported to improve heart failure symptoms in pregnancy related cardiomyopathies[15].Bromocriptine which decreases the effect of

Prolacti non cardiacmyocytes has been associated with better outcomes[16].

# Conclusion

Our prospective cohort study concluded that the maternal outcome was poor in cases with decreased ejection fraction and severe symptoms. Hypertension was found to be an important contributing factor. Early identification and management of the disease is a crucial step for improvising the feto-maternal outcome. An integral slant comprising of the cardiologist, intensivist, obstetrician and perinatologist is required for a successful fetomaternal outcome.

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# **Original Article**

# Maternal And Perinatal Outcome Of Ante Partum Haemorrhage (APH) In A Tertiary Care Hospital

Nikita Gandotra, Shagufta, Shah Nawaz

## Abstract:

**Background**: Antepartum haemorrhage (APH) is an obstetrical emergency that accounts for 3-5% of pregnancies and is a leading cause of maternal and perinatal morbidity and mortality.

**Materials And Methods**: This retrospective study was conducted in the department of obstetrics and gynaecology ,SMGS Hospital , GMC Jammu over a period of 1 year from 1st January 2022 to 31<sup>st</sup> December 2022.Data was collected from records kept in the hospital .179 cases of APH were studied during the study period. The maternal baseline characteristics, mode of delivery, pregnancy outcome and obstetrical complications were studied. The study was approved by the Institutional Ethics Committee. The objective of this study was to determine the maternal and perinatal effects of APH.

Results: Majority of the patients (67) were in the age group of 26-30 years (37.43 %). Majority of the patients (62) were primigravida (34.63 %), 47 patients were gravida 2 (26.25 %),41 patients were gravida 3 (22.90 %),18 patients were gravida 4(10.05 %) and 11 patients were gravida 5 and more (6.14 %). Majority of the patients (87) presented at 33-36.6 weeks of gestation (48.60%) followed by more than 37 weeks (39.10 %). Majority of the patients (72) had previous vaginal delivery (40.22 %) followed by primigravida (27.93 %), previous abortions (18.99 %), previous 1 LSCS (15.64 %) and previous 2 LSCS (7.26 %).130 patients had placenta praevia (72.62 %) ,abruption (20.67 %),accreta (3.35 %), Percreta (1.67 %) and increta (1.67 %). Majority of the patients underwent LSCS (75.55 %), LSCS WITH B/L UA Ligation (8.88 %), caesarean hysterectomy (10 %), vaginal delivery (4.44 %) and laparotomy with uterine repair (0.55 %). Majority of the babies had birth weight between 1.5 to 2.5 kg (69.27 %), more than 2.5 kg (24.02%) and <1.5 kg (8.37 %). Apgar score at birth >6 in 87.70%, < 6 in 10.05% and IUD in 3.88%.

**Conclusion:** APH cannot reliably be predicted. APH is associated with high maternal and perinatal morbidity and mortality. All the cases diagnosed as APH during antenatal period must be considered high risk and proper antenatal management plan should be formulated. In suspected cases of morbidly adherent placenta, senior obstetrician, paediatrician and anaesthetist must be available during delivery. In such cases, a preoperative planning with multidisciplinary approach should be followed. Patient counselling and proper consent should be taken which include possibility of hysterectomy and interventional radiology. JK-Practitioner2023;28(3-4):11-15

### Introduction:

Obstetrical haemorrhage is the leading cause of maternal mortality in world. [1] PH is defined as the bleeding from or in to the genital tract, occurring from 24+0 weeks of pregnancy and before the birth of the baby.APH complicates 3–5% of pregnancies and is a leading cause of perinatal and maternal mortality worldwide.[2]

The causes of antepartum haemorrhage can be classified as obstetric, local and unclassified. The common causes of APH are placenta praevia, abruption placentae and the other causes include cervical polyp, carcinoma cervix, vasa praevia, local trauma, condylomata etc.[3,4] When placenta is implanted wholly or partially in the lower uterine segment, it is defined as placenta praevia. Risk factors for placenta praevia include previous history of placenta praevia,

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Keywords APH, Haemorrhage, Hystrectomy, Morbidity, LSCS multiparity, previous history of miscarriages both induced and spontaneous, advanced maternal age, fibroid uterus, previous uterine scars such as myomectomy, evacuation of retained products of conception .[5] Studies have also shown that large size of the placenta, as seen in multiple pregnancy, severe anaemia, diabetes mellitus, smoking and polyhydramnios are associated risk factors for placenta praevia.

Placental abruption refers to premature separation of a normally situated placenta before the delivery of the baby. Risk factors for abruption are previous history of abruptio placentae, hypertensive disorders of pregnancy, polyhydramnios, multiparity, mal presentation, abdominal trauma have been implicated. [5]

Antepartum haemorrhage (APH) complicates about 2-5% of all the pregnancies.[6] Incidence of placenta previa at term is approximately 0.5%.Approximately 0.5-1% of all pregnancies are complicated by abruption.

Because of increase in the caesarean section rates, there is an increase in the incidence of placenta praevia and morbidly adherent placenta.

Recently, the use of ultrasound for placental placenta, localisation, diagnosis of abruption improved obstetrical and anaesthetic facilities, availability of blood transfusion and advanced neonatal care facilities increased survival of a preterm infant. The maternal complications include mal presentations, premature labour, postpartum haemorrhage (PPH), sepsis, shock and retained placenta, peripartum hysterectomies, coagulation failure and even death. Various fetal complications include preterm baby, low birth weight, intrauterine death, congenital malformations and birth asphyxia. The frequency of these complications depends on the amount of haemorrhage and gestational age at the time of delivery.

The objective of this study was to determine the maternal and perinatal effects of APH.

### **Materials and Methods**

This retrospective study was conducted in the department of obstetrics and gynaecology, SMGS Hospital, GMC Jammu over a period of 1 year from 1st January 2022 to 31<sup>st</sup> December 2022. Data was collected from records kept in the hospital .179 cases of APH were studied during the study period. The maternal baseline characteristics, mode of delivery, pregnancy outcome and obstetrical complications were studied. The study was approved by the Institutional Ethics Committee.

#### Inclusion criteria:

All cases of APH with gestational age more than 24 weeks.

#### **Exclusion criteria:**

1. Women with gestational age less than 24 weeks.

2. Women diagnosed with any bleeding disorder.

3. Women with bleeding from sources other than uterus.

# Results

Table 1: Age wise distribution of patients	Table 1	: Age wise	distribution	of	patients
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Age	Number	Percentage
21-25 years	57	31.84
26-30 years	67	37.43
31-35 years	38	21.22
> 35 years	11	6.14
< 20 years	6	3.35

In our study, majority of the patients(67) were in the age group of 26-30 years (37.43 %) followed by 21-25 years(31.84 %), 31-35 years (21.22 %),>35 years (6.14 %) and <20 years (3.35 %).

Table 2: Distribution of patient according to parity

Parity	Number	Percentage
PRIMI	62	34.63
G2	47	26.25
G3	41	22.90
G4	18	10.05
>G5	11	6.14

Majority of the patients (62) were primigravida (34.63 %), 47 patients were gravida 2 (26.25 %) ,41 patients were gravida 3 (22.90 %),18 patients were gravida 4(10.05 %) and 11 patients were gravida 5 and more (6.14 %).

 Table 3: Distribution of patients according to gestational age

GA		Number	Percentage
28-32.6		22	12.29
WEEKS			
33-36.6		87	48.60
WEEKS			
>	37	70	39.10
WEEKS			

In our study, majority of the patients (87) presented at 33-36.6 weeks of gestation (48.60%) followed by more than 37 weeks (39.10%).

Table	4:	Distribution	of	patients	according	to
obsteti	ric l	history.				

ОН	Number	Percentage
PRIMI	50	27.93
PREVIOUS	34	18.99
ABORTIONS		
PREVIOUS 1 LSCS	28	15.64
PREVIOUS 2 LSCS	13	7.26
PREVIOUS VD	72	40.22

Majority of the patients (72) had previous vaginal delivery (40.22 %) followed by primigravida (27.93 %),previous abortions (18.99 %),previous 1 LSCS (15.64 %) and previous 2 LSCS (7.26 %)

CAUSE	NUMBER	PERCENTAGE
PLACENTA	130	72.62
PRAEVIA		
ABRUPTION	37	20.67
ACCRETA	6	3.35
PERCRETA	3	1.67
INCRETA	3	1.67

# Table 5: Causes of APH.

In our study, 130 patients had placenta praevia (72.62 %), abruption (20.67 %), accreta (3.35 %), percreta (1.67 %) and increta (1.67 %).

#### Table 6: Types of placenta praevia

ОТҮРЕ	NUMBER	PERCENTAGE
1	8	4.46
2	30	16.75
3	15	8.37
4	80	44.69

Table 7: Risk factors.

RISK FACTORS	NUMBE	PERCENTAG
	R	E
PIH	20	11.17
PREECLAMPSIA	5	2.79
ECLAMPSIA	2	1.11
GDM	16	8.93
MULTIPLE	3	
PREGNANCY		1.66
MALPRESENTATIO	10	5.58
Ν		
HYPOTHYROIDISM	7	3.88

Table 8:Mode of delivery					
MODE OF	NUMBER	PERCENTAGE			
DELIVERY					
EM/EL LSCS	136	75.97			
EM LSCS WITH	16	8.93			
B/L UA Ligation					
СН	18	10.05			
VD	8	4.46			
LAPAROTOMY	1	0.55			
WITH UTERINE					
REPAIR					

Majority of the patients underwent LSCS (75.55 %), LSCS WITH B/L UA Ligation (8.88 %), caesarean hysterectomy (10 %), vaginal delivery (4.44 %) and laparotomy with uterine repair (0.55 %).

Table	9:Birth	weight	distribution.

EFW	NUMBER	PERCENTAGE
<1.5 KG	15	8.37
1.5 -2.5 KG	124	69.27
>2.5 KG	43	24.02

Majority of the babies had birth weight between 1.5 to 2.5 kg (69.27 %), more than 2.5 kg (24.02%) and <1.5 kg (8.37 %).

A/S	NUMBER	PERCENTAGE
<6	18	10.05
>6	157	87.70
IUD	7	3.91

Apgar score at birth >6 in 87.70% ,< 6 in 10.05 % and IUD in 3.91 %.

#### Discussion

APH is the most common life threatening condition. This retrospective study was carried out on 179 patients who presented with antepartum haemorrhage in the department of obstetrics and gynaecology ,SMGS Hospital, GMC Jammu over a period of 1 year from 1st January 2022 to 31<sup>st</sup> December 2022. Majority of the patients were un booked and were from low socioeconomic status. In our study, majority of the patients(67) were in the age group of 26-30 years (37.43 %) which is similar to study conducted by Kulkarni et al<sup>[7]</sup> and Yadav et al.<sup>[8]</sup> Incidence of APH were more common in multigravida (65.36 %) followed by primigravida (34.63 %). which was comparable to Adekanle, et al.[9] with 75.2% multipara and 24.8% nullipara. Thus, confirming the role of endometrial damage caused by repeated childbirth, a risk factor for uteroplacental bleeding in pregnancy.[10]

In our study, majority of the patients (87) presented at 33-36.6 weeks of gestation (48.60 %) followed by more than 37 weeks (39.10 %). Bhandiwad, et al.[11] who reported that 70% of cases of placenta previa had a gestational age of 28-32 weeks .Whereas in the study done by Archana, et al.[12], 63% of patients had gestational age  $\geq$  37 weeks . Majority of the patients (72) had previous vaginal delivery (40.22 %) followed by primigravida (27.93%), previous abortions (18.99 %), previous 1 LSCS (15.64 %) and previous 2 LSCS(7.26 %).

In our study, 28.07 % patients had history of previous LSCS which is less than study conducted by Purohit A, et al. (40%) . [13] In our study, 18.88 % had history of previous abortions, In Bako, et al. [14] 43.8% showed high incidence of prior abortion history, Purohit et al (16%) showed low incidence, Taylor et al [15] who reported that 30% patients of placenta previa had a previous abortion .Previous history of caesarean section, prior abortions and dilatation and curettage increases the risk of placenta previa due to decreased vascularity noted in fibrosed tissues.

Majority of the patients were presented with bleeding per vaginum followed by abdominal pain.

In our study, 130 patients had placenta praevia (72.62 %) followed by abruption(20.67 %), which is similar to study done by Yadav et al., but in the study done by Takai et al, [16] abruptio placentae were the most

common cause.12 patients had Morbidly adherent placenta [accreta (3.35 %),percreta (1.67%) and increta (1.67%).Majority of the patients underwent LSCS(75.97%),LSCS WITH B/L UA Ligation (8.93%). 75.97% of the patients underwent LSCS, most of them were emergency LSCS. These findings are comparable with the study conducted by Yadav et al and Khouri et al. [17]

Early and timely caesarean section improves perinatal outcome in patients with abruption .

In our study, 18 patients underwent caesarean hysterectomy (10.05%), vaginal delivery (4.46%) and laparotomy with uterine repair (0.55%).2 patient underwent bladder repair.

In our study, postpartum haemorrhage was the most common complications in patients with antepartum haemorrhage which was observed in 23 % cases which is similar to the study conducted by Chakraborty, et al [18] who reported 16.2% incidence of PPH .25 patients(13.96 %) underwent haemorrhagic shock. Anaemia was present in 54 % of cases and require blood transfusion.109 patients(60.89 %) underwent preterm delivery (60.89 %).No maternal mortality was reported in our study.

Majority of the babies had birth weight between 1.5 to 2.5 kg (69.27 %), more than 2.5 kg (24.02 %) and <1.5 kg (8.37 %). Apgar score at birth >6 in 87.70 %, < 6 in 10.05 % and IUD in 3.88 %.

Prematurity was the most common complication. Therefore, early detection of high risk patients with regular antenatal care, timely diagnosis and proper management, timely caesarean section with availability of blood and blood products, good neonatal intensive care unit will help to lower the perinatal and maternal morbidity and mortality.

# Conclusion

APH cannot reliably be predicted. APH is associated with high maternal and perinatal morbidity and mortality.Ultrasound can be used for the diagnosis of placenta praevia, but ultrasound scan does not exclude abruption. Placental abruption is a clinical diagnosis and no sensitive or reliable diagnostic tests are available.All the pregnant women should be aware of regular antenatal check-up, iron and folic acid supplementation, adequate nutrition, correction of anaemia during antenatal period, importance of institutional family delivery, planning and immunization.

All the cases diagnosed as APH during antenatal period must be considered high risk and proper antenatal management plan should be formulated. In suspected cases of morbidly adherent placenta, senior obstetrician, paediatrician and anaesthetist must be available during delivery. In such cases, a preoperative planning with multidisciplinary approach should be followed. Patient counseling and proper consent should be taken which include possibility of hysterectomy and interventional radiology.

Various government programs including the recent PradhanmantriSurakshitMatrutya Abhiyan and previously schemes like Janani Suraksha Yojana should be followed.

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# **Original Article**

# Minimally invasive calcaneal fracture fixation by using two-point distractor -A Prospective Observational Cohort Study

Iftikhar H Wani, Jawaher Mehmood Khan, Mushtaq Ahamd, Naseem ul Gani, Ajaz Ahmad Bhat

## Abstract:

**Introduction:** A displaced fracture of calcaneum is serious and disabling injury. Treatment options have evolved from conservative to open surgical alternatives and include a variety of minimally invasive techniques also. We hypothesise that minimally invasive surgery of calcaneal fractures by using a distractor achieves a good clinical and functional outcome with minimum wound complications.

**Aims and objectives:** The aim of our study was to assess the functional outcome of minimally invasive surgery in the management of calcaneal fractures and the subsequent complication rate in the management of displaced intra-articular fractures.

**Methods:** Between April 2018 and March 2021, patients with unilateral or bilateral closed calcaneal fractures, treated operatively with minimally invasive technique using distractor were included in the study. 64 patients with 60 calcaneal fractures were included in the study. Pre operatively CT scan evaluation was done and fractures were classified as per Sander's classification. Only type II and type III were included in the study. Pre operatively Pre operatively both Bohler's and Gissane's angles were measured. **Maryland foot and ankle score** was used for evaluation and effectiveness of intervention.

**Results:** The average operative time in our study was  $45\pm 11.2$  minutes. No major wound complications were reported in our study. Screw prominence was seen in three patients. Complex regional pain syndrome was seen in seven of our patients. Both Gissane and Bohlers angles were restored in 94% of our patients. Maryland foot and ankle score was excellent in 20 % (11) of patients, Good in 60% (33), Fair in 15% and Poor in 5%.

**Conclusion:** We concluded that management of calcaneal fractures with the use of distractor helps to restore the articular congruity of subtalar joint with minimum soft tissue complications.

### Introduction:

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Calcaneal fractures are the most common among tarsal bone fractures and constitute around 65% of all tarsal bone fractures.[1] Treatment options vary from conservative treatment to operative extensile approach and minimally invasive techniques of fixation. Although the ideal treatment is still controversial, but operative treatment has been found to have superior results in terms of pain and disability in the long run. [2,3]. The advanced minimally invasive techniques fair better in of wound complications, terms skin necrosis and early rehabilitation.[4]. Moreover, early surgical intervention is possible by means of minimally invasive techniques which in turn decrease the overall morbidity and rehabilitation time. The primary aim of our study was to assess the functional outcome of minimally invasive calcaneal surgery by using two-point distractor.

### Methods

This was a prospective observational study undertaken from April 2018 to March 2021 at our hospital. The study was approved by the institutional ethical committee and was laid down in accordance with the declaration of Helsinki.

The mean age of our patients was 45 years. 64 calcaneal fractures in 60 patients were operated by using two-point distractor during this period

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# Keywords

Distractor, Calcaneal fractures; Screw fixation.

and were included in the study. Four patients had bilateral fractures. Out of 64 calcaneal fractures, 45 were male and 19 were female. Pre-operatively fractures were evaluated by axial view, lateral view, Broden's views and a CT scan. Fractures were classified based on CT scan classification by Sander's. [5] Only patients with displaced type II and III Sander's were included in our study. Patients with open calcaneal fractures and type IV Sander's were excluded from the study. The average time from injury to surgery was 5.5 days. The average preoperative Bohler's angle was  $12 \pm 5.6^{\circ}$  and the average preoperativeGissane's angle was 75.0  $\pm$ 10.3°. Mechanism of injury is given in Chart 1. Marvland foot and ankle score was used for evaluation and effectiveness of intervention.

# Surgical technique

Patients were positioned in a lateral position with the side to be operated up. Two trans fixation collinear 2.5 to 3mm pins were placed in talus and calcaneal tuberosity for attachment to distractor. Two-point calcaneal distractor was placed in a manner so that it does not come in the field of vision [Fig. 1].

The placement of pins was confirmed under fluoroscopy. The initial lateral view, axial view and







Fig 2: Articular step correction by use of two point distractor

Broadens view were done at this point to check for varus/valgus alignment, posterior facet depression and articular malalignment. The pins are distracted on either side by means of a distractor to correct corresponding malalignment and confirmation is done under fluoroscopy [Fig. 2]

Once reduction was found to be satisfactory one or two cannulated 4mm sustentacular screws were placed under fluoroscopy followed by 6.5mm screws along the axial length of the calcaneum [Fig. 3]. The distractor was removed at this point of time and final fluoroscopic picture is taken followed by application of short leg slab [Fig.4 and 5].

Stab incisions are sutured and dressed and short leg slab is applied for three weeks. At three weeks sutures were removed and patient is encouraged for ankle and foot range of motion exercises. Patient is followed at 6 weeks, 10 weeks and 12 weeks. Patient is allowed partial weight bearing after 8 weeks and full weight bearing only after 3 months. Evaluation at the final follow up was done using Maryland foot and ankle score. Any complication arising during the course of treatment was noted down and managed appropriately.



Fig 1: Placement of pins in talus and calcaneum with application of distractor



Fig 3: Placement of Sustentacular screw



Fig 4: Final fluoroscopic picture

#### Results

The study was conducted for a period of 3years with a mean follow up around 22 months (16 -36 months). At final follow up 55 calcaneal fractures were reviewed with a follow up rate of 85%. The average operative time in our study was around  $45\pm11.2$  minutes. No major wound complication or deep infection was reported in our study. Three of our patients had minor superficial wound infections which resolved with antibiotics and dressings. Screw prominence at tuberosity was seen in three of our patients which were removed after the fractures united. Complex regional pain syndrome was reported in 7 patients which was managed conservatively.

The average length of hospital stay in our patients was  $5.3\pm3.2$  days. We did not report any sural nerve involvement or peroneal tendon dislocation in our patients. Reduction of posterior facet has been restored in 96% of patients. The average postoperative Bohler's angle was  $28.5 \pm 3.6^{\circ}$  and the average postoperative Gissane's angle was  $125.0 \pm 10.3^{\circ}$ . Both Bohlers and Gissane angles were restored in 94 % of the patients. Varus was corrected in all patients. Calcaneal height and length were restored in 92%. Loss of reduction was seen in five of our patients in view of lateral wall comminution. Maryland foot and ankle score was excellent in 20 % (11) of patients, Good in 60% (33), Fair in 14% and Poor in 6%. We achieved anatomically satisfactory reduction in majority of our patients.

#### Discussion

Displaced calcaneal fractures are very serious injuries and the optimal management of these fractures is still controversial. There are many studies which have been published regarding the optimal management of intra articular calcaneal fractures [6-8], but most of them lacked representative number of patients to develop a valid consensus. [6,7, 9-13].We employed technique of minimally invasive fixation of intra-



Fig 5: Final AP view

articular calcaneal fractures using the two point distractor. We believe that this mode of fixation has less number of wound complications as compared to the open reduction internal fixation [10 to 20 %]. In conventional plating, chances of main blood supply disruption which comes through lateral aspect are high and wound complications are severe as compared to minimally invasive technique. [14,15] De wall et al reported a deep wound infection and superficial wound infection of 14.3% and 21.4% respectively in open reduction and internal fixation of calcaneal fractures. [16] Buckley et al reported a 25 % rate of wound complications after open reduction and internal fixation. [17] It also allows early return to activities as patients can be operated as early as possible without waiting for the soft tissues to consolidate. We did not report any major wound complication in our study. In a meta-analysis by Fan et al the clinical results of minimally invasive technique were compared with that of ORIF. The lower incidence of soft tissue wound complications and reduced duration of surgical procedure was noted.[18] Moreover, arthrodesis becomes technically easier after minimally invasive technique of fixation.

The incidence of sural nerve injuries in minimally invasive calcaneal fracture fixation is negligible. The incidence of sural nerve injuries in extended approach can go up to 10% as there is a risk of injury to nerve at both proximal and distal part of the incision. Approximately 7.7% of sural nerve injuries have been reported by Weber et

al in extended approach.[19] No injuries to sural nerve were reported in our series as only stab incisions at anatomically safe points were given.

Our study had several limitations. First, the exact power analysis was not possible and the sample size was not that large to draw a meaningful conclusion. We had a midterm follow up only, as longer follow up is need to comment on arthritis which is the most common complication. Therefore, further studies are needed with larger sample size and longer follow up to ascertain a more precise and meaningful understanding of the clinical efficacy of distractor and minimally invasive technique in calcaneal fractures.

# Conclusion

We believe that minimally invasive technique with two-point distractor is ideal for treatment of joint depression and comminuted calcaneal fractures. It helps us to achieve length, width, joint congruity and varus-valgus alignment with rapid recovery and minimal wound complications.

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# **Original Article**

# Spectrum of radiological findings on HRCT temporal bone in patients with CSOM: A hospital based study from South Kashmir

Mir Saiqa Shafi, Sabeeha Gul, Arif Ahmad Wani

## Abstract:

**Background:** Chronic suppurative otitis media is one of the most common childhood infections worldwide and represents a leading cause of hearing impairment in resource-limited settings. Although a clinical diagnosis, imaging plays a crucial role in cases where there is suspicion of cholesteotoma and to look for the associated intracranial complications, which may otherwise prove fatal. Due to its excellent spatial resolution, HRCT has emerged as the modality of choice in diagnosing, surgical decisions, and further follow-up of patients.

**Aims and Objectives:** The present study aimed to study the radiological findings in the temporal bone in patients with CSOM, to look at the extent and sites of involvement in the middle ear and mastoid air cells, and to look for the complications of CSOM (if any).

**Materials and methods:** 150 patients referred for HRCT evaluation to the Radiology department over 1 year were enrolled in the study. HRCT evaluation of the study participants was done as per the set temporal bone protocol. The contrast was administered only in those patients where there was suspicion of intracranial complications. The HRCT images were evaluated for the presence or absence of abnormal soft tissue density, the status of the ossicles & the integrity of the ossicular chain, the integrity of the bony landmarks including the scutum, tegmen, mastoid cotes, & sigmoid sinus plate. Assessment of the mastoid pneumatisation was done in all cases.

**Results:** The mean age in our study population was 24.81 years. The majority of the patients belonged to the age group of 21-30 years. In our study, males were affected more frequently than females. The most common presenting complaints were ear discharge, decreased hearing, and ear aches. On HRCT evaluation, abnormal soft tissue density was seen in 100 cases(66.67%), with involvement of mastoid antrum and aditus ad antrum in all cases, followed by epitympanum, mesotympanum, and hypotympanum in that order. Ossicular erosions were seen in 89 cases(59.33%), with incus being the most frequently involved ossicle, followed by stapes malleus in that order. Scutum erosions were seen in 70 cases (46.67%) and erosions of the tegmen were seen in 38 cases (25.33%). Facial canal dehiscence/erosions were seen in 3 cases each (2%). Labrynthine fistula & extratemporal complications were noted in 2 patients each (1.33%).

**Conclusions:** HRCT of the temporal bone is an efficacious modality for the accurate delineation of the anatomy and pathological involvement of the temporal bone. It is a unique method to detect early cholesteotoma & also to detect cholesteotoma in hidden areas. HRCT is useful for diagnosis, surgical planning & management of temporal bone pathologies.

### Introduction:

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Chronic Suppurative otitis media is a chronic inflammation of the middle ear cleft of more than two-week duration. Clinically it is characterized by discharging ear, decreased hearing, fever, and nostalgia. Chronic suppurative otitis media is the leading cause of the chronic aural discharge. As per WHO estimates, it affects 65-330 million individuals globally with its prevalence ranging from as low as 1% in the developed world to as high as 30-45% in underdeveloped countries. Among them,50% of the patients have a hearing impairment

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**Keywords** HRCT, Chronic Suppurative otitis media, diagnosis and 28000 deaths are attributed to the complications clinical examination with an otoscope or otoendoscope. However, given the location of the tympanomastoid compartment, being separated from the middle cranial fossa and posterior cranial fossa by a thin bony partition, both short and long-term sequelae of otitis media may be devastating. If recognized early and treated appropriately, these complications can be avoided.[2]As the such radiological examination of the temporal bone provides crucial information to the clinician which guides both the medical and surgical management of patients with middle ear disease.

HRCT and MRI are the two most important imaging modalities in the evaluation of patients with chronic ear discharge. Conventional techniques of temporal bone imaging like the X-ray(Schuller's view,Stenvers, Townes, and submentrovertical projections) have been replaced by HRCT. It confirms the otoscopic findings to a greater extent, clears many clinical doubts, and helps in determining when surgery will be necessary and also in planning the approach for surgery. With its excellent submillimetric resolution, HRCT has emerged as the imaging modality of choice for the evaluation of middle ear pathologies. Being a highly sensitive tool, if normal, it virtually excludes any middle ear pathology.[3,4] It is the best modality to look for the integrity of the ossicles and the bony confines of the middle ear. HRCT can detect exposed dura, semicircular canal dehiscence, and facial canal dehiscence. It can effectively assess anatomical pitfalls like a high-riding jugular bulb. Having preoperative knowledge of anatomy and anomalies is crucial to prevent post-operative morbidity among patients who require surgery for middle ear disorders. Due to its superior contrast resolution, MRI serves as a problem-solving tool in indeterminate, complicated CSOM cases to look for the involvement of facial nerve canal, inner ear structures, and intracranial complications. It is the most useful modality for distinguishing residual or recurrent cholesteotoma from the granulation tissue or post-operative scar formation.[4,5,6]

The present study aims to study the radiological findings in the temporal bone in patients with CSOM, to assess the severity of the pathological changes in CSOM patients, to look at the extent and sites of involvement of the middle ear and mastoid air cells, and to look for the complications of CSOM (if any).

### Materials and Methods

The present study was conducted on 150 patients who were clinically diagnosed with chronic suppurative otitis media and were referred to the Radiology department of a tertiary care hospital, between June 2021 to June 2022 over a one year period. This was a of otitis media per year.[1]The diagnosis is mostly on prospective observational study with descriptive statistics. The study was performed after ethical clearance & informed consent.

Inclusion criteria:

All patients with chronic middle ear infections who were referred to the radiology department for HRCT evaluation.

Exclusion criteria:

Pregnant females, patients with a cochlear implant, those who had undergone previous temporal bone surgeries, patients with a history of previous skull base trauma, and patients are known to have temporal bone neoplastic pathology were excluded from the study.

All the CT scans were performed at our institute on a 128-slice Philips Incisive CT scanner. Non-contrast HRCT of the temporal bone was performed parallel to the orbito-meatal line by a spiral technique using the multislice CT scanner. Contiguous axial and coronal thin slices of both temporal bones were reconstructed using a high-resolution matrix and bone algorithm. Soft tissue windowing and sagittal reformatting were done wherever required. Intravenous contrast was given in patients with suspected intracranial complications. CT images were analyzed for the presence of soft tissue attenuation in middle ear clefts, ossicular erosions, erosions of the scutum, tegmen, and semicircular canals, facial canal erosions or dehiscence, mastoid cortex erosions, dural exposure & intracranial complications.

Data analysis:

The data was entered in Microsoft excel & analyzed with SPSS 23.0 software. Continuous variables like age were expressed as mean and standard deviation or median with the interquartile range depending on the normality distribution. Categorical variables like sex and temporal bone findings were expressed as proportions and percentages.

#### Results

**Table 1:** Distribution of age among the studyparticipants.

Age Group (Years)	Number (n=150)	Percentage
<10	10	6.67%
11-20	37	24.67%
21-30	49	32.67%
31-40	28	18.67%
41-50	16	10.67%
51-60	6	4.00%
>60	4	2.67%
total	150	100.00%



**Fig 1:** Graphical representation of the distribution of age among the study participants.

**Table 2:**Distribution of gender among the studyparticipants.

Gender	Number (n=150)	Percentage
Male	88	58.67%
Female	62	41.33%
Total	150	100.00%



Fig 2: Graphical representation of the distribution of gender among the study participants.

 Table 3: Distribution concerning the side of the affected ear.

Size	Number (n=150)	Percentage
Left	76	50.67%
Right	66	44.00%
Bilateral	8	5.33%

	Chief Complaints	Number (n=150)	Percentage
i	Ear Discharge	134	89.00%
ii	Decreased Hearing	121	80.67%
iii	Earache	55	36.67%
iv	Headache	15	10.00%
v	Vertigo/Giddiness	8	5.33%
vi	Tinnitus	5	3.33%
vii	Bloodstained discharge	6	4.00%
viii	Fleshy mass in the	3	2.00%
	ear		
ix	Facial Paralysis	1	0.67%

**Table4:**Distributionofpresentingsymptoms/complaints among the study participants.

Almost all the patients presented with multiple symptoms. The most common presenting symptoms were discharged from the ear and hearing impairment.



**Fig 3:** Graphical representation of the distribution of presenting symptoms/complaints among the study participants.

Distribution of the impression of CSOM type based on HRCT findings.



**Fig 4:** Graphical representation of the impression of CSOM type.

Findings on HRCT	Present	Absent
Abnormal soft tissue	100(66.67%)	50(33.33%)
mass		
Ossicular involvement	89(59.33%)	61(40.67%)
(erosions/displacement)		
Scutum erosions	70(46.67%)	80(53.33%)
Tegmen erosions	38(25.33%)	112(74.67%)
Semicircular canal	2(1.33%)	148(98.67%)
erosions		
Facial canal erosions/	20(13.33%)	130(86.67%)
dehiscence		
Mastoid cortex	3(2%)	147(98%)
erosions		
Sinus plate erosions	3(2%)	147(98%)
Aural polyp	3(2%)	147(98%)
Extra temporal	2(1.33%)	148(98.67%)
complications		

**Table 5:** Distribution of findings on HRCTevaluation.

**Table 6:** Distribution of site and extent of involvement of middle ear and mastoid in patients with abnormal soft tissue density (n=100).

Site	Number	Percentage
Epitympanum	98	98.00%
Mesotympanum	50	50.00%
Hypo tympanum	18	18.00%
Mastoid Antrum	100	100.00%
Aditus-ad-antrum	100	100.00%

**Table 7:** Distribution of the HRCT findings of Temporal bone concerning the status of mastoid pneumatisation.

Status of mastoid	Number (n=150)	Percentage
pneumatisation		
Loss of	91	60.67%
pneumatisation		
Mastoid air cell	14	9.33%
opacification		
Coalescent	3	2%
mastoiditis		
Well	42	28%
pneumatised		
mastoid bone		



**Fig 5:** Graphical representation of the status of mastoid pneumatization. The pattern of involvement of ossicular erosions



**Fig 6:** Graphical representation showing pattern of involvement in individual ossicles.



Image 1: Abnormal Soft tissue density in the left middle ear cavity with associated ossicular erosions.



**Image 2:** (a) Abnormal soft tissue density in the middle ear cavity with erosions involving the tegmen tympani. (b) Soft tissue density in the left EAC in the same patient is consistent with an aural polyp.



**Image 3:** (a) Focal erosions in the tegmen in a CSOM patient with abnormal soft tissue density in the epitympanum. (b) Loss of the normal ice-cream cone configuration of the middle ear ossicles in the same patient.



**Image 4:** (a) Ossicular displacement with maintained integrity. (b) Mastoid air cell opacification with associated mastoid sclerosis.



**Image 5:** (a) Facial canal dehiscence (FCD)in a normal middle ear cavity.(b)Another patient with abnormal soft tissue in the middle ear & mastoid antrum & associated FCD.



**Image 6:** (a) CSOM on the right side with erosions of the long process of the incus. left side of the same patient with normal incus.

(b) CSOM on the



Image 7: (a) Bilateral chronic sclerosing mastoiditis. (b)Mastoid air cell opacification on the left side.



Image 8: Abnormal soft tissue in epitympanum & mastoid antrum with blunt scutum.



**Image 9:** (a and b) Abnormal soft tissue in the left middle ear cavity with displacement & erosions of the middle ear ossicles. Articulation between the incus & the malleus is maintained. (c) Coronal HRCT of the same patient as above demonstrates abnormal anterior displacement of the ossicles. (d) Coronal HRCT image in the same patient at the level of scutum demonstrates scutum erosions.



**Image 10:** (a) Abnormal soft tissue density in left mesotympanum. (b) Abnormal soft tissue density filling the left external auditory canal. (c)Erosions involve the long process of incus, with a normal appearing handle of malleus & stapes superstructure.

# Discussion

Imaging techniques in the medical field have undergone tremendous changes ever since the first discovery of the X-ray by Sir William Roentgen on 8th November 1895. With the advent of HRCT with a submillimetric resolution, HRCT has emerged as the modality of choice for patients with CSOM. Although not a routine investigation in all CSOM patients, HRCT is especially useful for patients where the clinical examination is confounded due to one reason or the other or when there is a clinical suspicion of an unsafe type of CSOM (Atticoantral type). From an imaging perspective, the atticoantral CSOM can be further classified into the cholesteotomatous& noncholesteotomatous types. Classical HRCT findings in atticoantral CSOM with cholesteotoma include a nondependent abnormal soft tissue density, with erosion and blunting of scutum/lateral attic wall, widening of the aditus-ad-antrum, displacement of the ossicular chain and destruction of the ear ossicles. HRCT of the temporal bone has revolutionized the pre-operative assessment of the disease by picking up the anatomical variations in the temporal bone, delineating the extent of the disease, erosion of the ossicles, erosion of the dura, facial canal, etc, thereby allowing better pre-operative planning of surgery.

This prospective study was undertaken to study the imaging features of CSOM patients referred for HRCT to the radiology department.

We studied a total of 150 patients with a clinical diagnosis of CSOM. In this study, the mean age of the patients was 24.81 years. Thukral et al found that the mean age of the patients was 27.95 years which was similar to our study. A maximum number of patients in our study belonged to the age group of 21-30 years (32.67%) followed by the 11-20 year age group (24.66%). A minimum number of patients belonged to the age group of more than 60 (2.66%).

In our study, the males were more commonly affected than females. These results were following studies by Sharma et al, Dhulipalla et al, Chatterjee et al &Kanotra et al [7, 8,9,10]. In all these studies, males were affected more frequently than females (60%, 58%, 68.86% & 57.44% respectively).

In our study, the left side ear was affected more commonly than the right side with bilateral involvement in eight cases.

The majority of our patients had the presenting complaints of ear discharge (89%) followed by decreased hearing (80.66%), earache (36.67%), headache (10%), vertigo/giddiness (5.33%), blood-stained discharge (4%), tinnitus (3.33%), fleshy mass in the ear (2%) & facial paralysis (0.67%). Our results were comparable with Jadia et al [11] who in their study observed that otorrhea/ear discharge was the most common presenting feature (100%) followed by hearing loss (98.1%) with facial weakness being the least common(1.92%). Similarly, Tamilarasan etal [12] reported that the symptoms in their study population were Otorrhoea (91.95%), Hearing loss

(59.77%), otalgia (29.89%), nausea & vomiting (11.49%), headache (10.34%), tinnitus (9.20%) & facial weakness (5.75%).

HRCT evaluation of the temporal bone revealed the presence of abnormal soft tissue mass in 100 patients (66.67%). The presence of a non-dependent soft tissue mass in the middle ear cavity is highly suggestive of cholesteotoma. Payal et al [13] observed the presence of soft tissue mass in 86.67% of the patients. Similarly, Chatterjee etal found the presence of soft tissue mass in 100% of the patients [9]. This variation in our results was likely because our study was not limited to the unsafe type of CSOM rather it included all patients of CSOM referred for HRCT evaluation.

Regarding the site of involvement of this abnormal soft tissue mass, epitympanum was involved in 98% of the cases; mesotympanum was involved in 50% of the cases followed by hypotympanum which was involved in 18% of the cases. The mastoid antrum and aditus and antrum were involved in 100% of the cases which showed an abnormal soft tissue mass. Our observations are comparable to the findings by Jadia etal [11]who found the extension in epitympanum in 100% of cases followed by mesotympanum in 78.85% and hypotympanum in 55.57%. In their study, antrum was involved in 84% of the cases, and aditus adantrum in 78.85%. Similarly, the most frequently involved sites observed by Sirigri et al [14] were epitympanum in 88% of the cases, mastoidantrum in84% of the cases, aditus ad antrum in 76%, mesotympanum in 44% and hypotympanum in 44%. The order of the involvement was comparable to our study.

Loss of pneumatisation of the mastoid air cells was seen in 91 cases (60.67%), whereas mastoid air cell opacification was noted in 14 patients (9.33%) and findings suggestive of coalescent mastoiditis was noted in 3 cases (2%). The rest of the study participants showed well-pneumatised mastoid bone(28%). These findings were consistent with those of Mandal P et al[15] who reported the presence of mastoiditis in 60% of the cases. Similarly, our findings corroborated with those of Thukral et al [16] who observed mastoiditis in 76% of the cases.

Our study revealed ossicular erosions in 89 patients (59.33%). These results were comparable with the studies by Chatterjee et al [9] & Gul et al [17] where ossicular erosions were present in 62.28% and 54.57% respectively. Malleus erosions were present in 15 patients (10%), incus erosions were present in 82 patients(54.67%) & stapedial erosions were present in 41 cases (27.33%). However, our study did not match the results of Sharma et al [8] and Bathla et al [18] who reported ossicular erosions in 84 and 73 % of the cases respectively. This was likely due to the general inclusion of CSOM patients referred for temporal bone. Although both types of HRCT CSOM, tubo-tympanic which is considered safe, as well as attico-antral which is considered unsafe, may lead to the erosions of the ossicular chain. This propensity for ossicular destruction is much greater in cases of unsafe CSOM, due to the presence of cholesteotoma and/or granulations.[19]

Among the patients with ossicular erosions, incus was involved in 92% of the cases, followed by stapes in 46% of patients and malleus in 16.85% of the patients. Malleus was found to be the most resistant ossicle & the incus was found to be the most common ossicle to get necrosed in cases of CSOM. These results were comparable with the findings of Tamilarasan et al & Payal etal [12,13].

Regarding the pattern of involvement in individual ossicles, among a total of 15 patients with malleus erosions, the handle of the malleus was involved in 9(60 %) cases followed by the head of the malleus in 5 cases (33.33%) with non-visualization in 1 case (6.67%).These findings were comparable with those of S Varshney et al[20].In their study, the handle of the malleus was the most commonly necrosed part of the malleus.

Similarly out of the 82 patients with incus erosions, the long process was the most frequently involved in 60 patients (73.17%), followed by a short process of incus in 17 cases(20.73%) with non-visualization in 5 cases (6.10%). These findings were comparable with those of Austin et al[2], Kartush et al [22] & Mathur et al [23].

Stapes superstructure erosions were seen in all 41 cases (27.33%) with the involvement of the stapes on HRCT. These findings were comparable with those of S Varshney et al [20] where involvement of the stapes superstructure was noted in 21.33% of the cases of CSOM and the footplate was found intact in all cases.

Erosions of the scutum were seen in 46.67% of the patients enrolled in the study. These results were comparable with the study by Thukral et al [16] where scutum erosions were seen in 42% of the patients. Similarly, Tamilarasan et al [12]identified eroded scutum in 34.48% of the cases. Sharma et al [8] identified erosions in scutum in 84% of the cases and Chatterjee et al found erosions of the scutum in 67.07% of the cases[9]. The higher proportion of erosions in the latter two studies was likely attributed to the fact that the former study included only those patients with unsafe chronic suppurative otitis media and the latter was done in patients who were planned for mastoid exploration & as such were likely to have cholesteotoma.

Regarding the erosions in the tegmen, our study documented the same in 38 patients (25.33%). Our results were comparable to those of Jadia et al [11] who reported the tegmen erosions in 23.1 % of the cases. Similarly, Keskin et al [24] mentioned the tegmen erosions in 19.6% of the study population.

Our study reported labyrinthine fistula (lateral semicircular canal erosions) in 2 patients (1.33%). Our results were comparable with those of Tamilarasan et al [12], Mandal et al [15], and Sharma et al [8] who reported this finding in 3.8%, 4% & 6% respectively. Our study reported a lower rate which

may be attributed to the fact that our study was not limited to the unsafe CSOM only. Further, it could be attributed to the fact that patients report to the hospital much earlier in the course of the disease.

Regarding the facial canal dehiscence/erosions, our study reported it in 20 cases (13.33%) whereas an intact facial canal was demonstrated in 130 cases (86.67%). Selesnick and Lynn-Macrae [25] reported that fallopian canal dehiscence was seen in 33% of the patients with cholesteotoma. The accuracy of the CT scan for detecting the FCD is not constant & sometimes it may be impossible to detect it in the thin bony canal of the facial nerve [26,27,28]. The Facial canal dehiscence may be a normal anatomical variant due to a congenital process or may be an associated feature of chronic otitis media, particularly with cholesteotoma. In either case, it is very important to document this finding. It can lead to one of the ominous intra-temporal complications of facial nerve paralysis or can lead to an intra-operative complication of facial nerve trauma.

Similarly, mastoid cortex erosions were seen in 3 cases (2%) and sigmoid sinus plate erosions were seen in 3 cases (2%). We reported only two cases with extratemporal findings, one had an epidural abscess and the other case had skull base osteomyelitis.

# Conclusion

HRCT of the temporal bone is an efficacious modality for the accurate delineation of the anatomy and pathological involvement of the temporal bone. It is a unique method to detect early cholesteotom & also to detect cholesteotoma in hidden areas. HRCT is useful for diagnosis, surgical planning & management of temporal bone pathologies.

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# **Original Article**

# Screening and treatment of infants with retinopathy of prematurity at a tertiary care hospital in Kashmir

Tufela Shafi, Zainab Haroon, Haniyaa Mufti, Snober Yousuf, Tasneem Muzaffar

# Abstract:

**Background:** Retinopathy of prematurity (ROP) is a vasoproliferative disorder seen in the retina of preterm infants. It is a major cause of irreversible, though preventable childhood blindness. Hence screening for ROP and timely intervention is necessary to prevent a lifetime of blindness in the affected babies.

**Objective:** The study was conducted to report on the incidence of ROP in preterm babies referred for ROP screening to a tertiary care hospital in Kashmir and to assess the outcome of the disease after laser photocoagulation.

**Materials and Methods:** Retrospective, non interventional study, analysing the hospital records of 103 patients who attended the referral ROP Clinic in a tertiary care hospital in Kashmir between January 2018 – December 2018.

**Results:** Incidence of ROP in our cohort of 103 patients was 68.93 % (71 patients) out of which laser was required by 23 patients (32.39%), 3 of whom worsened (4.22%). Normal weight babies did not have any incidence of ROP.

**Conclusion:** Incidence of ROP in Kashmir is quite high and ROP is seen across all gestational age groups and birth weight groups except normal weight groups.

# Introduction:

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Retinopathy of Prematurity (ROP) is a vasoproliferative disorder seen in the retina of preterm infants[1] and is a major cause of preventable childhood blindness.[2,3] Recent advances in neonatal care has resulted in increasing survival of preterm babies, hence the incidence of ROP has also seen a rise, particularly in the developing countries like India.[4-6]

First described by Terry in 1942 as fibroblastic proliferation of tunica vasculosa lentis [7], the pathogenesis of ROP is better understood now. Around 12 weeks of gestation, vasculogenesis of retina commences, from the optic nerve head, in a centrifugal fashion completing the vascular architecture of the retina between 36-40 weeks of gestational age. Preterm birth disrupts this pattern of vascularisation and instead vaso obliteration and subsequent neo vascularisation of the immature retina may take place.[8]This may ultimately result in tractional retinal detachment with subsequent blindness.

The term ROP was coined by Heath in 1952 and later on a universally accepted classification of the disease called as International Classification of Retinopathy of Prematurity (ICROP) was universally accepted in 1983.[9] Subsequently the classification underwent further revisions.

Multiple risk factors associated with the disease have been identified which include low gestational age, low birth weight, prolonged exposure to supplementary oxygen, cardio respiratory support, transfusions, sepsis, respiratory distress syndrome and intra ventricular hemorrhage.[10-13]

ROP is an underestimated disease, with studies from India reporting incidence between 22% to 52%.[14,15] With improvement in neonatal care in India, the number of preterm babies requiring screening for ROP is increasing. Hence reduced exposure to known risk factors along with timely screening and intervention is needed to reduce the visual loss due to the disease.

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**Keywords** ROP, laser photocoagulation, APROP. Treatment of vision threatening disease involves ablation of the non vascularised retina by laser photocoagulation or cryotherapy in centres where laser is not available. With the advent of anti VEGF drugs for the treatment of vasoproliferative diseases of the retina, the use of these agents in treatment of ROP is increasing day by day.

Different screening criteria are being followed around the world for ROP, and in India also from time to time, various screening guidelines have been formulated. The guidelines currently in place are the "Revised guidelines for neonatal screening including ROP (RBSK 2017 guidelines)".[16]At our hospital also, these guidelines have been put into effect and we wanted to determine the ROP incidence/ positivity rate in the babies screened ,using the RBSK guidelines and treatment outcome of these babies. To our knowledge, this is the first such study from Kashmir Valley.

# Materials and Methods

It was a retrospective, observational study conducted in the ROP Clinic of the Government Pediatric Hospital (Government Medical College) which is a tertiary care pediatric hospital in Kashmir, with a level III NICU and gets referrals from all over the valley. Hospital records of patients referred for ROP screening between 1st January 2018 and 31st December 2018 were analysed in the study. The infants had been screened using the RBSK guidelines and hence all preterm infants with birth weight <2000gm and age <34 weeks as well as preterms with gestational age between 34-36 weeks with high risk factors and infants with unstable clinical course deemed to be at risk for ROP by the attending neonatologist/pediatrician were included in the study. All the babies had been seen by a single examiner (TS). The first examination had been carried out at 3-8 weeks of post natal age depending upon the time of referral from the attending neonatologist. The examination was done using topical proparacaine drops. ICROP Classification was used and ROP was classified into Type 1 and Type II disease( using the ETROP guidelines<sup>17</sup> and APROP.

Infants with mature vascularisation were not examined again. Those with type II ROP were serially examined till regression occured or till mature vascularisation occurred whereas laser treatment was carried out in type I ROP, and APROP; laser being the gold standard of treatment, and the most easily available modality of treatment in the hospital. Non response to laser , requiring surgical intervention was categorized as worsening.

On basis of prematurity, babies were grouped into

- Extreme preterm (EPT) with gestational age <28 weeks
- Very preterm (VPT) Gestational age 28-31 6/7weeks
- Moderate preterm Gestational age 32-33 6/7

• Late Preterm (LPT) gestational age 34-37

On the basis of birth weight the babies were grouped into

- Extreme Low birth weight (ELBW) <1000gms
- Very low birth weight (VLBW) 1000-1499gms
- Low birth weight 1500-2500gms
- Normal birth weight >2500gms.

# Results

103 preterm babies were enrolled in the study. The mean  $\pm$ SD gestational age was  $30.32 \pm 2.490$  weeks whereas the mean  $\pm$ SD birth weight was  $1495 \pm 0.431$  gms.11 babies were in EPT, 60 in VPT and 22 in MPT,10 in LPT group (fig 1) .None of the babies referred had term gestation. 5 babies were in ELBW, 46 in VLBW, 48 in LBW and 4 babies in normal weight group (fig 2). The ROP positivity or incidence among these screened newborns was 68.93% (71/103).

ROP positivity /incidence ,of any stage was highest in the EPT group and was seen to successively decrease with increasing gestational age group (fig 3). All preterm babies had presence of one or the other stage of ROP.As far as birth weight was concerned all babies in various low birth weight groups developed ROP(fig 4). 4 babies were seen to belong to normal weight group, out of which none developed ROP.

Out of the 71 babies who developed ROP, 23(32.39%) required laser treatment. 95.7% (68/71) babies showed regression (either spontaneous or post laser). 87% (20/23) of babies who underwent laser showed complete regression whereas 13% (3/23) worsened and had to be referred outside the valley for surgical treatment.

# Discussion

The ROP positivity among our study was high as compared to other studies, which have reported a rate ranging between 20-52%.[16,17] This can be attributed to a rigorous screening protocol ,inclusion of wider range of gestational age and birth weight cutoffs for screening, combined with increasing referrals by the neonatologists, increased awareness about the disease amongst the neonatologists, ophthalmologists and general population, along with the setting up of a dedicated ROP screening clinic, the first of its kind in the valley, within the premises of a tertiary level pediatric hospital, which gets referrals from all over the valley.

The guidelines of RBSK have recommended screening in higher weight babies as well, if they have significant risk factors or an unstable clinical course or if the treating neonatologist deems babies to be at high risk for ROP. Many reports indicate that in developing countries, neonates with higher gestational age and birth weight were seen to have severe retinopathy.[18,19] This was explained by Vinekaret al[18] on the basis of exposure to uncontrolled and unmonitored oxygen, lack of awareness of the disease
and intrinsic nature of the disease itself, that may contribute to severe retinopathy in such infants. And in fact, the application of western screening criteria for ROP, for developing countries like India, has been questioned by Jalaliet al[20] and the revised guidelines for neonatal screening (RBSK) have taken these facts into consideration. However, in this study we observed that though all 5 cases in ELBW group had ROP, no case of ROP was seen in the babies born with term weight and above, even though they were also preterm babies, in terms of gestational age. This could be explained on the basis of the fact that incidence of ROP decreases with increasing birth weight and increasing gestational age group, since higher birth weight and gestational age correspond to a more mature and well developed retina. Good quality care and monitoring in the NICU may also have had a contributory role.

33.39% of our babies needed laser photocoagulation. Similar results have been observed by Chaudhariet al. [16] We observed laser requiring babies were from all gestational ages as well as all birth weight groups except the normal birth weight, which did not have any case of ROP. Though all babies in the ELBW group developed ROP, one did not progress to the stage of intervention.

Post laser, 20 (87%) patients showed complete regression of the disease. Laser photocoagulation being an effective, safe and complete treatment continues to serve as a gold standard in the treatment plan of ROP. Several studies have reported that extreme prematurity and more severe forms of the disease strongly correlated with unfavorable outcome. And though we also observed severe and more posterior disease in the 3 babies who had unfavorable outcome, all such cases were also seen to have delay in referrals and hence delay in undertaking treatment. These three babies had been referred at 6-8 weeks post natal age, even though in all the three cases, gestational age was less than 32 weeks.

We conclude that the incidence of ROP might be high in our valley and more rigorous awareness campaigns need to be put in place so that no baby escapes the net of screening. However effective tracking and surveillance is needed to ensure compliance and timely reporting for screening and treatment and given the shortage of trained manpower, it can be a particularly challenging situation. More people need to be trained in ROP screening at district levels so that time delay in screening and treatment is avoided. The number of cases in our study is not large enough to effectively draw a conclusion and we need to undertake more studies with larger numbers to finalise our observations.



gestational age groups.



Fig 2. Distribution of cases across different birth weight groups.



Fig 3. Results of screening in different gestational groups



Fig 4. Results of screening in different birth weight groups.

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#### **Original Article**

#### Prevalence and Distribution of Vancomycin Resistant Enterococci in a Tertiary Care Hospital of Northern India

Unairah Naqash, Asifa Nazir, Rukhsana Taj, Junaid Mehraj Lone

#### Abstract:

**Background:** There are no eradication approaches for Vancomycin Resistant Enterococci(VRE) so infection control strategies rely only on screening and isolation of colonised patients.

**Objective:** To find the prevalence and distribution of Vancomycin Resistant Enterococci(VRE).

**Methodology:** This was an observational study from a tertiary care hospital which was completed over a period of 18 months.

**Results:** The prevalence of Enterococcal isolates was3.9% in our hospital out of which 19.6% were Vancomycin Resistant Enterococci(VRE). Among male subjects the prevalence was much higher (27.5%)in comparison to females(12%) and the difference was found to be statistically significant (p < 0.001).

**Conclusion**: This study emphasizes on the prevalence of vancomycin resistant Enterococci in Tertiary care hospital of Kashmir valley. Enterococcus species has been of particular concern due to their increasing incidence and paucity of drugs available to treat them.

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#### Introduction

Enterococci are normally considered as bacteria of low pathogenicity, which only infect persons with special immunodeficiency disease.[1] They are most common cause of urinary tract infections, second most common cause of intra-abdominal and intra-pelvic abscesses or post-surgery wound infections and third most common cause of blood stream infections.[2]

The SENTRY Antimicrobial Surveillance Program carried out in the Asia- Pacific (APAC), European, Latin American (LATAM), and North American (NA) regions through 1997 to 2016 found that the overall average frequency of VRE increased from 8% to 15.4% over time in all monitored regions.[3]The prevalence of VRE infections in India is also increasing in the past one decade. Mathur P et al., from New Delhi were the first to report VRE from India in 1999. [4] The reported prevalence from tertiary care hospitals across India ranges from 1.7% to 20%.[5-8] This increase was higher among patients in ICUs, rising from 0.4% to 13.6% in the same time interval. Further, the risk of death from vancomycin resistant Enterococci (VRE) is 75%, compared with 45% for those infected with a susceptible strain.[9] Infection with these organisms causes an estimated 1,300 deaths eachyear.[10]

The natural ability of *Enterococci* to acquire, accumulate and share extra chromosomal elements encoding virulence traits or antibiotic resistance genes explains their increasing importance as nosocomial pathogens. Acquired resistance to various antimicrobial agents and available antibiotics currently limits the therapeutic options. Furthermore Enterococci have different mechanisms for the transfer of resistance genes, to other pathogenic Gram positive bacteria such as *Staphylococcus aureus* which is very important clinically. The proposed study is an effort to determine the prevalence of Vancomycin Resistant Enterococcal(VRE) infections and also to access some of the risk factors associated with acquisition of these infections.

#### Aims and objectives

To find the prevalence and distribution of vancomycin resistant *Enterococci* (VRE).

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Keywords

Enterococcus, drug,strain, vancomycin,

#### Results

A total of 19617 samples were received and processed in our lab out of which 11576 were found to show the growth for various bacteria on culture media. Among the samples, 6003 were isolated from urine, 3944 from pus other body fluids, and 1629 from blood. Out of these 455 Enterococcus were

isolated; 306 from urine, 93 from pus and other body fluids and 56 from blood. The total prevalence of Enterococcal infections was 3.9% and the prevalence among urine, blood and pus and other body fluids was 5.1%, 3.4%, 2.4% respectively. (**Table 1**)

Table 1: Prevalence of Enterococcal Infections								
	No. of samples	No. of samples received (N)		No. of samples positive for Enterococcus				
		N	%	N	%			
Urine	8519	6003	70.4	306	5.1			
Pus and other fluids	6166	3944	64	93	2.4			
Blood	4932	1629	33	56	3.4			
Total	19617	11576	59	455	3.9			

Table 2: Prevalence and Distribution of VRE and VSE Isolates									
Sample	Total	VRE	VSE	p-value					
Urine	306	58 (18.9%)	248 (81.1%)	p = 0.02296					
Blood	56	18 (32.1%)	38 (67.9%)	[Chi square = $7.548$ , Df = 2]					
Pusand other fluids	93	13 (13.9%	80 (86.1%)	DI = 2					
Total	455	89 (19.5%)	366 (80.5%)						

A total of 455 non-duplicate isolates of Enterococcus were isolated out of which 89 were resistant and 366 were found sensitive depicting the prevalence of vancomycin resistant Enterococcus as 19.5% and vancomycin sensitive Enterococcus as 80.5%. From Enterococcal isolates the VRE percentage was 18.9 in urine, 32.1% in blood and 13.9 in pus and other body fluids[**Table 2**]. The difference of VRE isolates from different fluids was found to be statistically significant.

Table 03: Gender Wise Distribution of Enterococcal Isolates								
Gender	VRE (n=89)	VSE (n=366)	Total (n=455	Odds Ratio (95% CI)	P Value			
Male	61 (27.5%)	161 (72.5%)	222	2.774	p<0.001			
Females	28 (12.0%)	205 (88.0%)	233	(1.694 – 4.540)	[Chi-square=17.27 df=1]			

**Table 3** shows the gender distribution of enterococcal isolates. Out of 455 samples, 222 were isolated from males where in 61(27.5%) were VRE and 161(72.5%) were VSE. Among 233 samples from females 28(12.0%) were VRE and 205 (88.0%) were VSE. The difference in percentage of VRE isolates from males and females was found to be statistically significant (p < 0.001) and the odds of having more VRE isolates in males was found to be 2.774 (1.694 - 4.540).



**Figure 1** shows the ward wise distribution of VRE isolates wherein VRE were recovered mainly from patients in ICU (32%), followed by general surgery (16%), general medicine (12%), urology (9.0%), cardiology (8%), nephrology (8%) and gastroenterology (6%). Least number of VRE isolates were recovered from neurosurgery and ENTwards.

Table 4: Risk Factors Associated with Vancomycin Resistant Enterococci         (multiple responses)							
Risk factors	VRE (N=89)	Percentage					
IV line	89	100.0%					
Antibiotic intake	83	93.3%					
Urinary catheter	68	76.4%					
Duration of hospital stay >10 days	58	65.2%					
Hypertension	21	23.6%					
Renal insufficiency	15	16.9%					
Steroid intake	9	10.1%					
Malignancy	9	10.1%					
Diabetes	7	7.9%					
Autoimmune disorder	3	3.4%					
COPD	3	3.4%					

**Table 4** depicts the risk factors associated with Vancomycin Resistant Enterococci. Among the 89 patients from whom VRE was isolated, 89(100%) had IV line, 83 (93.2%) had history of antibiotic intake; urinary catheterisation was seen in 68(76.0%) of the patients, 58 of patients (65.1%) had a hospital duration stay of more than 10 days. Co-morbidities like hypertension, diabetes, COPD was seen in 21(23.5%), 7(7.8%) and 03(3.3%) of the patients respectively. Renal insufficiency was seen in 15(16.8%) where as 10.1% (09) had an associated malignant condition and steroidintake.

#### Discussion

This cross sectional study was carried out in a tertiary care hospitalin Kashmir valley in the Post Graduate Department of Microbiology Govt Medical College, Srinagar for a period of eighteen months. Samples including urine, blood, pus, and other body fluids were processed in the laboratory. Out of the total 19,617 samples received from Oct 2019- May 2021, 11576 were found to show growth on culture media for various bacteria. Enterococcal growth was found in 455 samples;366 of which were sensitive and 89 showed resistance to vancomycin. The overall prevalence for Enterococcal infections in our study was found to be 3.9% which is in accordance with studies all over India. **Kalyan R et al (2013) [11]** in their study found the prevalence to be 1.46%, **Kolli HR et al (2016)** [12] reported 4.4%, **PurohitG et al (2017)[2]** reported a prevalence of 5.9%, **Khandelwal N et al. (2020) [13]** reported the prevalence to be 1.5%. Variations in prevalence are attributed to various factors including the type of study, sample size, duration o fstudy

In our study, the data from urine reflected 8519 samples out of which 6003 showed a growth on culture media (hereby referred to as culture positive) for various bacteria.306 (5.1%) Enterococcal species were isolated out of which 58 were resistant to vancomycin. Pus and other body fluids accounted for 6166 samples with 3944 being determined culture positive for various bacteria;2.4% of these tabulating to 93 samples were positive for various Enterococcal species out of which 13 were vancomycin resistant.4932 blood samples were receivedoverthestudyperiodoutofwhich1629werecult urepositive.3.4%. 56 of these were growth positive for Enterococcus out of which 18 showed resistance tovancomycin.Our study included the 455 samples from different clinical specimens which showed the growth of Enterococcus. Of these 455 isolates, 89 (19.56%) were found to be vancomycin resistant and 366 (80.4%) were sensitive to this glycopeptide. All of 89 VRE isolates had high level vancomycin resistance (MIC>64µg/ml) as confirmed by VITEK 2 (bio Merieux). Similar results were reported by Deshpande VR et al. (2013) [14], in their study titled "Prevalence of multidrug resistant Enterococci from a tertiary care hospital in India" and Oberoi A et al. (2014) [15], who in their study found vancomycin resistance in 20% of the isolates. ArifD et al. (2019) [15]however in their study reported VRE to be 30% (16/53) which is high as compared to most of the earlier studies from India. From Kashmir valley the earlier studies by Ahmad J et al. (2015) [17] and ManzoorM et al. (2016)[18] reported a prevalence of 6.5 % and 7% respectively. The above results point towards a steady increase in the prevalence of vancomycin resistant Enterococci in the last decade in India. This increasing trend of VRE bacteremia is a red alert to the clinicians and the infection control practitioners, so that strict antibiotic policies and proper adherence to the infection control practices can be initiatedtoreducetheVRE rate as was quoted by Sivaradjy M et al. [19] in their three-year prospective study October 2017 and September between 2020. Enterococcus were isolated more from females (51.2%) than males (48.8%) but VRE were isolated more from males (68.5%) which was statistically found significant in our study. Majority of the VRE recovered belonged to the patients in age group of

60-69 years (29.2%), followed by (14.7%) in age group of >50-59 years; the least number of VRE were recovered from patients under age of 0-9 years. Of many risk factors that have been identified with vancomycin resistant infections increasing age has been shown significant in earlier studies done by Ahmad J et al. (2015) [17] and Tripathi A et al.(2015) [20]. Vancomycin-resistant Enterococcus is particularly a problem in the elderly because they are exposed to infections at higher rates in hospital and institutional settings. More over with advancing age infections become a leading cause of morbidity and mortality due to various factors like decreased immunity, presence of chronic co-morbid conditions and alterations in normal physiological organ function which all modifies the severity of infections in elderly patients making them vulnerable to infections. However, both these parameters (age and gender) as per previous study by Rajkumari N et al. [21] were found (2014)statistically insignificant. Among the clinical samples, urine had the maximum isolation rate of Enterococci (67.3%) followed by pus and other body fluids (20.4%) and least from blood (12.3%). Results similar to ours were found by Kolli HRet.al(2016) [12] with percentage of 57.4%, 31.5% and 11.1% respectively, Nautiyal S et al. (2016) [22] with percentage of 46.0%,28.3% and 7%, ManzoorM et al. (2016)[18] with a percentage of 50.8%, 35.3%, and 13.8 % respectively. FawziaA et al. (2017) [23] with 46.6% isolation rate from urine. Similarly, ArifD et al. (2019) [16] reported 66% Enterococcal isolates from urine,24.4% from puts and 1.8% from blood. Boccella M et al. (2021 [24] had reported 32.5% of the isolates from urine. The above data highlights the prevalence of Enterococci in urinary tract infections. There are discrepancies in some studies as by GeetaraniPurohit et al. (2017) [2]and Rajkumari N et al. (2014) [21] where in Enterococcus was isolated more from blood than urine. Most of the studies support the same findings as ours the reason being Enterococcus is encountered as the most frequent uropathogen, and also being a commensal of GIT, it may be reason for UTI due to the close proximity of anal opening to urethra. Urinary catheterization in some cases may also have contributed to higher isolation of Enterococci from urine. VRE was isolated more from blood (32.1%), followed by urine (18.9%) and (14%) in pus. The isolation of VRE from blood in our study was significant with a p value =0.02296. In the recent survey (2011- 2014) conducted by the National Healthcare Safety Network (NHSN) at the US Centres for Disease Control and Prevention (CDC), Enterococci ranked first among pathogens associated with central line- associated bloodstream infections (CLABSIs). Enterococcal bloodstream infections(BSI)areassociated with a highlevel of mortalit y.Mostcasesofenterococcal BSI are thought to result from translocation of Enterococci from the gut into the bloodstream. Other routes of infection include along intravenous lines, endocarditis, urinary tract infections and other abscesses. The results of our study are consistent with studies done by ManzoorM et al. (2016) [18] and Chaudhary S et al. (2014) [25] who reported higher isolation of VRE from blood (34.3%) and (57.1%) respectively. Other studies by Gupta V et al. (2007) [26], Ghoshal U et al. (2006) [27], Kapoor L et al. (2005) [28], MathurP et al. (2003) [29], also reported a higher isolation of VRE from blood samples. However, some recent studies by ArifD et.al (2019)[16] and Khandelwal N et al (2020) [13]reported majority of VRE isolates from urine.

In our study risk factors were accessed for patients from whom VRE were isolated. Most of the patients (31.5%) were admitted in ICU at the time of sampling, followed by patients in surgical and medicine wards (15.7) % and (12.4%) respectively; the next high percentage of patients was seen in urology (9%) followed by nephrology and cardiology wards, each with 7(7.9%) of the total 89 patients 93.2% of the patients with VRE had history of antibiotic administration. The patients had prolonged stay in hospital with 65.1% being admitted for more than 10 days; 100% of patients had IV line, where as urinary catheterization was seen in 76%;9 out of 89(10%) of the VRE patients were diagnosed with a malignant condition whereas renal insufficiency was seen in 16.8% of the VRE patients. Other co morbid conditions like hypertension, diabetes, and COPD was seen in 21(23.5%),07(7.8%) and 3(3.3%) respectively. Our findings are consistent with the studies done earlier Ahmad J et al. (2015) [17]. In their study they demonstrated a significant relation for antibiotic intake. IV line and urinary catheterization for vancomycin resistant enterococci. TripathiA et al. (2015) [20]found significant association of VRE with renal insufficiency, surgery, hospital stay of >48 hrs, ICU admission and use ofantibiotics.

#### Conclusion

The prevalence of Enterococcal isolates in our study wasfound to be 3.9% which was comparable to other studies. The VRE isolates were more common in males and in blood samples. As there are no eradication approaches for VRE so infection control strategies rely only on screening and isolation of colonised patients. Also antibiotic stewardship programs that limit the use of cephalosporins, antibiotics against anaerobes, vancomycin and broad spectrum antibiotics can play an essential role in preventing the emergence and spread of this pathogen.

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#### **Original Article**

### A cross-sectional study, to access the awareness regarding antibiotic usage and anti-microbial resistance among general Kashmiri population

Naser Shaheen Mir, Mehwish Majeed , Zuryat Ashraf, Samina Farhat

#### Abstract:

**Background:** Antibiotic resistance has now a days become one of the greatest threats to global health and development. Antibiotic resistance can occur naturally but antibiotic misuse further accelerates the process. Since general public can play a pivotal role in checking inappropriate use of antibiotics, hence it is important to work on their awareness levels.

Aim: to assess the awareness regarding antimicrobial usage and its resistance among general Kashmiri population.

**Material and methods:** This **cross-sectional study was conducted in the** Department of Pharmacology, Government Medical College Srinagar from 1<sup>st</sup> October 2022 to 1<sup>st</sup> January 2023.A questionnaire based on previous studies was framed and circulated through whats app. **273** responses were obtained. Responses were compiled using Microsoft Excel Sheet and then analyzed. Statistical analysis was done using SPSS version 25.0 software. Demographic characteristics were analyzed using descriptive statistics. Categorical variables were measured as percentages.

**Results:** In this study (261) 96% participants were of the opinion that antibiotics are used to treat infections. (243) 89% were aware that antibiotics act against bacteria. (147) 53% believed that anti-microbial agents should be brought after proper medical consultation. (267) 98% had idea that antibiotics can cause side effects. (141) 52% left their antibiotics midway during the course and among them (105) 68% believed that symptomatic improvement was the main reason behind it. (258) 96% knew that effectiveness of antibiotics is reduced if antibiotics are left midway. (249) 89% had an idea about antibiotic resistance and the same percentage considered self-medication as its main contributor. Only (90) 32% participants had heard about antibiotic stewardship program.

**Conclusion:** This study showed that a lot of difference exists between knowledge and actual practice. Although the study population was aware about proper antibiotic usage, but in reality they did not practice it. Intensive awareness campaigns regarding proper antibiotic usage and antibiotic resistance should be carried out focusing health care professionals as well common public, so that misuse of antibiotics can be prevented. Further there should be a strict check on availability of antibiotics as over the counter drugs.

#### Introduction:

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One of the greatest contributions to therapeutics was with the advent of antibiotics. Antibiotics are substances produced by microorganisms, which selectively suppress the growth of or kill other microorganisms at very low concentrations while Antimicrobial agent (AMA) are synthetic as well as naturally obtained drugs that attenuate microorganisms [1]. Antibiotics, the frequently prescribed drugs are used for the treatment and prevention of infectious diseases [2,3]. Unprofessional use of antibiotics not only hampers their actual role resulting in failure of therapy but also in the development of antibiotic resistance. Antibiotic resistance has now a days become one of the greatest threats to global health and development. Antibiotic resistance can occur naturally but antibiotic misuse further accelerates the process. According to the study published in Lancet Planetary Health by

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Keywords

Adverse effects, Culture sensitivity, Stewardship.

Global Research on Antimicrobial Resistance (GRAM) Project, antibiotic consumption has increased by 46% in the last two decades (from 2000-2018) [4]. Antimicrobial resistance has given birth to superbugs (resistant pathogens) which do not respond to conventional antimicrobial therapies. In USA it is estimated that about 2.8 million population get infected with antibiotic resistant pathogens and there are 35000 antibiotic related deaths annually [5]. It has also been stated that Asia has the highest rate of antimicrobial resistance and in India 80% E.coli has resistant to drugs become like penicillins, cephalosporins and fluroquinolones [6].

Unprofessional antibiotic use includes self-medication of antibiotics, inadequate education and training in health care professionals, promotion of drug companies, over the counter sales. Among this selfmedication seems to be the main culprit. It is commonly practiced in both developed and developing countries. It is more of a concern in developing third world, where health care needs out weight the facilities available. Especially among health care professionals tendency of self-prescription of antibiotics has been reported to be very high [7]. Access to antibiotics is not strictly prescription bound in India as well as in Kashmir [8]. Antimicrobial agents are easily available as over the counter drugs. This free access to antibiotics further escalates the issue of antibiotic resistance which is a serious concern in health care system today.

WHO in 2015 in collaboration with 12 countries conducted a survey to observe public awareness and knowledge of antibiotic use and its resistance and revealed that education and financial status were the main culprits behind antibiotic resistance [9-11]. Inspite of regular reminders from WHO, low public knowledge about antimicrobial use and its resistance still remain as the major challenge.

Since general public can play a pivotal role in checking inappropriate use of antibiotics, hence it is important to work on their awareness levels. Keeping this thing in mind we framed our current study to assess awareness regarding antimicrobial usage and its resistance among general Kashmiri population.

A collection of coordinated efforts that encourages the prudent use of antibiotics is known as antimicrobial stewardship (AMS). This concept was introduced to describe acts that affect the environment, animal health, and human health on a local, national, and international scale. Among other things, antimicrobial stewardship programs optimize the use of antibiotics, enhance patient outcomes, lower AMR and healthcare-associated infections (HAIs), and save healthcare expenditures.

Unprofessional use of antibiotics has become one of the greatest worry for health care system today. Researchers have shown that numerous health conditions caused by multi drug resistant pathogens have come into existence [12,13]. There have been limited studies assessing the knowledge of antibiotic usage among general public [14,15]. Common people form a significant portion of the society and as such it's important to gauge their understanding regarding antibiotic usage and antibiotic resistance. Hence, we conducted the current study to assess awareness regarding antimicrobial usage and its resistance among general Kashmiri population.

#### Methodology

Our study was conducted in the Department of Pharmacology, Government Medical College Srinagar from 1<sup>st</sup> October 2022 to 1<sup>st</sup> January 2023, after getting approval from Institutional Ethics Committee. An electronic questionnaire to assess the awareness regarding antibiotic usage and its resistance was prepared using Google forms and circulated through social media platform (whatsapp). Identity of the respondents was kept highly confidential. The questionnaire was prepared based on previous studies. The questionnaire had 26 questions divided into four sections and was prepared in English language. The first section consisted of basic demographic profile of respondents like age, sex etc. The second section inspected the use of antimicrobial agents by the participants in the last three months, the reasons for consuming the drug and the source from which the drug was obtained. The third section dealt with the awareness regarding antibiotic usage and section four contained information regarding knowledge of participants about antibiotic resistance. Options of questions in section four were framed on 3-point Likert scale.

We received responses from 279 participants which were then included in the study. Responses were compiled using Microsoft Excel Sheet and then analysed. Statistical analysis was done using SPSS version 25.0 software. Demographic characteristics were analyzed using descriptive statistics. Categorical variables were measured as percentages.

#### Results

Table 1 shows the Demographic profile of study population. Table 2 lists the Participants awareness regarding antibiotic usage. Figure 1 describes the Conditions for which antibiotics were consumed by the respondents. Figure2 shows the knowledge of respondents regarding antibiotic resistance. Table 3 depicts the Education of the study participants where they obtain antibiotics from. Table 4 depicts the Education with respect to the idea about Antibiotic Stewardship program.

Table 5 shows the participants know self medication of antibiotics may lead to antibiotic resistance. Table 6 shows whom the participants consult in case their symptoms don't improve and if they want to change their antibiotic.

Parameter	Number
AGE	
18 - 28	63(23%)
29-38	144(52%)
39-48	45(17%)
49 and above	21(8%)
GENDER	
Male	108(40%)
Female	165(60%)
MARITAL STATUS	
Single	72(26%)
Married	198(73%)
Divorced	3(1%)
RESIDENCE	
Urban	201(74%)
Rural	72(26%)
EDUCATION	
High school	24(9%)
Graduate	57(21%)
Post graduate	189(70%)

Table 1: Demographic	profile of study population.
Parameter	Number

## Table2:Participantsawarenessregardingantibiotic usage.

	Number
Have you consumed antibiotics in	
the last three months	
Yes	204(75%)
No	69(25%)
Don't know	0
If yes, then how long	
3 days	81 (40%)
5 days	93 (46%)
10 days	15 (7%)
>10 days	15 (7%)
What are antibiotics used for	
To decrease fever	9 (3%)
To relieve pain	3 (1%)
To overcome fatigue and malaise	0 (0%)
To treat infections	261 (96%)
No idea	0 (0%)

Where do you obtain antibiotics	
	147 (520/)
From pharmacy with prescription	147(35%)
From pharmacy without	111 (41%)
prescription	15 (6%)
Classical formation of the last of the las	0(0%)
Obtained from some friend	
Do you have idea against which	
organisms antibiotics act	<b>2 1 2 1 2 1 2 1 2 1 3 1 1 1 1 1 1 1 1 1 1</b>
Bacteria	243 (89%)
Virus	0 (0%)
Fungi	24 (9%)
No idea	6 (2%)
Do you know antibiotics cause side	
effects	
Yes	267 (98%)
No	6 (2%)
Don't know	0 (0%)
Should antibiotics always be	
purchased after a valid prescription	
Yes	252 (92%)
No	15 (6%)
Don't know	6. (2%)
Have you ever left antibiotics	
Nag	141 (520/)
i es	141 (52%) 122 (48%)
	152 (48%)
	0 (0%)
If yes, what was the reason	105 (740)
Symptomatic improvement	105 (74%)
Medicine got finished	5 (4%)
Cost issue	2 (1)0/2 )
	3(270)
Busy schedule	$3^{(2\%)}$ 25 (18%)
Busy schedule Misguidance	$\begin{array}{c} 5 & (2\%) \\ 25 & (18\%) \\ 0 & (0\%) \\ 2 & (2\%) \end{array}$
Busy schedule Misguidance Experienced adverse effects	$\begin{array}{ccc} 3 & (2\%) \\ 25 & (18\%) \\ 0 & (0\%) \\ 3 & (2\%) \end{array}$
Busy schedule Misguidance Experienced adverse effects What do you do with the medicines	3       (2%)         25       (18%)         0       (0%)         3       (2%)
Busy schedule Misguidance Experienced adverse effects What do you do with the medicines left after your course is completed Save the remaining dames for future	$ \begin{array}{c} 3 & (2\%) \\ 25 & (18\%) \\ 0 & (0\%) \\ 3 & (2\%) \\ \end{array} $
Busy schedule Misguidance Experienced adverse effects What do you do with the medicines left after your course is completed Save the remaining drugs for future	$\begin{array}{c} 3 & (2\%) \\ 25 & (18\%) \\ 0 & (0\%) \\ 3 & (2\%) \end{array}$
Busy schedule Misguidance Experienced adverse effects What do you do with the medicines left after your course is completed Save the remaining drugs for future use Discard the left over medicines	$\begin{array}{cccc} 3 & (2\%) \\ 25 & (18\%) \\ 0 & (0\%) \\ 3 & (2\%) \\ \hline 205 & (75\%) \\ 49 & (18\%) \\ 11 & (4\%) \\ \end{array}$
Busy schedule Misguidance Experienced adverse effects What do you do with the medicines left after your course is completed Save the remaining drugs for future use Discard the left over medicines Cine it to some friend when they	$\begin{array}{cccc} 3 & (2\%) \\ 25 & (18\%) \\ 0 & (0\%) \\ 3 & (2\%) \\ \end{array}$ $\begin{array}{cccc} 205 & (75\%) \\ 49 & (18\%) \\ 11 & (4\%) \\ 8 & (2\%) \\ \end{array}$
Busy schedule         Misguidance         Experienced adverse effects         What do you do with the medicines         left after your course is completed         Save the remaining drugs for future         use       Discard the         left over medicines         Give it to some friend when they         basement eight       No ideo	$\begin{array}{cccc} 3 & (2\%) \\ 25 & (18\%) \\ 0 & (0\%) \\ 3 & (2\%) \\ \end{array}$ $\begin{array}{cccc} 205 & (75\%) \\ 49 & (18\%) \\ 11 & (4\%) \\ 8 & (3\%) \\ \end{array}$
Busy schedule         Misguidance         Experienced adverse effects         What do you do with the medicines         left after your course is completed         Save the remaining drugs for future         use       Discard the         left over medicines         Give it to some friend when they         become sick       No idea	$\begin{array}{cccc} 3 & (2\%) \\ 25 & (18\%) \\ 0 & (0\%) \\ 3 & (2\%) \\ \end{array}$ $\begin{array}{cccc} 205 & (75\%) \\ 49 & (18\%) \\ 11 & (4\%) \\ 8 & (3\%) \\ \end{array}$
Busy schedule Misguidance Experienced adverse effects What do you do with the medicines left after your course is completed Save the remaining drugs for future use Discard the left over medicines Give it to some friend when they become sick No idea Do you have idea that effectiveness	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
Busy schedule         Misguidance         Experienced adverse effects         What do you do with the medicines         left after your course is completed         Save the remaining drugs for future         use       Discard the         left over medicines         Give it to some friend when they         become sick       No idea         Do you have idea that effectiveness         of antibiotics is reduced if full         paperagies and completed	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
Busy scheduleMisguidanceExperienced adverse effectsWhat do you do with the medicinesleft after your course is completedSave the remaining drugs for futureuseDiscard theleft over medicinesGive it to some friend when theybecome sickNo ideaDo you have idea that effectivenessof antibiotics is reduced if fullcourse is not completed	3       (2%)         25       (18%)         0       (0%)         3       (2%)         205       (75%)         49       (18%)         11       (4%)         8       (3%)
Busy schedule         Misguidance         Experienced adverse effects         What do you do with the medicines         left after your course is completed         Save the remaining drugs for future         use       Discard the         left over medicines         Give it to some friend when they         become sick       No idea         Do you have idea that effectiveness         of antibiotics is reduced if full         course is not completed         Yes	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
Busy schedule         Misguidance         Experienced adverse effects         What do you do with the medicines         left after your course is completed         Save the remaining drugs for future         use       Discard the         left over medicines         Give it to some friend when they         become sick       No idea         Do you have idea that effectiveness         of antibiotics is reduced if full         course is not completed         Yes         No	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
Busy schedule Misguidance Experienced adverse effects What do you do with the medicines left after your course is completed Save the remaining drugs for future use Discard the left over medicines Give it to some friend when they become sick No idea Do you have idea that effectiveness of antibiotics is reduced if full course is not completed Yes No Don't know	$\begin{array}{cccccccccccccccccccccccccccccccccccc$



Figure 1: Conditions for which antibiotics were consumed by the respondents.



Figure2 : Knowledge of respondents regarding antibiotic resistance.

### Table 3:Education- Where do you obtain antibiotics from.

			Where do yo	u obtain antibio	otics from			
			From	From	Left	Total		
			pharmacy	Pharmacy	over			
			with	without	medicine			
			prescription	prescription	at home			
Residence		Rural	12	8	0	20		
Count			60.0%	40.0%	0.0%	100.0%		
% within Education								
	Urban		6	0	2	8		
Count			75.0%	0.0%	25.0%	100.0%		
% Within Education								
			31	29	3	63		
Count			49.2%	46.0%	4.8%	100.0%		
% within Education								
Total			49	37	5	91		
Count			53.8%	40.7%	5.5%	100.0%		
% within Education								
Chi-Square Test								
	Value	Df		Asymptotic		Exact sig.(2-sided)		
				Significance	e(2-			
				sided)				
Pearson Chi-Square	11.459"	4		0.022		0.022		
Likelihood Ratio	13.125	4		0.011		0.013		
Fisher"s Exact Test	10.145					0.023		
N of Valid Cases	91							

p value= 0.023

#### Table 4: Education-do you have idea about Antibiotic Stewardship program.

			Do you have any idea about Antibiotic Stewardship					
			program					
			Don't know		No	Ye	s	Total
Residence		Graduate	0		19	1		20
Count			0.0%		95.0%	5.0	)%	100.0%
			0		5	3		8
% within Education			0.0%		62.5%	37	.5%	100.0%
	High	school	1		36	26		63
Count			1.6%		57.1%	41	.3%	100.0%
% Within Education								
	Postgraduate							
Count								
% within Education								
Total			1		60	30		91
Count			1.1%		65.9%	33.	.0%	100.0%
% within Education								
Chi-Square Test								
	Value	Df		Asy	Asymptotic		Exact si	g.(2-sided)
				Sigr	nificance(2-			
				side	d)			
Pearson Chi-Square	9.872"	4		0.04	3		0.103	
Likelihood Ratio	12.457	4		0.01	4		0.009	
Fisher"s Exact Test	11.964						0.009	
N of Valid Cases	91							
$p_{\rm value} = 0.000$	•						•	

p-value= 0.009

	•		Do you know self medication of antibiotics may lead to				
			antibiotic	resistance		-	
			Don't	No	Yes	Total	
			know				
Residence		Rural	0	4	20	24	
Count			0.0%	16.7%	83.3%	100.0%	
			3	1	63	67	
% within residence			4.5%	1.5%	94.0%	100.0%	
	Urban						
Count							
% Within Residence							
Total			3	5	83	91	
Count			3.3%	5.5%	91.2%	100.0%	
% within Residence							
Chi-Square Test	T			•		1	
	Value	Df		Asymptotic		Exact sig.(2-sided)	
				Significar	ice(2-		
				sided)			
Pearson Chi-Square	8.701"	2		0.013		0.026	
Likelihood Ratio	8.334	2		0.016		0.026	
Fisher"s Exact Test	6.955					0.033	
N of Valid Cases	91						

#### Table 5: Residence-Do you know self medication of antibiotics may lead to antibiotic resistance.

p-value=0.033

#### Table 6: Residence- whom do you consult in case your symptoms don't improve and you want to change your antibiotic.

			If yes then whom					
			99	pharmacist	physician	self	Total	
Residence		Rural	5	3	16	0	24	
Count			20.8%	12.5%	66.7%	0.0%	100.0%	
% within residence								
	Urban		11	0	50	6	67	
Count			16.4%	0.0%	74.6%	9.0%	100.0%	
% Within Residence								
Total			16	3	66	6	91	
Count			17.6%	3.3%	72.5%	6.6%		
% within Residence								
Chi-Square Test								
	Value	Df		Asympto	tic	Exact sig	.(2-sided)	
				Significat	nce(2-			
				sided)				
Pearson Chi-Square	10.875	3		0.012		0.014		
Likelihood Ratio	12.017	3		0.007		0.011		
Fisher"s Exact Test	8.816					0.021		
N of Valid Cases	91							
$\mathbf{p}$ value $-0.021$	•					•		

p-value= 0.021

#### Discussion

In the study we conducted we found, that majority of the respondents (52%) were in the age group of 29-38 years, with female predominance 60%. Most of the participants (73%) were married. 70% participants were post graduates and 74% lived in urban areas.

In the current study when asked about consumption of antibiotics in the last three months, 75% participants responded in the affirmative. Similarly in the study conducted by El Zowalaty ME et al [16],71% subjects had used antibiotics in the last 6 months while 59% had consumed antibiotics in the last 12 months, in the

research conducted by Zajmi D et al [17]. As is evident from figure 1, major portion of the study population (37%) had consumed antibiotics for the treatment of sore throat, followed by cough with sputum,17%. In the previous similar studies conducted by Mir SA et al [18], sore throat with cough (89%) was the leading cause of antibiotic usage. Another study was conducted by Zajmi D et al [17] where sore throat (20%), was the second most common cause of antibiotic usage. In the research when the respondents were asked about the conditions where antibiotics can be used, 96% correctly responded for the treatment of infections. Yin X et al [19] also reported that majority of the participants (72%), had agreed that antimicrobials can be used to treat infections. Similarly Sharif SI et al [20] conducted the study and reported that 50% participants agreed that antibiotics can be used for the treatment of various infections.

In this research, majority respondents obtained antibiotics from pharmacies after a valid prescription,53%. Similar results were reported by Sharif SI et al [20] from his study where 41% subjects had purchased antibiotics from medical stores after valid prescriptions. Another study was conducted by Tangcharoensathien V et al [21]where 98% respondents had received their medicines from pharmacies after consultation with health care professionals.

Self medication of drugs is rampant world wide but more so its a problem for third world countries [22]. Especially in case of antibiotics, self medication can result in inappropriate dosage which is one of the major contributors to antibiotic resistance [23]. In this research 47% participants reported that they either bought antibiotics from pharmacies without prescription or used drugs left behind at home. Almost similar results were reported by Sharif SI et al [20] were 40% study subjects practiced self medication of antibiotics. Only 10% respondents had self medicated themselves with antibiotics in the study conducted by Yin X et al[19]. The probable reason for this could be that we are still a third world country where public needs override the available health care facilities. Majority respondents in this study (89%), were aware of the fact that antibiotics act against bacteria. Similarly in the study conducted by André M et al [24],77% participants had correctly agreed that antibiotics are effective against bacteria. Participants in the study were well aware of the fact that antimicrobial drugs cause side effects,98%. Likewise 42% subjects had agreed that antibiotics cause side effects as per the study conducted by Javaeed A et al[25]. In this study, 52% subjects had left antibiotics midway and the most common reason for this was symptomatic improvement. Results of our study were comparable with the studies conducted by Sharif SI et al [20] and Mir SA et al [18] respectively. In the study conducted by Sharif SI et al [20], 62% participants had left antibiotics midway during the

course, while when the respondents in the study conducted by Mir SA et al [18]were asked about the reason of leaving the medicine midway, 58% replied that the felt improvement in their symptoms. 96% subjects in the study were well aware of the fact that effectiveness of antibiotics is reduced if full course is not completed. Our results were definitely better than the previous study conducted by Javaeed A et al [25] where only 2% participants were aware that antibiotics effectiveness is reduced if full course is not completed. This suggests better knowledge about antibiotic usage in our study group. Figure 2 consisted of factors to scrutinize the knowledge of participants regarding antimicrobial resistance. 89% subjects in our study had idea about antibiotic resistance. Our findings were almost similar to the findings reported by André M et al [24], where 85% subjects were familiar with antibiotic resistance. Again 89% participants knew that self-medication was one of the main culprits behind it while only 62% participants said so in the previous study conducted by Karandikar YS et al [26] .67% respondents in our study changed their medication in case their symptoms did not improve after consultation with some health care professional. The results of our study were contrary to the findings reported by Mir SA et al [18], where only 16% subjects had changed their antibiotics when their symptoms had not improved. In our study 86% participants knew about culture sensitivity testing which should ideally be done before prescribing antibiotics, while only 23% had actually undergone such a test and only 32% had heard about antibiotic stewardship program. Fisher exact test was done to find out the association between variables. On statistical analysis between education and where the respondents obtained antibiotics from, it was found that a higher percentage of subjects (75%) with high school education bought antibiotics from pharmacies using a valid prescription, and this was found to be statistically significant with a p-value= 0.023 (table 3). This meant that the post graduates in our study were more adamant that they are in no need of prescriptions to get drugs from medical stores. This attitude of theirs needs to be addressed as people with higher education influence the society more. When relationship between education and idea regarding antibiotic stewardship program was analyzed, it was found that higher percentage of postgraduates (41.3%) were aware about the program and the association was found to be statistically significant with a p-value of 0.009 (table 4). The association between residence and awareness that self medication of antibiotics may lead to antibiotic resistance was analysed and it was found that that urban population was more aware about this fact (94%). This association was found to be statistically significant with a p-value of 0.033 (table 5). When the relationship between residence and the person whom the respondents consulted in case their symptoms did not improve and they wanted to change their antibiotics, higher percentage of urban population (75%) consulted physicians before doing so. This association was seen to be statistically significant with a p- value of 0.021 (table 6). This is probably due to more exposure of urban people to awareness programs.

#### Conclusion

The discovery of antimicrobial agents was a major breakthrough in the field of medicine. It proved life saving for a variety of infectious conditions. Then came an era when these magic bullets began to be used indiscriminately resulting in the development of antimicrobial resistance. Various factors contribute to the development of antimicrobial resistance, the first being the level of awareness regarding its proper use. In our study 96% participants were of the opinion that antibiotics are used to treat infections. 89% were aware that antibiotics act against bacteria. 53% believed that anti-microbial agents should be brought after proper medical consultation. 98% had idea that antibiotics can cause side effects. 52% left their antibiotics midway during the course and among them 68% believed that symptomatic improvement was the main reason behind it. 96% knew that effectiveness of antibiotics is reduced if antibiotics are left midway. 89% had an idea about antibiotic resistance and the same percentage considered self-medication as its main contributor. Only 32% participants had heard about antibiotic stewardship program. Our study showed that a lot of difference exists between knowledge and actual practice. Although our study population was aware about proper antibiotic usage, but in reality they did not practice it. Intensive awareness campaigns regarding. proper antibiotic usage and antibiotic resistance should be carried out focusing health care professionals as well common public, so that misuse of antibiotics can be prevented. Further there should be a strict check on availability of antibiotics as over the counter drugs.

#### **Conflict of interest:**

There is no conflict of interest among the authors. **References:** 

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#### **Original Article**

# Molecular characterization Beta-Lactamase Gene Variants in Escherichia coli in the northern Indian region

Hamid Ahmad Shah, Dalip K. Kakru, Mohd Altaf Bhat

#### Abstract:

**Background:** With the rise of bacteria that are multidrug-resistant, antimicrobial resistance (AMR) is an extensive public health problem. *Escherichia coli*, a common bacterial pathogen, has demonstrated resistance to beta-lactam antibiotics through the formation of beta-lactamase enzymes. Understanding the genetic diversity of  $\beta$ -lactamase genes in *E. coli* is essential for developing effective strategies to combat AMR.

**Methods:** In this study, we conducted a comprehensive molecular characterization of beta-lactamase gene variants in *E. coli* isolates collected from clinical in the northern Indian region. To find and categorize beta-lactamase genes, 210 *E. coli* isolates were submitted for phenotypic and genotypic investigation. Different beta-lactamase gene variations were detected using DNA sequencing and polymerase chain reaction (PCR).

**Results:** Our findings revealed a diverse range of beta-lactamase gene variants in the *E. coli* isolates, including SHV, TEM, and CTX-M types. Importantly, we seen a greater existence of extended-spectrum beta-lactamase (ESBL)-making the strains of E. coli, indicating the growing concern of ESBL-mediated resistance in the region.

**Conclusion:** This research provides valuable awareness of the molecular epidemiology of beta-lactamase gene variants in *E. coli* in the northern Indian part, highlighting the urgent need for targeted interventions to curb the spread of antimicrobial resistance. Understanding the genetic diversity and mechanisms of resistance is crucial for the development of effective antibiotic stewardship programs and the design of novel therapeutic approaches to combat AMR in this region.

#### Introduction:

#### JK-Practitioner 2023;28(3-4):50-56

The Major public health concern globally nowadays is antibiotic resistance caused by enteric bacteria.[1] Numerous resistance mechanisms were reported in Enterobacteriaceae and non-fermentative gram-negative bacilli.[2-4] The enteric bacteria are primarily causative agents of septicemia, urinary tract, wound, and respiratory infections. The usage of beta-lactam antibiotics has increased which has resulted in an increase in Enterobacteriaceae resistance because of the formation of the  $\beta$ -lactamases which act on the beta-lactam ring of antibiotics. ESBL are a subset of  $\beta$ -lactamases generated by gram-negative bacteria, primarily Enterobacteriaceae and *Pseudomonas aueruginosa*.[5] Klebsiella & E.coli are the most common strains that produce ESBLs.[6,7] The emergence of ESBL-producing bacteria places restrictions on the prescribing of beta-lactam antibiotics, has led to numerous disease outbreaks around the world, and poses challenging infection control measures. The emergence of beta-lactamases E. coli is a serious concern in hospital settings. Only a few genes, particularly TEM-1, TEM-2, and SHV-1 were described during early phases of resistances.[8,9] More than 450 variants of /TEM, SHV, and CTX-M enzymes are found which are produced by ESBL harboring bacteria.[10] The goal of the current research had been to detect the ESBL isolates from various clinical isolates. There hasn't been any research done to use molecular cloning and sequencing analysis to find distinct variations of the ESBL resistance genes. The current research focused on detecting variants likeTEM-1,TEM-2, SHV-1, and CTX-M15.

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#### Keywords

Antimicrobial resistance, DNA sequencing, *Escherichia coli*, ESBLmediated resistance, Molecular epidemiology.

#### Materials and Methods

### Collection of isolates and ESBL identification

From January 2021 to December 2022, the research was conducted in the Department of Veterinary Microbiology, FVSc & AH., SKUAST-K, and the Department of Microbiology, SMSR, Sharda University. A total of 210 isolates of the *E. coli* have been gathered through the various sites in the Noida, Uttar Pradesh, and Kashmir valley regions. These isolates were from people who may have had *E. coli* infections. Phenotypic identification was done by using ESBL chromogenic agar, Double disc synergy test, E-test, and Disk diffusion test. Presumptive isolates found to be positive in phenotypic tests underwent genotypic detection by multiplex PCR amplification utilizing specific primers set.

#### **Extraction of bacterial DNA**

Utilizing a DNA extraction kit that is available commercially, the DNA was isolated from the bacterial lysate (Wizard Genomic DNA purification kit, Promega). This helps us to achieve the pure DNA without any PCR inhibitors. The DNA extracted was subjected to O.D check before using them as a template in the PCR reaction. A ratio of 260/280 in the range of 1.6-1.8 was appropriate to consider.

Detection of ESBL gene variants *TEM* group, *SHV* group, and *CTX-M*15

Using the Go-green Master mix, all of the PCR experiments in this investigation were carried out in a  $25\mu$ l reaction volume (Promega). DNA taken by the lysate subjected to PCR amplification for the detection of ESBL gene variants utilizing a set of primers as mentioned in Table-1 The cyclic conditions are mentioned in Table-2

S.N 0	PCR name	β- lactamase(s) targeted	Sequence (50 –30)	Length (bases)	Amplicon size (bp)	Primer concentr ation (pmol/m L)	Ref ere nce
1	Multiplex I	TEM variants	F- CATTTCCGTGTCGCC CTTATTC	22	800	0.4	[11]
	TEM	TEM-1 and TEM-2	R- CGTTCATCCATAGTT GCCTGAC	22	800	0.4	[11]
2.	Multiplex	SHV variants	F- AGCCGCTTGAGCAA ATTAAAC	21	712	0.4	[11]
	SHV	including SHV-1	R- ATCCCGCAGATAAA TCACCAC	21	/13	0.4	[11]
3	Sin alandar	CTV M 15	F- CACACGTGGAATTTA GGGACT	21	006	0.1	[12]
	Singlepiex	CIX-M-15	R- GCCGTCTAAGGCGA TAAACA	20	990	0.1"	[12]

. Table-1 Details of Primer sets used in this "study

Table-2: Cyclic conditions for PCR amplification of ESBL gene variants

"Gene	Initial	Denaturation	Annealing	Extension	Final
	Denaturation				Extension"
TEM Variants	94°C for 10 min	94°C for 40s	60°C for 40s	72°C for 1	72°C for 7 mins
including TEM-				min	
1 and TEM-2					
SHV variant	94°C for 10 min	94°C for 40s	60°C for 40s	72°C for 1	72°C for 10
including SHV-				min	mins
1					
CTX-M 15	95°C for 10 min	94°C for 40s	50°C for 40s	72°C for 1	72°C for 10
				min	mins

#### **Electrophoresis and Documentation**

A 500 ml Erlenmeyer flask has been utilized to heat the necessary agarose quantity (Sigma Aldrich, St. Louis, USA) with 50 ml of a 1X tris acetate EDTA (TAE) (appendix) buffer. This resulted in an agarose gel that had a weight-to-volume ratio of 1.5 percent. After the flask had been chilled to 60 degrees Celsius, ethidium bromide has been poured until the final concentration read 0.5 µg per ml. After allowing the heated agarose solution to totally set at room temperature for 30 mins, the solution was poured into a plastic holder equipped with an appropriate comb (with one mm wells). Following the removal of the comb, the gel was installed on an electrophoresis tank (manufactured by Amersham Pharmacia Biotech. UK), and the electrophoresis tank was then filled with 1X TAE buffer. On the submerged gel, individual PCR samples were placed into wells of their own. In addition, the standard molecular weight (100 bp) marker that was supplied by promega was injected into one well. A voltage ranging from 1 to 5V/cm was applied across the gel till the yellow dye of the master mix migrated to the correct distance. After removing the gel, it was recorded using ultraviolet light, and photographs were taken using the Gel Documentation System (Ultra-lumInc.Imaging System, UVP, UK).

### 2.5 Cloning of gene variants *TEM* group, *SHV* group, and *CTX-M*15

The representative positive samples, one from each of the SHV group, CTX-M group (CTX-M15), and 2 from the TEM group had been cloned in a pGEMTeasy cloning vector (Promega Corporation, Madison, USA) and then sent out to be sequenced so that the identity of ESBL E. coli could be determined. To summarise, the PCR products have been ligated into the pGEMT-easy cloning vector in accordance with the proposed procedure provided by the manufacturer. In order to convert DH5a Escherichia coli cells, a heat shock treatment was performed in a water bath while the ligation combination was present. Two types of colonies were observed on the plates white (positive) and blue (negative). 5 positive (white) colonies were selected for every transformation, placed in Luria Bertani (LB) broth (Difco), and afterward placed in a rotary shaking incubator set to 37 ° C for one night. The shaking rate of the incubator was 200 revolutions per minute (JEIO TECH, Korea).

#### **Screening of Recombinant Colonies**

Both colony PCR and restriction enzyme analysis were used to screen the recombinant colonies to determine whether or not they contained the insert in addition to the plasmid DNA. Each pellet was suspended in 500 l distilled water and heated for 10 minutes followed by rapid cooling over ice for 15 minutes. then centrifuged at 10,000rpm for 10 min the supernatant had been kept in another 1.5ml microcentrifuge tube and has been utilized as the template for PCR. The PCR was carried out using *TEM-2*, *TEM-1*, *CTX-M* 15 and *SHV-1* primers as described previously to confirm the presence of insert. The amplicons were checked by agarose gel electrophoresis.

### Extraction of Recombinant plasmid and Restriction digestion

After utilizing QIAprep® Miniprep Kit (Qiagen, Hilden, Germany) to extract the plasmid DNA from chosen colonies, the concentration of the DNA was modified to be 200 ng/µl. The isolated plasmids were digested separately with restriction enzyme EcoRI for the confirmation of insert. Each of the digestion reactions consisted of  $\sim 5\mu g$  of plasmid (2  $\mu$ l), 1 $\mu$ l of Fast Digest green buffer, 10 units of EcoRI enzyme, and remaining nuclease-free water to make up an overall volume of 10 µl. The reaction solutions has been incubated in a water bath at the temp of 37°C for the time of 20min and then 2 µl of this plasmid was loaded onto 0.8% agarose gel and subsequently visualized under a UV gel documentation system for the presence of the insert. After determining the concentration of the isolated plasmid using absorbance at  $\lambda 260$  (using a Biophotometer made by Eppendroff in Germany), the sample was placed in a 1.5 ml centrifuge tube and frozen before being sequenced. The plasmids were sequenced by Sanger's dideoxy chain termination method [13] in Unipath Specialty Laboratory Ltd. India. Following the completion of the sequencing, homology searches have been carried out by utilizing the BLAST aproach.(http://blast.ncbi.nlm.nih.gov/Blast.cgi).

#### Results

### Occurrence of ESBL *E. coli* in clinical isolates

During the study period out of 210 clinical isolates collected only 158(75.23%) isolates were phenotypically presumptive positive ESBL *E. coli* based on the phenotypic confirmatory test (ESBL Chromogenic agar), E-test, and double disk synergy test as depicted in Fig-1a, 1b,1c. All these presumptive isolates underwent molecular detection by PCR utilizing a particular set of primers for the determination of the ESBL gene in isolatesof *E. coli*. Only 124 isolates were positive for *bla* SHV, *bla* CTX-M, and *bla* TEM as depicted in Fig-2.

### Detection of ESBL gene variants *TEM* group, *SHV* group, and *CTX-M*15

All these 124 isolates that have been positive for the *bla TEM*, *bla SHV*, and *bla CTX-M* were subjected to another round of PCR to determine the type of variants using a specific set of primers. Out of 124 ESBL *E. coli* isolates, 54(43.5%) were *TEM* variants, 14(11.29%) were *SHV* variants and 46 (37.09%) were *CTX-M15* variants. The *bla*-CTX-M15 strain was the one that was found the most frequently. Isolates that carried the *bla* TEM variant gene created an amplicon with 800 bp, those that carried the *bla* CTX-M variant displayed an amplicon with 996 bp, and the existence of the *bla* SHV gene variant had been identified by the amplification of 713 bp, as shown in Figure 3a, 3b, and 3c.

Table 3.	Repartition	of the Detect	ed ESBL Genes
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ESBL Genes	Types of Variant Group	No. (%)
Bla TEM	TEM Variants including TEM-1 and TEM-2	54(43.5)
	СТХ-М15	46(37.09)
Bla CTX-M	SHVVariants including SHV-1	14(11.29)
Bla SHV		

**Cloning of gene variants** 

One representative amplicon of SHV and CTX-M15 and two from TEM group were purified and cloned separately in E. coli DH5a cells, using cloning vector pGEM-T. The existence of altered colonies on the LB/Ampicillin agar plates served as the basis for determining whether or not the cloning attempt was successful. The colonies with and without insert appeared white and blue, respectively as depicted in Fig-4.The white colonies were further confirmed for the presence of the respective inserts by colony touch PCR depicted in Fig-5.Restriction digestion by EcoRI also confirmed the presence of insert. Four gene amplicons from the above gene variants were sequenced commercially. BLAST analysis of nucleotide sequences of the TEM group showed 100% homology to the E. coli class A broad-spectrum beta-lactamase TEM-1 (blaTEM) gene, SHV group showed 99.85% of homology to beta-lactamase SHV-1 precursor gene, and CTX-M15 showed 99.90% of homology to extended-spectrum class A betalactamase CTX-M-15 gene. The sequences of CTX-M-15, SHV-1, and blaTEM-1 from the isolates were submitted to Genbank under accession numbers OR350836, OR350837, and OR350838 respectively. Discussion

The first-line drugs in infections caused by Enterobacteriaceaeare  $\beta$ -lactam antibiotics.[14] The present study investigates the ESBLproducing Enterobacteriaceae in two tertiary care Indian hospitals. There is variation in the existence of ESBL-producing Enterobacteriaceae around the globe. In most of the countries, where the patients are treated with antibiotics, a high prevalence rate of multidrug-resistant Enterobacteriaceae has been observed.[15] However, lower rates were found in North America and Europepreviously [16,17] and high rates in Asia. [18]. South America[19], and Africa.[20] The factors responsible for the spread are encouraged by indiscriminate antimicrobial use without a prescription, use of counterfeit drugs, poor hygiene, a high prevalence of infectious diseases, and lack of diagnostic tools for detecting antibiotic resistance.[21,22] In our research, the isolation of MDR ESBL strains that expressed the CTX-M-15 gene restricted the treatment options available to clinicians for their patients. It is not enough to just focus on the strains themselves to prevent the resistant gene isolates spread; rather, continuous surveillance and the application of effective methods for infection control are essential. The findings that the majority of beta-lactam-resistant isolates had blaTEM genes emphasize the significant contribution of non-ESBL blaTEM genes to resistance. This is caused by the gene product's enzymatic capacity to hydrolyze the majority of penicillin medications, historical cephalosporins, and contemporary betalactams.[23,24] In our study, Bla-CTX-M15has been themajor represented *bla-CTX-M* type which is also confounded by previous findings from ESBL isolates from camel and domestic livestock origin in Africa[25-28] Interestingly, the isolates harboring blaCTX-M-15 and blaTEM-1 gene exhibited an MDR phenotype. This phenotypic emergence corroborated findings from prior research indicating ESBLproducing Enterobacteriaceae frequently display an MDR phenotype against nonbeta-lactam antibiotics as a result of their plasmids containing numerous resistance genes[26,27,29]



Fig-1a: Isolation of ESBL producing *E. coli* on Chromogenic agar.1b: Phenotypic confirmation of ESBLs production in *E. coli* isolates by Etest using ceftazidime/ ceftazidime + clavulanic acid Strip.1c: Phenotypic confirmation of ESBLs production in *E. coli* isolates by disk diffusion method using cefotaxime (CTX) and cefotaxime+clavulanic (CEC)acid disks.



Fig-2: Representative *bla<sub>SHV</sub>*, *bla<sub>TEM</sub>* and *bla<sub>CTX</sub>*. Mgenes profile of phenotypically positive isolates using multiplex polymerase chain reaction (m-PCR):- Lane M: 100 bp DNA Ladder; Lane 1: Positive control for *bla<sub>SHV</sub>*, *bla<sub>TEM</sub>* and *bla<sub>CTX</sub>*. Mgenes; Lane 2: Negativecontrol Lane 3: *bla<sub>SHV</sub>*positive; Lane 4: *bla<sub>TEM</sub>* positive; Lane 5: *bla<sub>CTX-M</sub>* positive; Lane 6:*bla<sub>TEM</sub>* and *bla<sub>CTX</sub>*. Mpositive and Lane 7:bla<sub>SHV</sub>, bla<sub>TEM</sub> and bla<sub>CTX</sub>. **M**positive



Fig-3a: PCR detection of *bla<sub>TEM</sub>* group:- Lane M: 50 bp DNA Ladder; Lane 2: Positive control for *bla<sub>TEM</sub>* group; Lane 1: Negativecontrol; Lane 5 and 6: *bla<sub>TEM</sub>*grouppositive;



Fig-3b: PCR detection of *bla<sub>CTX-M15</sub>* group:- Lane M: 50 bp DNA Ladder; Lane 1: Negativecontrol; Lane 3 and 4: bla<sub>CTXM</sub>. <sup>15</sup>grouppositive, Lane 5: Positive control for *bla<sub>CTXM-15</sub>* group



Fig-3c: PCR detection of *bla<sub>SHV</sub>*group:- Lane M: 50 bp DNA Ladder; Lane 2: Negativecontrol; Lane 1: *bla<sub>SHV</sub>*group positive



Blue colony without insert)

White colony (with insert)

Fig-4: Blue/white screening for recombinant DH5a (LB/Amp. Agar) carrying blagene in pGEM-T vector on Luria Bertaini agar.



**Fig-5:** Colony touch PCR confirming the presence of *bla<sub>TEM</sub>*, *bla<sub>CTXM-15</sub>* and *bla<sub>SHV</sub>* inserts in *E. coli* DH5 - a clone using pGEM-T vector Lane M: 50 bp DNA Ladder

Lane 1-2: DH5- $\alpha$  clones on LB/Amp Agar showing amplification of approx. 800bp amplicons, upon colony touch PCR, confirming the presence of  $bla_{TEM}$ insert. Lane-3: DH5- $\alpha$  clones on LB/Amp Agar showing amplification of approx. 996bp amplicons, upon colony touch PCR, confirming the presence of  $bla_{CTX-MI5}$ insert. Lane-4:DH5- $\alpha$  clones on LB/Amp Agar showing amplification of approx. 800bp amplicons, upon colony touch PCR, confirming the presence of  $bla_{TEM}$ insert. Lane 5: Negativecontrol

#### Conclusion

In this study, we conclude the isolates as phenotypically presumptive positive ESBL *E. coli* based on the phenotypic confirmatory test (ESBL Chromogenic agar), E-test, and double disk synergy test. On molecular evaluation, 124 isolates were positive for *bla* TEM, *bla* SHV, and *bla* CTX-M genes mainly expressed by MDR ESBL isolates. Thus the indiscriminate use of antibiotics in the food industry is one reason for AMR development and in order to prevent the spread of ARGs among humans while also preserving the cultural practices of the pastoral communities, efforts should be taken to develop medical practices and husbandry practices to widen up the antibiotic options availability while fighting any medical health problem.

#### **Conflict of Interest**

All authors declare there is not any conflict of interest or any affiliation or involvement in any organization whether it is academic, commercial, financial, personal and professionally.

#### Authors' Contribution

HAS, DKK, MAB conceptualized the work and conducted research. HAS also wrote the manuscript. **References** 

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#### **Original Article**

# Prevalence of whole blood adverse donor reactions in SKIMS medical collegeand hospital –A study at health care of North India

Faisal Ashraf, Mohammad Suhail Malik

#### Abstract:

**Background and Purpose:** To find the incidence and analysis of adverse donor reactions in whole blood donations.

**Materials and Methods:** This study has been done for a period of three years in Department of Blood Transfusion Medicine and Immunohaematology SKIMS, MCH Srinagar from May 2020 – April 2023. Donors were accepted for blood donations only after proper screening and counseling as per the national guidelines. Any adverse reaction during and post donation was managed conservatively successfully and recorded accordingly.

**Results:** Out of 5952 donors comprising of both voluntary and replacement donors. Males comprised of 5426 (91.16%) and females 526(8.84%) donations. Male to female blood donor ratio is 10:1. 4635 i.e. (77.87%) of total donors were on replacement basis. Prevalence of the donors experiencing adverse reactions was 177 (2.97%). Female donors 171 (57.77%) are most susceptible to reactions. Vasovagal reactions141 (79.73%) were found to be among most common reaction with its mild grade in majority of cases.

**Conclusion:** Only 177 (2.97%) of blood donors had some kind of adverse reactions. As we know that the cause of blood donation reactions varies, most of which can be easily mitigated through strict adherence to guidelines and competence of blood centre staff.

#### Introduction:

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Uneventful blood donations are backbone of a successful blood transfusion service. Developing countries usually have less blood donations due to lack of unmotivated population and if an adverse reaction will happen will lead to weak blood transfusion service (BTS) in a population. [1]Educated and well informed population leads to healthy non remunerated blood donors, but despite of that adverse reactions can occur at beginning, during and end of donation [2]. The most common type of reaction is a vasovagal reaction. Fainting (syncope) has found to be more in female gender, low body weight and first time donors. >7% of the donors don't come back after suffering any adverse event. Even after thorough screening of donors adverse reactions still can occur hence the need to observe and report the events become more necessary to mitigate the chances. The nature of reactions can vary from severe to mild. A blood donation which is goes smoothly increases the chances of retaining the donor for future as a regular voluntary donor. Apart from starting Hemovigilance Programmes for surveillance of transfusion reactions in 1900's soon it was felt important to record analyse and mitigate blood donation related reactions [3]. After ISBT [International Society of Blood Transfusion] and IHN [International Hemovigilance Network] Working Party and AABB Hemovigilance Programme, India also started reporting its own blood donation related reactions under National Blood Donor Vigilance Programme[NBDVP]on14<sup>th</sup> June, 2015 on world blood donor day in Kolkata [4].

#### **Data Collection:**

Variables such as age, gender, weight, donation status and type of adverse reaction were collected from departmental data registers. Also recorded concerned data such as type of adverse events and its management was piled up and inserted on MS Excel sheets. Author Affiliations Faisal Ashraf, Resident, Mohammad Suhail Malik, Associate Professor and Head, Department of Immunohematology and Blood Transfusion Medicine, SKIMS, MCH, Jammu and Kashmir India.

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Keywords Adverse Donor Reactions, Immunoheamatology

#### **Statistical Analysis:**

The overall analysis of the data was descriptive with results presented as percentage for categorical data. Statistical analysis was done using Statistical Package for the Social Sciences Version 22.0. If  $p \le 0.05$ , it was considered to be statistically significant.

#### Material and Methods:

This hospital based single centre retrospective study was conducted over a period of 3 years from May 2020 to April 2023 on voluntary and replacement based whole blood donors in Department of Blood Transfusion and Immunohematology SKIMS, MCH. Both voluntary and replacement non remunerated donors aged 18-65 years and having body weight equal to and more than 45 kg's were properly counselled and screened under the guidelines provided by Director General of Health Services prior **Results:**  to donation. Asepsis was maintained by disinfecting the site of venipuncture properly by using betadine and alcohol preparation. The lower limit of acceptable hemoglobin concentration was at 12.5 gm/dl.

At every step of donation proper SOP was followed. Prior informed consent was taken from donors and confidentiality maintained. The blood donors were observed during and 20 minutes post donation for any adverse event. All adverse reactions were noted accordingly in departmental register. Data entry was done in Microsoft excel and appropriate Statistical test were applied. All blood donors who experienced reaction in blood centre as well as during blood donation camps were included in our study. All donor reactions were conservatively managed successfully as per the SOP.

Total Donations (N)(%)	5952 (100%)
Males(%)	5426 (91.16%)
Females(%)	526 (8.84%)
Replacement donation(%)	4635 (77.87 %)
Voluntary donation(%)	1317 (22.13%)

*Table 1.Total number of blood donations with gender and donation type wise distribution.* Figure 1 displays that total 5952 whole blood donors were recorded in our data system. Male donors were 5426 (91.16%) and females comprised of 526 (8.84%) donations. Male to female ratio was 10:1. As per donation status replacement donors4635 (77.87%) surpassed voluntary donations.



*Figure 2: Prevalence of adverse donor reactions* According to this figure about 177 (2.97%) blood donors experienced some kind of adverse reactions.



Figure 3 displays total blood donation as per body weight .It can be seen that 1658 (27.85%) donors were between 45-50 kg's while as 4294 (72.15%) of donors were above 50 kg's.



Figure 4:Age wise distribution of total blood donations.

In the above figure, blood donors within age group 18-35 years contributed 2668 (44.82%),36-50 years 2064(34.67%) followed by age group51-65 years 1222 (20.52%) of total blood donations. Hence younger age group seem to donate more oftenly.





A significant and sharp decrease in donor reactions with increase in age is seen in the above figure. [p value  $\leq 0.05$ ].



Figure: Gender wise donor reactions Above figures shows us that female gender donors 102 (57.77%) are most susceptible to experience adverse donorreactions than male donors 75 (42.23%).



First time donors Repeat donors Figure 5: First time and repeat blood donations. Figure 5 displays that among the all blood donations, first time donors were in majority i.e. 4008 (67.34%) hile repeat donors comprised 1944 (32.66%) donations.

REACTION CLASS	TOTAL NO. OF	CTIONS(%)
	REACTIO NS(N)	
VASOVAGAL	141	79.73%
REACTIONS		
НЕМАТОМА	17	9.46%
TINGLING/NUMBNE SS	11	6.42 %
EXTRAVASATIONS (BRUISES)	08	4.40%
	177	100

Table 8: Percentage and number of reactions bymajor reaction class

The above figure displays all the reactions experienced overall by the donors in terms of both the number and percentage. It is clearly seen that vasovagal reactions 141 (79.73%) are the most common of them all.



Figure: Distribution of Vasovagal adverse donor reactions as per grading.

The above figure displays that among all adverse reactions mild form of vasovagal reaction was most

common reaction experienced by donors, comprising of majority i.e. 127 (71.61%) of reactions. 42 (23.73%) developed moderate reactions and 08 (4.66%) experienced severe vasovagal reaction.



Hematoma Numbness/Tingling Extravasations

#### Figure10: Needle injuries

Figure 10 shows that total percentage of needle injuries experienced by donors is 36 (20.27%). Here hematoma was shown by 17 (9.46%) of donor population followed by tingling/numbness 11 (6.42%) and extravasations (bruises) 08 (4.40%).

#### Discussion

Only 296 (2.97%) of blood donors showed adverse donor reactions with vasovagal reaction being most common but still it is a potential problem for the donor retention, especially the new donors. All donors especially first time should be counselled properly prior to donation about the benefits and probable side effects of donation to alleviate their anxiety. Any query should be competently and empathically answered. Blood donation has proven to be a safe and uneventful procedure when applied with some of mitigations such as effective pre donation counseling and screening, attentive and skilled staff, timely refreshment and post donation counseling. Thus helping eventually to meet all challenges and maintain an optimum blood transfusion services.

In our study, 2.97 % of all whole blood donations were complicated by adverse events. This is in concordance to various studies conducted all over the world in which the rate of adverse events associated with donations ranged from 0.3% to 3.8% [9–11,13, 14, 17, 18] Also some studies showed the incidence of adverse reactions to be in

between 2% to 7% [18-21]. Although whole blood donation is considered to be quite safe, reports in the medical literature about the frequency of adverse events during donation show broad heterogeneity. [12-14]

Our study found that out of total 5952 donors, 5426 [91.16%] belonged to male gender & only 526 [8.84%] were female donors. Similar studies by Mangwana S 2013; [21] Majlessi F et al, 2008; [22]

Chowdhury FS et al, 2011; [23] Jain N et al, 2014 [24] showed almost same frequency of male [96.96 %, 94 %, 92.5%, 96.1 %] & female [3.04 %, 6 %, 7.5 %, 3.9 5] donors respectively. As male have bigger social circles, can be contacted more easily and have higher chances of eligible hemoglobin levels therefore all these factors contribute towards majority of donations. In present study, age group between 18-35 years 2668 (44.82%) were found to be in majority of blood donations which was found to be in accordance with study conducted by Mahbub-ul-Alam M et al, 2007 [15] Rohra D K et al, 2010 [16] & Agnihotri N et al, 2012 [17]. These studies also concluded increased incidence of donors in younger age groups. The reason of young people being in high number can be due to the fact that younger population are comparatively more energetic, have altruistic behavior and more enthusiasm in them.

It was found in our study, that most of the donors who experienced adverse donor reactions, 79.93 % [141] belong to the younger age groups i.e ,< 40 years. There was a significant decrease in the reaction percentage as the age increased [p value  $\leq 0.05$ ]. In various studies done by Mangwana S 2013; [25] Rathod K 2014; [26] Rohra DK 2010;

[27] Tondon R et al 2008; [28] they also reported that the adverse reaction percentage decreased as the age of donors increased. A study by Newman B H [29] postulated that baroreceptor sensitivity is decreased in healthy young individuals when they are physically or psychologically stressed. With increasing age, the human body becomes more stable hemodynamically. Also, the reason may be due to the fact young donors have first time anxiety and are more apprehensive to the pain of phlebotomy.

The present study also found that female donors 102 (57.77%) experienced reactions more than those of male 75 (42.23%).donors also seen in study by Miah M. [30]

Under the class of needle injuries 36 (20.27%), hematomas 17 (9.46%) were more commonly observed similar to Tiwari *et al.*'s [31] study and whereas the bruises (extravasations) were also observed in regular donors [32] Most of

the hematomas took more than 7 days to resolve. These results were documented, as donors with hematoma usually followed up again at a later date to ensure its resolution.

Finally, like various other authors [33-35] we found a low incidence of severe reactions (major syncopal reactions (3.72%, 11/296) with no episodes necessitating hospitalisation or administration of intravenous fluids. It is also to be mentioned that the maximum volume of blood withdrawn during the donation (450 mL  $\pm$  10%) is only about 10% of the total blood volume in an adult donor. Since at least 800-1,500 mL of blood, i.e. 15-20% of the total blood volume would have to be lost in order to be in at least class I risk of hypovolaemia, blood donors are unlikely to experience severe vasovagal reactions. [36] As blood donors are screened properly under strict guidelines, which leave less chance of severe adverse reactions.

#### Conclusion

Blood donation is a safe process but still some adverse reactions can occur. These unpleasant events although less in percentage have gross and significant effect on donor retention rate. So it's very important to find the cause, and accordingly mitigate the occurrence of blood donation related adverse events. As offsite reactions go un-noticed and un-marked less data regarding it is found. As blood transfusion service centres have both responsibility of maintaining optimum blood and its components with assuring safety for blood donors too. Hence even a minor class of reaction drastically reduces repeated donations [5-11].

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#### **Conflicts of Interest:**

The Authors declare no conflicts of interest.

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#### <u>Original Article</u> Impact Of Introduction Of Nucleic Acid Test And Its Role In Improving Blood Safety In A Tertiary Care Hospital

Mohd Zubair Qureshi, Shazia Handoo, Aruj bin Rashid, Sheikh Bilal

#### Abstract:

**Background:** Nucleic Acid Testing (NAT) is a molecular technique for screening blood donations to reduce the risk of Transfusion Transmitted Infections (TTIs) in the recipients, thus providing an additional layer of blood safety. It is a highly sensitive test which reduces the window period by detecting low levels of viral genomic materials that are present soon after infection but before the body starts producing antibodies in response to the virus.

**Material and method:** The study was conducted over a period of 10 months from September 2020 to June 2021.All samples were examined for HbsAg, HCV, HIV I & II by Enzyme Linked Immunosorbent Assay (ELISA). All seronegative cases by ELISA were subjected to Minipool-NAT in small pools of six to detect HBV DNA,HCV RNA and HIV 1 & 2 RNA.

**Result:** Out of all 15569 blood donations collected over study period, reactive samples by serological test (ELISA) were 40.

All the seronegative 15529 samples were tested by Minipool-NAT, out of which 22 were positive with total NAT yield of 1 in 706.

**Conclusion:** The routine use of NAT for detection of HBV, HCV & HIV should be mandatory for all seronegative donor blood to reduce the serological window period and hence reduce the incidence of transfusion transmission infections and increase the safety for the patients.

#### Introduction

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Nucleic Acid Testing (NAT) is a molecular technique for screening blood donations to reduce the risk of Transfusion Transmitted Infections (TTIs) in the recipients, thus providing an additional layer of blood safety. [1] The traditional method which is used for screening blood donations, known as immunoassay (or serology) testing, detect antibodies to viruses or viral antigens. With immunoassays, there is an interval between the donors' exposure to a virus until antibodies against the virus are produced, known as "window period". During this period there is risk of infection being missed in donated blood by immunoassay testing. These undetected window period infections are responsible for most of TTIs. Thus, NAT takes care of the dynamics of window period of viruses and provide safe blood for donation. [2]

Despite the current practice of screening blood with the newest generation serological tests of different sensitivities, a considerable residual risk of TTIs remains. Although these tests have shortened the pre-sero conversion window period, they still are not able to identify a number of newly infected blood donors. [3] NAT is highly sensitive test which detects the viral ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) by the amplification method. It reduces the window period by detecting low levels of viral genomic materials that are present soon after infection but before the body starts producing antibodies in response to the virus. This allows for earlier detection of infection and further decrease the possibility of transmission via transfusion and also detects mutants and occult cases. [4] Although NAT screening cannot completely eliminate the risk of TTIs, but it has reduced the risk of HBV, HCV and HIV-1, where it has been implemented. [5]

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#### Keywords

Nucleic acid testing, Transfusion transmitted infections, window period. HBV, HCV and HIV Implementation of NAT has introduced not only a new methodology and new logistic but when combined with sensitive serology it provides the most sensitive and specific screening platform for blood screening. [6] In India as per the regulatory requirements of the drug and cosmetics act of 1940 (1st amendment 1992) it is mandatory to test each unit of blood for markers of HIV 1 and 2, Hepatitis B and C, malaria and syphilis. [7] Various screening tests available for screening blood donors are Rapid tests, Enzyme Linked Immunosorbent Assay (ELISA), Chemiluminescence (CLIA) and Nucleic Acid Testing (NAT). There are two types of NAT, Individual donor (ID) NAT and Minipool (MP) NAT. Both are recognized by FDA as valid instruments for NAT testing. [8] NAT is a highly sensitive and advanced technique which has reduced the window period of HBV to 10.34 days, HCV to 1.34 days and HIV to 2.93 days. [9]

The AIM of this study is to assess the impact of the introduction of Minipool-NAT for HBV, HCV and HIV and its role in improving blood safety in a tertiary care hospital.

#### Materials and methods

The study was conducted at Blood Centre of Shri Maharaja Hari Singh (SMHS) Hospital / Government Medical College (GMC) Srinagar over a period of 10 months from September 2020 to June 2021. After Physical examination all medically fit donors were allowed to donate blood after obtaining informed consent for blood donation and screening for TTIs. Blood samples were collected in pilot test tubes at the time of bleeding. It was a non-interventional, retrospective, observational study.

All samples were examined for five TTIs namely HIV I & II, HBsAg, HCV, syphilis and malaria. Blood samples of six milliliters collected in a clean and dry test tube for the TTIs screening were centrifuged for serum and then tested by ELISA for HBsAg (HEPALISA by J Mitra& co Pvt Ltd) and anti-HCV antibody (OSCAR by Oscar Medicare PvtLtd.), anti-HIV 1+2 (MERILISA by Merilisa Diagnostic Pvt Ltd). Rapid kit tests were performed for Syphilis (RECKON by Reckon Diagnostic P Ltd) and Malaria antigen to Plasmodium Falciparum (RELIABLE By Reliable Pro-detect Biomedicals Pvt Ltd). All the data was stored for future reference.

All seronegative cases by ELISA were subjected to Minipool-NAT in small pools of six on Roche's CobasTaq Screen MPX assay v2.0 on Cobas System s 201(Roche Diagnostics Gmbh, Mannheim) to detect HIV-1 (groups M and O RNA), HIV-2 RNA, HCV RNA and HBV DNA.

The CobasTaq Screen MPX assay comprises of four automated steps which include (i) pooling of samples, (ii) sample preparation, (iii) real time Polymerase Chain Reaction (PCR) amplification, detection, (iv) data management and reporting. This also involves quality control by processing one replicate of the Negative Control (MPX (–) C, v2.0) and one replicate of each of the three Positive Controls (MPX M(+)C, v2.0, MPX O(+)C, v2.0 and MPX 2(+)C, v2.0) in each batch. Reactive (created) pools were retested individually to confirm and to know the infection in donor sample. Limits of detection (with 95% probability) for various analytes on Taqscreen MPX v 2.0 are : HIV-1 Group M - 46.2 IU/mL, HIV-1 Group O - 18.3 Copies /ml, HIV-2-56.2 copies /ml, HCV6.8 IU /mL, HBV- 2.3 IU /mL. HIV-1 Group M, HCV and HBV are calibrated against WHO International Standards while HIV-1 Group O and HIV-2 are calibrated against FDA Reference reagents.

The data were recorded on specially formed proforma, the recorded data were tabulated and analysed.

#### Results

A total of 15569 blood donations were collected over the period of 10 months from Sep 2020 to June 2021. Of these, the majority of the donors 15190 (97.57 %) were males and 379 (2.43%) were females. There were 11852 (76.13%) replacement donors and 3717 (23.87%) voluntary donors. Out of a total 3717 voluntary donors 3499 (94.14%) were first time voluntary donors and only 218 (5.86%) were repeat voluntary donors (Table1). Out of all 15569 blood donations, reactive samples by serological test (ELISA) were 40, consisting of 17 (0.11%) of HBV, 23 (0.14%) of HCV and 0 for HIV (Table 2). All the Sero-negative 15529 samples were tested by Minipool-NAT out of which 22 were positive, 16 were positive for HBV, 6 were positive for HCV & 0 for HIV. NAT yield i.e., Units reactive by NAT and Non-reactive by Serology was 1 in 970 for HBV, 1 in 2588 for HCV, with total NAT yield of 1 in 706 (Table 3).

#### Discussion

The purpose of introduction of NAT in Blood Centres is to provide an additional layer to blood safety. NAT is highly sensitive and specific for viral nucleic acids and is based on amplification of targeted regions of RNA and DNA and thus is the technique of choice. By early detection than serology, the window period of HBV, HCV and HIV infections narrows. In India, mandatory blood screening for HBV, HCV and HIV done by serological tests. The screened is seronegative donations are still at risk for TTIs and thus, need for a sensitive screening test arises. The residual risk has been significantly reduced over the last two to three decades in western countries by implementation of NAT. In order to mitigate the residual risk, NAT has been started in few centers in India, but it is not a mandatory screening test for TTIs as per Drug and Cosmetics Act, 1940. [10]

However because of continued hemovigilance it is now being considered that NAT screening may prove to be more beneficial keeping in view the burden of

#### Table1: Demographic details of donation

	Donor Demographics (n=15569)		
	(Number)	(%)	
Gender			
Male	15190	97.57%	
Female	379	2.43%	
Donation Type			
Replacement	11852	76.13%	
Voluntary	3717	23.87%	
Donor Repeatability			
First time Voluntary Donors	3499	94.14%	
Repeat Voluntary Donors	218	5.86%	

#### Table 2: Seroreactivity of HBsAg, HCV and HIV by ELISA

Screening (By Elisa)	Screen Reactive (n=15569)
HBsAg (3 <sup>rd</sup> Generation)	17 (0.11%)
HCV (3 <sup>rd</sup> Generation)	23 (0.14%)
HIV (4 <sup>th</sup> Generation)	0
HbsAg + HCV + HIV	40 (0.25%)

### Table 3: NAT Yield per donation tested.

Virus detected	Total no of Seronegative donation (N=15529)		
	No. of NAT yield donation	NAT yield	
HBV	16	1:970	
HCV	6	1:2588	
HIV	0	0	
Total NAT yield donations	22	1 : 706	

the transfusion transmissible infectious and the endemicity of Hepatitis B and C with high seroprevalence of transfusion transmissible infectious agents.

The studies done so far are also in favour of introduction of NAT on a wider basis to enhance the safety of blood and blood products in India. [11-15]

In the present study 15569 blood donor samples were tested, by serology tests (ELISA), out of which 40 were seropositive with seroprevalence of 0.11% for HBV, 0.14% for HCV & 0% for HIV. Among all the seronegative 15529 samples tested by Minipool-NAT 22 were positive, 16 for HBV, 6 for HCV and none for HIV. The combined NAT yield for blood donors of all three viruses was 1 in 706 samples tested, which was comparable with study from Kumar R etal. [16] The NAT yield rate from other Blood Centres in India is 1 in 3182, [17] 1 in 2972, [12] 1 in 2622, [18] and 1 in 1528, [11] which is lower than our NAT yield rate.

NAT Yield obtained from developed countries is much lower compared to India. A study conducted in USA found a NAT yield of 1: 2 million for HIV and 1: 270,00 for HCV for 66 million donations. [19] Another study from Europe found a NAT yield of 1: 600,000 for HCV and 1: 1.8 million for HIV after screening 3.6 million donations. [20] One of the reasons for this lower NAT yield is that these countries mostly collect blood through voluntary blood donations and much lower prevalence of these viral infections in the population. NAT screening may thus prove to be more beneficial where the seroprevalence of transfusion transmissible infectious agents is high, as is the case in most developing countries.

In our study, there were 23.87% voluntary blood donors (which included only 5.86% repeat voluntary blood donors) and the remaining 76.13% were replacement donors. The majority of voluntary donors being first-time voluntary donors may not be safer than replacement donors and it could explain the higher NAT yields in our study as compared to some other centers. [21]

The implementation of NAT as an add on test for blood safety has been reported in various studies in India. The cost of implementation of NAT as a quality and safety measure is much lower than the cost of treating infected patients after receiving blood from window period donations. The cost of disease burden and treatment of HBV and HCV is very high and cannot be overlooked in view of millions of carriers already in the country and the lack of facilities and resources for treatment including hepatocellular carcinoma or liver transplantation. The benefits of NAT are especially important in patients who receive multiple blood transfusions for diseases such as thalassemia, chronic kidney disease, malignancies etc. Such patients need regular, repeated and life-long blood transfusions and are at higher risk of being infected with serious TTIs.

There are certain limitations of this study. First the sample size was relatively small and secondly we have used Minipool-NAT in our study as compared to ID-NAT in most of the other studies. But it should be kept in mind that ID-NAT marginally reduces the window period of the three infections compared to Minipool NAT by 2 days only, moreover several developed countries continue to use Minipool-NAT even today. [22]

#### Conclusion

By implementing Minipool-NAT we detected TTIs in 22 samples of donated blood which were missed by serological tests with an overall NAT yield of 1 in 706. The routine use of NAT for detection of HBV, HCV & HIV should be mandatory for all seronegative donor blood to reduce the serological window period and hence reduce the incidence of TTIs and increase the safety for the patients. The issue of higher cost in the developing countries accounts for the limitation of ID-NAT, hence if finance is the problem then Minipool-NAT also could be an acceptable beginning in the road to transfusion safety.

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#### **Original Article**

### Role of Adenosine Deaminase in Diagnosis of ExtrapulmonaryTuberculosis: Study from a Tertiary Care Hospital of North India

Rukhsana Taj, Unairah Nagash, Shazia Mushtag

#### **Abstract:**

**Background:** Tuberculosis has been reported worldwide. Mycobacterium tuberculosis (MTB) primarily affect the lungs but can eventually spread to any other organ resulting in extra pulmonary tuberculosis (EPTB). The high morbidity associated with EPTB necessitates rapid development of sensitive tests. Adenosine Deaminase (ADA)is a proven biochemical marker with several advantages over conventional and molecular methods having high sensitivity and specificity for diagnosing TB.

Aims and Objective: To evaluate the sensitivity and specificity of Adenosine Deaminase (ADA) in diagnosis of extrapulmonary tuberculosis from different body fluids.

Methods: The current study was carried out on 190 specimens collected from different body fluids in orderto rule out extrapulmonary tuberculosis. The smearswere confirmed for presence of tubercular bacilli through ZN staining, LJ Media (Gold standard) andGeneXpert (CBNAAT). Simultaneously the ADA estimation was done from supernatant and readings were taken and expressed in IU/L.

Results: Out of the total 190 samples taken31 (16.3%) samples tested positive for TB on culture media, 30 (15.8%) through GeneXpert and 2 (1.1%) on ZN staining. Through ROC analyisADA estimation achieved the sensitivity of 100% in pleural, ascetic and synovial fluid. In CSF only 94.1% of sensitivity was achieved through ROC analysis. The specificity achieved was 100% for synovial fluid; however it reached to a maximum of 93.2% for pleural fluid, 95% for CSF and 96.4% for ascitic fluid.

**Conclusion:** Although conventional culture methods and GeneXpert are established diagnostic tools for identification of TB;the ADA levels estimation showed high sensitivity and specificity for diagnosis of tuberculosis in our study.

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#### Introduction:

Tuberculosis has been found to infect all age groups and its occurrence has been reported worldwide. The causative organism Mycobacterium tuberculosis (MTB) is the 13<sup>th</sup> leading cause of death world-wide.[1] The bacteria primarily affect the lungs but can eventually spread to any other organ directly or via lymphatics or hematogenous routes, resulting in extra pulmonary tuberculosis (EPTB).[2] In India 15%-20% of TB cases were reported to have TB involving extrapulmonary sites. 50% cases were seen in HIV positive individuals. [3] Extrapulmonary TB was seen mostly in adults above 44 years and children below 14 years of age.[4] Clinical presentation in EPTB is variable, depending on the organ involved, host immune response and the degree of tissue damage that has occurred. [5] Common disease manifestations include meningitis, lymphadenitis, pleuritis, pericarditis, peritonitis cutaneous, musculoskeletal, abdominal, genitourinary and miliary forms of tuberculosis.[6] The most frequent extrapulmonary sites of disease seen in India were extra thoracic lymph nodes (35%), pleural tuberculosis (20%), abdominal (14%) bone and joint tuberculosis (10%), genitourinary (5%), central nervous system (4.5%).[7]

The high morbidity associated with extra pulmonary tuberculosis (EPTB) necessitates rapid development of sensitive tests, the preliminary aim being to identify the presence of mycobacteria tuberculosis. Although a variety of tests including traditional,

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Keywords Diagnostic ADA. Accuracy, Extrapulmonary Tuberculosis
Conventional culture-based techniques, Molecular Methods and Adenosine deaminase assay are available but the current study was limited to determine the diagnostic accuracy of ADA levels and a comparison to that of conventional and molecular methods for diagnosis of tuberculosis.

ADA is a proven biochemical marker that offers several advantages of being simple, rapid, low cost and easy to perform in most clinical laboratories.[8] The sensitivity and specificity of ADA in the different body fluids including those of pleural, pericardial, ascitic fluid etc has been ascertained in many studies.[9] In lieu of above facts the current study was undertaken to investigate the accuracy of ADA levels over other diagnostic approaches, wherein the specimens were collected from those of pleural fluids, ascitic fluids, synovial fluids, cerebrospinal and pericardial fluids for the diagnosis of EPTB. To evaluate the sensitivity and specificity of Adenosine Deaminase (ADA) in diagnosis of extrapulmonary tuberculosis from different body fluids.

#### **Materials and Methods**

This cross-sectional study was conducted at Postgraduate Department of Microbiology Govt. Medical College, Srinagar for a period of 18 months. A total of 190 specimens were collected from different body fluids like pleural fluid, ascitic fluid, cerebrospinal fluid (CSF), synovial fluid and pericardial fluid under all proper aseptic precautions from patients suspected of extra pulmonary tuberculosis. Specimens were collected in sterile, leak-proof, disposable, and appropriately labelled containers without fixatives and were transported to laboratory immediately. By keeping in consideration, the RNTCP guidelines for grading of ZN-stained smears, the differential staining technique (Ziehl -Neelson) was done for proper visualization and separation of acid-fast bacilli through microscope. Further, the specimens were concentrated by sedimentation in a refrigerated centrifuge at 3000 g for 30 minutes. The sediments were used for preparation of smears and were inoculated with 2-4 drops (0.2ml - 0.4ml) of centrifuged sediment on Lowenstein Jensen (LJ) media and were incubated at 35°C in the dark atmosphere and high humidity. Culture media was incubated in slanted position with screw caps and most isolates appeared between 3 and 6 weeks of incubation. After 8 weeks of incubation,

negative cultures (those showing no growth) were reported, and the culture bottles were discarded. The sediments were further analysed through GeneXpert /MTBRIF which is a rapid, nested real-time PCR for diagnosis of tuberculosis and drug resistance. It is a cartridge based nucleic acid amplification test (CBNAAT) which simultaneously detects DNA of Mycobacterium tuberculosis complex (MTBC) and resistance to rifampicin (RIF) in less than 2 hours. The supernatant was used for detecting adenosine deaminase (ADA) levels at the Department of Biochemistry through calorimetric method using the ADA assay kit in analyzer. Reading of ADA levels in different body fluids was done and ADA level was expressed in IU/L. The whole procedure was carried out in the biological safety cabinet.

#### **Data Collection**

The detailed history including chief complaints, co morbidities, history of contact with patients of tuberculosis and diagnostic resultswere entered on a self devisedproforma. The data was entered in excel and analysed using SPSS version 20.0.

#### **Ethical clearance**

The ethical clearance for the study was granted by Ethical Clearance committee of Government Medical College, Srinagar.

#### **Results:**

The current study was conducted to rule out the efficiency of elevated Mean ADA levels in suspected cases along with a comparison to different multimodalities for the diagnosis of extrapulmonary tuberculosis. (**Table:1**) below shows the summarized report of different body fluids wherein a total of 190 samples were investigated for EPTB, out of which 64 (33.7%) samples were of pleural fluid, 57 (30.0%) of CSF, 33 (17.4%) of ascitic fluid, 32 (16.8%) of synovial fluid and 4 (2.1%) of pericardial fluid.

Outcome of culture on LJ media is shown in **Table 1**. In pleural fluid 64 samples were inoculated on LJ media and growth was seen in 5 (7.8%) samples and the same samples also tested positive on Genexpert. In 57 CSF samples growth was seen on 17 (29.8%) samples and same tested positive on GeneXpert. After inoculating 33 samples of ascitic fluid on LJ media 5 (15.2%) samples were positive and same tested also positive on GeneXpert.Four samples of synovial fluid tested positive on LJ

Table: 1 Exudate types and their outcome on different diagnostic modarities.						
Type of fluid	Total Samples	<b>Culture Positive</b>	GeneXpert Positive	ZN Staining		
				Positive		
Pleural Fluid	64	5 (7.8%)	5 (7.8%)	0 (0.0%)		
CSF	57	17 (29.8%)	17 (29.8%)	1 (1.8%)		
Ascitic Fluid	33	5 (15.2%)	5 (15.2%)	0 (0.0%)		
Synovial Fluid	32	4 (12.5%)	3 (9.4%)	1 (3.1%)		
Pericardial Fluid	4	0 (0.0%)	0 (0.0%)	0 (0.0%)		
Total	190	31 (16.3%)	30 (15.8%)	2 (1.1%)		

Table:1 Exudate types and their outcome on different diagnostic modalities

Table 2: Comparison of Mean ADA levels according to culture results in different body fluids								
Type of sample & ADA Cutoff	No. of Samples	Overall Mean ADA	Std. Deviation	Mean ± SD ADA levels among Culture	Mean ± SD ADA levels among Culture	P-value		
				Positives	Negatives			
Pleural Fluid	64	35.2077	46.57159	100.40 ±22.490	29.68 ±20.858	< 0.001		
CSF	57	18.6335	28.81398	$51.00 \pm 34.808$	$4.877 \pm 1.660$	< 0.001		
Ascitic Fluid	33	35.6430	56.71333	129.00±103.114	18.97 ±8.293	< 0.001		
Synovial Fluid	32	22.2941	20.77581	73.25±19.653	15.01 ±10.632	< 0.001		
Pericardial Fluid	4	17.0750	10.49170	-	$17.07 \pm 10.491$	-		

media and 3 of them were positive on GeneXpert also.Only 1 sample each from CSF and synovial fluid tested positive for TB on ZN staining. All the 4 pericardial fluid samples were negative on all testing modalities.

**Table 2** shows comparison of mean levels of ADAamong tuberculosis positive and negative patients indifferent body fluids. In pleural fluid the Mean ADAlevelamongculturepositivesampleswas100.4 $\pm$ 22.490and amongculturenegativesampleswas29.68 $\pm$ 20.858. The mean ADAactivityamong

culture positive CSF samples was  $51.00\pm34.808$  and among the culture negative samples it was  $4.877\pm1.660$ . In ascitic fluid mean ADA level was  $129.00 \pm 80.114$  among culture positive subjects and among culture negative mean ADA was  $18.97\pm8.293$ . In synovial fluid the mean ADA level among culture positive samples was  $73.25\pm19.653$  and in culture negative samples it was  $15.01\pm10.632$ . The mean difference was statistically significant among positive and negative samples of pleural fluid, CSF, ascetic fluid and synovial fluid [p value (<0.001)].

Table 3: Performance characteristics of ADA Levels in different types of fluids as compared to culture on         LJ media in diagnosis of EPTB								
Type of			Culture on LJ media		Considerates	Crossificity	DDV	NDV
fluid			Positive	Negative	Sensitivity	specificity	<b>FFV</b>	
Pleural	ADA Levels	Positive	5	10	100.0%	<b>Q1</b> 404	21.204	100.0%
Fluid	(Cut off 40U/L)	Negative	0	49	100.0%	01.4%	31.2%	100.0%
CSE	ADA Levels	Positive	16	2	04.1%	95.0%	88.9%	07 404
CSF	(Cut off 10U/L)	Negative	1	38	94.1%			97.4%
Ascitic	ADA Levels	Positive	5	2	100.0%	02.0%	71 404	100.0%
Fluid	(Cut off 40U/L)	Negative	0	26	100.0%	92.9%	/1.4%	100.0%
Synovial	ADA Levels	Positive	4	0	100.0%	100.0%	100.00/	100.0%
Fluid	(Cut off 40U/L)	Negative	0	28	100.0%	100.0%	100.0%	100.0%
Dominandial	ADA Levels	Positive	0	0				
Fluid	(Cut off 40U/L)	Negative	0	4	-	100.0%	-	100.0%
Total	ADA Lovela	Positive	48	17	0/ 10/	92.6%	72.00/	00 (0/
Total	ADA Levels	Negative	3	213	94.1%		13.0%	<b>70.0</b> %

Performance characteristics of ADA in different body fluids (at conventional cut off) when culture results were taken as gold standard is shown in **Table 3**. The sensitivity of ADA for the diagnosis of tuberculosis on pleural fluid was found to be 100% and specificity was 81.4%.In CSF the sensitivity and specificity of ADA levels in the diagnosis of tuberculosis was found 94.1% and 95.0% respectively. In case of ascitic fluid the sensitivity of ADA for the diagnosis of TB in ascitic fluid is 100% and specificity was92.9%. Synovial fluid showed complete correspondence between ADA levels and culture positive growths, hence the sensitivity and specificity were calculated at 100% for both.

**Table 4**shows performance characteristics of ADA in different body fluids with geneXpert as gold standard. The sensitivity of ADA for the diagnosis of tuberculosis in pleural fluid was found to be 100% and specificity was 81.4%. In CSF the sensitivity and specificity of ADA levels in the diagnosis of tuberculosis was found 94.1% and 95.0% respectively. In case of ascitic fluid the sensitivity of ADA for the diagnosis of TB in ascitic fluid is 100% and specificity was 92.9%. The ADA levels in synovial fluid showed sensitivity and specificity 100% & 96.6%, respectively.

Table 4: Performance characteristics of ADA Levels in different types of fluids as compared to         GeneXpert in our study population								
Type of			Gene	GeneXpert			DDL	
fluid			Positive	Negative	Sensitivity	Specificity	ΡΡν	NPV
Pleural	ADA Levels	Positive	5	10	100.00/	01.40/	21.201	100.0%
Fluid	(Cut off 40U/L)	Negative	0	49	100.0%	81.4%	31.2%	
CSF	ADA Levels	Positive	16	2	94.1%	95.0%	88.9%	97.4%
	(Cut off 10U/L)	Negative	1	38				
	ADA Levels	Positive	5	2	100.0%	92.9%	71.4%	100.0%
Ascitic Fluid	(Cut off 40U/L)	Negative	0	26				
Synovial Fluid	ADA Levels	Positive	3	1		96.6%	75.0%	100.0%
	(Cut off 40U/L)	Negative	0	28	100.0%			
Pericardial	ADA Levels	Positive	0	0		100.0%	-	100.0%
Fluid	(Cut off 40U/L)	Negative	0	4	1 -			

Fig. 1: ROC analysis of ADA in different body fluids when compared to culture (gold standard) for EPTB diagnosis.



Cut-point = 53.5	Cut-point = 45.5
Sensitivity $= 100\%$	Sensitivity $= 100.0\%$
Specificity $= 96.4\%$	Specificity $= 100.0\%$

Figure 1shows receiver operating characteristic (ROC) of ADA in different body fluids. The area under curve achieved was 0.953 (0.900-1000) for ADA in pleural fluid. At a cutoff of 74.0 IU/L for ADA in pleural fluid the sensitivity and specificity achieved was 100% & 93.2%, respectively. In CSF the area under curve for ADA achieved was 0.982 (0.955-1000). At a cutoff of 10.75 IU/L for ADA in CSF the sensitivity and specificity achieved was 94.1% & 95.0%, respectively. In ROC analysis(ADA in ascitic fluid) the area under curve achieved was 0.986 (0.951-1000). At a cutoff of 53.5 IU/L for ADA in ascitic fluid the sensitivity and specificity achieved was 100% & 96.4%, respectively. Figure 1 also shows receiver operating characteristic (ROC) of ADA in synovial fluid. The area under curve achieved was 1.000 (1.000-1000). At a cutoff of 45.5 IU/L for ADA in synovial fluid the sensitivity and specificity achieved was 100%.

#### **Discussion:**

The present study was conducted on 5 different types of body fluids including those of Pleural fluid, CSF, Ascitic fluid, synovial fluid and pericardial fluid in order to find out the utility of ADA levels indiagnostic accuracy of EPTB. Out of the total 64 samples taken, 5 samples were positive in both ADA and culture media while 49 were being found negative. The Sensitivity of ADA for the diagnosis of extrapulmonary tuberculosis was found to be 100% while the specificity attained was 81.4% on both culture and GeneXpert. Thisanalysis showed a close resemblance with the studies of San José et al. [10] wherein they analysed the use of serum, pleural ADA and lysozyme in tuberculous pleurisy in Spain, and found that pleural ADA had a sensitivity of 100% and a specificity of 93% for the diagnosis of TB.Muranishi et al. [11] while working on measurement of ADA activity and tuberculostearic acid (TSA) in pleural effusions attained a sensitivity of 56% and specificity of 76% for the diagnosis of tuberculous pleuritis. However, the observed results were relatively low when compared with our data. Our results further showed a concordance with the studies of De Oliveira et al. [12] who concluded that the use of these tests in combination was a highly efficient diagnostic strategy of low cost that merits wider use. On ROC analysis of pleural ADA, at a cut off of 74.0 IU/L, 100% sensitivity and 93.2% specificity were achieved. The predictive value (cutoff) as reported by Villena et al.[13] in their study was 33 IU/L for ADA whereby a sensitivity of 90% and specificity of 85% was achieved for tuberculous effusion, however, this value was much lower than our study.

The mean ADA activity among culture positive samples in CSF was 51.00±34.808 and among culture negative samples was 4.877±1.660 with a significant p value (<0.001).Gambhir et al.[14] reported mean ADA of 9.6  $\pm$  4.1 U/L in 36 patients with tubercular meningitis, which was lower than the mean ADA in our study (18.6335  $\pm$ 28.813) however, the fact may be attributed to the inclusion of more adults in our study. Upon both culture media and GeneXpert, the sensitivity and specificity of ADA levels in the diagnosis of EPTB came out to be 94.1% and 95.0% respectively. The results went in a complete harmony with the studies of Choi et al. [15] who observed ADA activity in CSF of 36 TBM patients and reported that at a cut-off of 7 IU/L, the sensitivity of the test for TBM group as compared to aseptic meningitis group was 83% and the specificity was 95%. Same sensitivity and specificity like that on culture media and GeneXpertwas achieved upon ROC analysis, at a cut-off of 10.75 IU/L for ADA in CSF. However, Corral et al. [16] used ROC curve analysis and suggested a cut off value of 8.5 U/L for the diagnosis of TBM with 57% sensitivity and 87% specificity.

For ascitic fluid the mean ADA level observed among culture positive subjects was  $129.00 \pm 80.114$  and among culture negative subjects was 18.97±8.293. The sensitivity of ADA for the diagnosis of EPTB in ascitic fluid when compared with LJ media (Gold Standard) and GeneXpert was 100% and the specificity was 92.9%. UponROC analysis area under the curve achieved was 0.986 (0.951-1000) and at a cut-off of 53.5 IU/L for ADA in ascitic fluid the sensitivity and specificity achieved was 100% & 96.4%, respectively for diagnosis of peritoneal tuberculosis.However,Hillenbrand DJ et al. [17] obtained a sensitivity of only 30% in their study and concluded that the ADA is inferior in cirrhosis as a diagnostic method for peritoneal TB. Furthermore, they inferred that this could be because of a positive correlation between ADA and ascitic fluid total protein as cirrhotic patients generally have low ascitic fluid total protein. In a study conducted by Dahale AS et al. [18] the ADA had very high sensitivity (93%) and specificity (94%) at a cut-off of 41.1 IU/L. They also showed the presence of elevated ADA levels in the cirrhotic peritoneal TB group than that of cirrhotic non-peritoneal group and all other types of ascites patients in the control group.

Similarly, 4 samples of synovial fluid out of 32 samples taken were found positive on Culture media and there was a complete correspondence between ADA levels and culture growth, hence the sensitivity and specificity calculated was 100% for both. Upon ROC analysis thearea under curve achieved was 1.000

(1.000-1000) and at a cut-off of 45.5 IU/L, the sensitivity and specificity achieved was 100%. **Gupta VK et al.** [19] while studying Musculo-skeletal disease observed a positive predictive value of 85.71% and a negative predictive value of 66.67%, however, the predictive values being lower than that found in our study.

#### Conclusion:

Although culture and GeneXpert are good diagnostic tools for identification of TB yetestimation of ADA levels in patients suspected of TB especially EPTB is inexpensive, rapid and efficient with high sensitivity and specificity. It is also efficient in differentiating tubercular pulmonary infections from non-tubercular pulmonary infections thereby, suggesting that the test should be included in routine investigations in patients suspected of tuberculosis.

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#### **Original Article**

## Role of Feature Selection in CT Lung Nodule Classification: The modified Particle Swarm Optimization and Topology selection

Mohini Manav, Monika Goyal, Anuj Kumar

#### **Abstract:**

**Background:** In healthcare, machine learning is playing a significant role in computer-aided detection and diagnosis of lung nodules to reduce the load and increase the accuracy of radiologists. In the scenario where the datasize is limited, machine learning poses its advantage. The intrinsic information is discerned utilizing radiomics, which, in turn, serves as the foundational feature set for shaping the algorithmic framework employed in the classification process.

In this study, the Lung Image Database Consortium and Image Database Resource Initiative (LIDC-IDRI) database was used to study the lung nodule classification with different numbers of radiomic features selected.

Materials and Methods: A total of 1018 thoracic CT scans having lung nodules categorized as "nodule  $\geq$ 3 mm," "nodule <3 mm," and "non-nodule  $\geq$  3 mm," identified through a two-phase annotation process out of which, 300 CT scans with nodules  $\geq$  3 mm in size were used in our study. Four machine learning models, namely, Light GBM, Random Forest, XG Boost, and Support Vector Machine, were used with the optimum number of radiomic features selected using binary Particle Swarm Optimization combined with different topologies and time-varying inertia weights.

**Results and Conclusion:** The XGBoost classifier with ring topology and linear decreasing inertia weight presented the best results, achieving 97.67%, 95.74%, 100%, 95.12%, 97.83%, and 98.75% for accuracy, precision, sensitivity, specificity, f1-score, and AUC, respectively.

This outperformed a wide range of feature selection and machine learning approaches for lung nodule classification on the same data, as documented in numerous published academic papers. The proposed method demonstrated an improved nodule classification performance by utilizing optimal features obtained through the fusion of various inertia weights and different topologies in the feature selection method.

#### **1** Introduction

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Lung cancer is the most common reason for cancer-related fatalities worldwide.[1]In 2020, lung cancer leading with nearly 2.21 million deaths. [2] For a good prognosis, detecting lung cancer at an early stage is very important. [3] Calculating the likelihood of malignancy for early malignant lung nodules is a troublesome job. [3,4]Compared to standard chest radiography, computed tomography (CT) screening is more effective at lung cancer screening. [4,5] According to the report by The National Lung Screening Trial, there is a 20% reduction in lung cancer mortality using CT images for diagnosis. [6]

CT has emerged as an imaging technique with greater sensitivity in detecting lung nodules. [7]Pulmonary nodules are lung abnormalities that are crucial indicators of lung cancers visible to lung computed tomography (CT) scans as roughly round opacities. [8] Accurate diagnosis of lung nodules is challenging, laborious, and timeconsuming.[9]

Several computer-aided diagnosis and detection techniques have been developed to aid radiologists in detecting and diagnosing lung nodules with greater accuracy and efficiency. [10,11]Lung nodules can be differentiated based on features like shapes, contours, textures, etc.[12]

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#### Keywords

Machine learning, Particle Swarm Optimization (PSO), inertia weight, LIDC-IDRI, Medical Imaging, Medical Image classification. Computed Tomography

]The role of Machine Learning has shown its remarkable significance in healthcare by assisting in various tasks such as disease diagnosis.[13]

Feature selection is a vital pre-processing step in eliminating the redundant features and lowering the number of features.[14]In classification problems, where the quality of the selected features can significantly impact the accuracy and efficiency of feature classification models, selection is essential.[15] In cancer diagnosis and prognosis, selection can also improve models' feature interpretability and clinical relevance. [16]Deep learning, a subset of machine learning, acts as a blackbox solution to many problems, e.g., object recognition, natural language processing, disease detection in healthcare, etc. [17]

In recent years, bio-inspired algorithms have gained popularity due to their capability to resolve complex problems that traditional algorithms struggle with. [18] They are designed to mimic the behaviour of organisms in nature and apply these behaviours to solve optimization problems. [19] Feature selection is one of the most common applications of natureinspired algorithms. [20] Some popular natureinspired feature selection algorithms include Genetic Algorithm, Particle Swarm Optimization (PSO), Ant Colony Optimization, Artificial Bee Colony, and Grey Wolf Optimizer. [21-26]PSO is one of the natureinspired algorithms. PSO is a population-based optimization algorithm that mimics the social behaviour of swarms of birds or fish. The algorithm works by simulating the movement of particles in search of the optimal solution. It has been applied to many optimization problems in recent years. [27,28]

In the present paper, we have classified the lung nodule into malignant and benign categories from the CT images. To classify CT lung nodules, we explored multiple topologies, including the ring, star, pyramid, and random topologies, while simultaneously investigating various inertia weight adjustments such as exponential, linear, and nonlinear changes in PSO. [29-34]We utilized the selected features extracted from the CT images to perform classification using several popular supervised machine learning algorithms, namely LightGBM (LGBM), Random Forest(RF), XGBoost (XGB), and Support Vector Machines (SVM). [35-38]

The study results are presented as the performance of the various classification models in terms of accuracy, precision, sensitivity, specificity, f1-score, and AUC score based on the selected features. Through our experimentation, we strive to contribute to the advancement of accurate and efficient lung nodule classification. The subsequent sections will delve into the materials and methods, results, and discussions, and finally, the conclusion provides a comprehensive evaluation of the effectiveness of our integrated approach and the performance of the LGBM, RF, SVM, and XGB algorithms.

## 2. Materials and methods:

#### 2.1 Dataset used:

The dataset was obtained from the Lung Image Database Consortium and Image Database Resource Initiative (LIDC-IDRI) database, the largest available open-accessible dataset of lung nodules. [39-41]The dataset comprises1018 diagnostic and lung cancer screening thoracic computed tomography (CT) scans with marked-up annotated lesions. These scans were collected from 1010 patients through collaboration between academic centers and medical imaging experienced companies. Four radiologists independently reviewed the scans in a two-phase annotation process and marked the lesions which belong to one of three categories ("nodule > or =3mm," "nodule <3 mm," and "non-nodule > or =3mm").[41]

In the present study, we have used an initial 300 scans. The 80% consensus consolidation of the annotation contours was computed, which means the annotations from all annotators by considering regions where at least 80% of the radiologists' annotations agree or overlap were combined. This approach aims to create a consolidated segmentation representing a consensus among the annotators. Also, we limited the scope of our study to the nodules  $\geq$  3 mm.

#### 2.2 Pre-processing:

**Nodule segmentation:** For the nodule segmentation from the segmented lung images, the pylidc library, which is an Object-rational mapping (using SQL Alchemy) for the LIDC dataset, was used. [42]The XML file associated with each scan was analyzed using the scriptsto get the segmentation object.

**Feature Extraction:** For all the segmented nodules, features such as the First Order Statistics, Shapebased (3D), Gray Level Co-occurrence Matrix, Gray Level Run Length Matrix, Gray Level Size Zone Matrix, Neighbouring Gray Tone Difference Matrix, Gray Level Dependence Matrix were extracted for each nodule. For the feature extraction, the Python library PyRadiomics was used. [43]

**Feature selection:** For the feature selection process and to investigate the impact of different inertia weight variations with different topologies on the performance of the PSO algorithm, three types of inertia weight functions were employed: exponential, linear, and nonlinear. Each function served to modulate the inertia weight during the optimization process.

**2.3Time-Varying Binary Particle Swarm Optimization (TV-BPSO):** TV-BPSO is a BPSO algorithm variant that utilizes time-varying inertia weight to improve optimization capabilities. [44]The inertia weight influences the trade-off between exploration (global search) and exploitation (local search) during the optimization process. [45]

By dynamically adjusting the inertia weight over time, TV-BPSO enhances the search capability and helps to avoid premature convergence to suboptimal solutions.

# 2.4 Time-Varying Inertia Weight (TV-IW) techniques:

In this study, we enhanced the traditional BPSO by incorporating TV-IW techniques. TV-IW modifies the inertia weight during optimization to control the balance between exploration and exploitation. Specifically, we explore three types of time-varying inertia weights: linear, nonlinear, and exponential.[32-34]The following equations were used for the linear, nonlinear, and exponentially decreasing intertia weights respectively.

$$w = (w^{initial} - w^{final} - d_1) \exp\left[\left(\frac{1}{1 + \frac{d_2 \cdot iter_t}{iter_{max}}}\right) \\ w = w^{final} + (w^{initial} - w^{final}) \exp\left(\frac{iter_{max} - iter_t}{iter_{max}}\right) \\ w = w^{final} + (w^{initial} - w^{final}) \left(\frac{iter_{max} - iter_t}{iter_{max}}\right)^n$$

Where  $d_1$  and  $d_2$  are control factors to control w between  $w^{initial}$  and  $w^{final}$  and have values 2 and 7, respectively.  $w^{initial}$  represents the initial inertia weight at starting inertia weight, and  $w^{final}$  is the inertia weight value when the algorithm process runs the max iterations. The value of  $w^{initial}$  and  $w^{final}$  is 1.0 and 0.4, respectively. Iter<sub>max</sub> denotes the maximum iteration, and iter<sub>t</sub> denotes the t<sup>th</sup>iteration. n is the modulation index and has a value of 1.2 in the present study.

#### 2.5 Different Swarm Topologies:

Topology, which governs the interactionand information sharing among particles, plays a crucial role in the performance of BPSO. The choice of topology can significantly impact search behavior and convergence. The particles' interactions and information exchange in different topologies can impact the convergence speed and exploration capacity of TV-BPSO during the feature selection process. This study aims to comprehensively analyze BPSO using four topologies: Ring, Star, Pyramid, and Random.[46,47]

# 2.6 Image Classification using supervised machine learning:

Different supervised machine-learning models were used to classify the images using the reduced features from the abovementioned algorithms. These models were the LGBM classifier, RF classifier, XGB classifier, and SVM classifier.[35-38]

**2.7Performance evaluation:** The metrics used in the evaluation process for the model performance were accuracy, precision, sensitivity, specificity, f1-score, and AUC score.

#### 3. Results:

3.1 Experimental setup: In the present study, the CT scans from the LIDC-IDRI database were classified using different supervised machine learning models with the optimum number of features selected using binary PSO with the combination of different topologies and time-varying inertia weights. The data was divided into train and test data as 80:20. The experiments were performed using the Python programming language, and Google Colab was used as a computational platform to execute the experiments. For different feature extraction, the PyRadiomics library was used. [43]For the feature selection processfrom the training dataset, we utilized PySwarms library by the making specific modifications and customizations tailored to the requirements of our research. [48] For the classification model, the Scikit-learn library was used. [49]Figure 1 demonstrates the proposed method employed in the study for classifying CT scans from the LIDC-IDRI database.



Fig1.Block diagram for proposed method in the present study for classification of CT nodules

#### **3.2 Feature Extraction:**

A total of 111 features were extracted from the segmented nodule images.Different features extracted from the CXR images are given in Table 1:

Sr.	Feature Type	Number of features
No.		
1.	First Order Statistics	19
2.	Shape-based (3D)	17
3.	Gray Level Co-occurrence Matrix	24
4.	Gray Level Run Length Matrix	16
5.	Gray Level Size Zone Matrix	16
6.	Neighbouring Gray Tone Difference Matrix	5
7.	Gray Level Dependence Matrix	14
	Total	111

 Table 1: Features type and number of features

Figure 2 shows the graphical representation of selected features with different topologies and inertia weights.



Figure 2 bar plot depicting the selected number of optimal features for the different topology- inertia weight combinations with different classifiers

**3.3 Performances of feature selectionalgorithms:** Table 2 shows the number of optimal features selected for different combinations of classifiers, topologies, and time-varying inertia weights from the training dataset.

Models used for	Topology	Inertia weight	Selected optimized number
classification	Topology	mertia weight	of features
		Exponential	65
	Ring	Linear	50
		Nonlinear	53
		Exponential	57
LGB	Star	Linear	57
		Nonlinear	59
		Exponential	45
	Pyramid	Linear	56
		Nonlinear	54
		Exponential	64
	Random	Linear	54
		Nonlinear	57
		Exponential	60
	Ring	Linear	63
		Nonlinear	66
		Exponential	51
RF	Star	Linear	52
		Nonlinear	70
	Pyramid	Exponential	58
		Linear	61
		Nonlinear	52
	Random	Exponential	54
		Linear	66
		Nonlinear	58
		Exponential	54
	Ring	Linear	60
		Nonlinear	56
		Exponential	54
XGB	Star	Linear	59
nob		Nonlinear	61
		Exponential	56
	Pyramid	Linear	62
		Nonlinear	64
		Exponential	55
	Random	Linear	55
		Nonlinear	56
	D.	Exponential	50
	Ring	Linear	50
		Nonlinear	42
	C.	Exponential	55
SVM	Star	Linear	59
		Nonlinear	57
		Exponential	54
	Pyramid	Linear	56
		Nonlinear	53
		Exponential	63
	Kandom	Linear	59
		Nonlinear	49

Table 2.Comparative analysis of the selected number of features out of 111 extracted features for different combinations of topologies with time-varying inertia weights for different classifiers

**3.4 Classification algorithm comparison with different feature selection algorithms:** The performance of different classifiers on the test dataset with selected features in terms of accuracy, precision, sensitivity, specificity, F1-score, and AUC is shown in Table 3.

 

 Table3:Performance of classifiers with optimal features selected using different topologies with timevarying inertia weight in BPSO

Models used for classification	Topology	Inertia weight	Accuracy	Precision	Sensitivity	Specificity	F1-score	AUC
		Exponential	93.23	93.33	93.33	92.68	93.33	98.16
	Ring	Linear	95.35	91.84	100	90.24	95.74	98.54
		Nonlinear	97.67	95.74	100	95.12	97.83	98.00
		Exponential	94.19	93.48	95.56	92.68	94.51	98.16
LGB	Star	Linear	95.35	93.62	97.78	92.68	95.65	98.92
		Nonlinear	93.02	95.35	91.11	95.12	93.18	97.83
		Exponential	97.67	95.74	100	95.12	97.83	97.45
	Pyramid	Linear	93.02	93.33	93.33	92.68	93.33	98.05
		Nonlinear	95.35	95.56	95.56	95.12	95.56	98.43
		Exponential	91.86	93.18	91.11	92.68	92.13	97.72
	Random	Linear	93.02	93.33	93.33	92.68	93.33	96.91
		Nonlinear	96.51	95.65	97.78	95.12	96.70	98.86
		Exponential	97.67	95.74	100	95.12	97.83	97.67
	Ring	Linear	97.67	95.74	100	95.12	97.83	97.18
		Nonlinear	95.35	93.62	97.78	92.68	95.65	97.75
	-	Exponential	96.51	95.65	97.78	95.12	96.70	96.86
RF	Star	Linear	96.51	93.75	100	92.68	96.77	97.62
14		Nonlinear	96.51	93.75	100	92.68	96.77	97.43
		Exponential	97.67	95.00	100	95.12	97.83	97.48
	Pyramid	Linear	96.51	93.75	100	92.68	96.77	98.16
		Nonlinear	93.02	95.35	91.11	95.12	93.18	97.40
	5 1	Exponential	95.35	95.62	97.78	92.68	95.65	98.32
	Random	Linear	96.51	95.65	97.78	95.12	96.70	97.78
		Nonlinear	95.35	95.56	95.56	95.12	95.56	97.18
		Exponential	94.19	93.48	95.56	92.68	94.51	97.99
	Ring	Linear	97.67	95.74	100	95.12	97.83	98.75
		Nonlinear	95.35	93.62	97.78	92.68	95.65	97.78
	G.	Exponential	96.51	95.65	97.78	95.12	96.70	98.48
XGB	Star	Linear	94.19	95.45	93.33	95.12	94.38	98.05
		Nonlinear	95.35	95.56	95.56	95.12	95.56	97.99
	D 1	Exponential	95.35	93.62	97.78	92.68	95.65	98.54
	Pyramid	Linear	93.02	93.33	93.33	92.68	93.33	98.10
		Nonlinear	91.86	91.30	93.33	90.24	92.31	97.45
	D 1	Exponential	93.02	95.35	91.11	95.12	93.18	98.37
	Random	Linear	94.19	93.48	95.56	92.68	94.51	97.40
		Nonlinear	95.35	95.62	97.78	92.68	95.65	97.94
	Dina	Exponential	94.19	93.48	95.56	92.68	94.51	97.18
	Ring	Linear	96.51	93.75	100	92.68	96.77	96.91
		Nonlinear	95.35	93.62	97.78	92.68	95.65	97.54
CVD (	Stan	Exponential	91.80	91.50	93.33	90.24	92.31	98.54
SVM	Star	Linear	94.19	95.48	95.56	92.68	94.51	97.53
		Nonlinear	88.57	92.68	84.44	92.68	88.37	96.04
	D	Exponential	93.02	93.33	95.53	92.68	93.33	96.69
	Pyramid	Linear	93.02	93.33	95.55	92.68	93.33	97.24
		Nonlinear	94.19	95.45	95.55	95.12	94.38	98.05
		Exponential	91.86	93.18	91.11	92.68	92.14	96.91
	Random	Linear	96.51	93.75	100	92.68	96.77	98.00
		Nonlinear	96.51	93.75	100	92.68	96.77	96.26

LGB Model Perfor Accurac LGB Model Performance - Precision Exponenti Linear Non-linear ← Exponential ← Linear ← Non-linear • 95.5 95.0 96 94.5 Accuracy 5 94.0 YPC 93.5 94 93.0 93 92.5 92.0 92 Ring Star Pyramid Random Star Pyramid Random Ring LGB Model Performance - Sensitivity LGB Model Performance - Specificity 100 Exponential
 Linear
 Non-linear Exponential 95 Linear
 Non-linear 98 94 Sensitivity Specificity 93 94 92 92 91 Ring Star Pyramid Randon 90 Ring Star Pyramid Random Topology LGB Model Performance - AUC score LGB Model Performance - F1-score 99.00 98 Exponential
 Linear
 Non-linear ← Exponential ← Linear ← Non-linear 98.75 97 98.50 96 98.25 98.00 F1-score OP 97.75 94 97.50 97.25 93 97.00 92 Ring Star Pyramid Random Ring Star Pyramid Random RF Model Performance - Accuracy RF Model Performance - Precision Exponential
 Linear
 Non-linear Exponentia
 Linear
 Non-linear 95.5 97 96 95.0 Accuracy 95 Prec 04.5 94 94.0 93 Random Random Pyramid Ring Star Pyramid Ring Sta RF Model Performance - Sensitivity RF Model Performance - Specificity Exponential
 Linear
 Non-linear Exponentia
 Linear
 Non-linear 100 95.0 94.5 Sensitivity 94.0 94 93.5 92 93.0 Ring Star Pyramid Bandon Topology Pyramic Rand Ring RF Model Performance - F1-score RF Model Performance - AUC score 98 ← Exponential ← Linear ← Non-linear ← Exponential ← Linear ← Non-linear 98.2 97 98.0 97.8 96 96 F1-score 95 core 97.6 AUC 97.4 97.2 94 97.0 93 96.8 Ring Random Ring Star Pyramid Random Star Pyramid





Fig 3: graphical representation of different performance matrices of classifiers on test dataset utilizing distinctive feature sets derived from varied combinations of topologies and time-varying inertia weights in BPSO

#### 4. Discussion

The current study aimed to classify benign and malignant CT nodules from the LIDC-IDRI database

using different supervised machine learning models with optimal feature selection through binary PSO. The optimal feature selection was done by exploring various PSO topologies and different time-varying inertia weights to identify the most discriminative feature subsets. Each topology offers a unique communication mechanism among particles, influencing their exploration and exploitation in the feature space. In addition to exploring various topologies, we also incorporated time-varying inertia weights during the optimal feature selection process, which facilitated adaptability during optimization, allowing the algorithm to balance exploration and exploitation phases over time.

Overall, the best values of accuracy, precision, sensitivity, specificity, f1-score, and AUC on the test dataset were observed for the XGB classifier with ring topology and linear decreasing inertia weight. For this combination, the percentage values of accuracy, precision, sensitivity, specificity, f1-score, and AUC were 97.67, 95.74, 100, 95.12, 97.83, and 98.75, respectively.

On the meticulous evaluation of Table 3, we can divide the results broadly into two parts with an accuracy of more than 97% and more than 96%.For an accuracy of more than 97%, six combinations of different topology and inertia weights were observed for the test dataset.

For all six combinations with accuracy greater than

97%, the F1-score and specificity were also observed, with values of 97.83 and 95.12, respectively.

For ten combinations of different topologies and inertia weight, more than 96% accuracy was observed. Two combinations show AUC greater than or equal to 98%, one with random topology and nonlinear inertia weights for the LGB classifier and the second with star topology with exponential inertia weight for the XGB classifier. In all combinations where the classifiers achieved accuracy greater than 96%, the corresponding F1-score was measured to be 96.70%.

Average accuracy with different combinations of topology and inertia weight for different classifiers LGB, RF, XGB, and SVM is 94.69, 96.22, 93.79, and 94.67, respectively.

Compared to other combinations of classifiers, topologies, and inertia weights, the LGB classifier with ring topology and nonlinear decreasing inertia weight demonstrated the highest values in accuracy, precision, sensitivity, specificity, and AUC score when considering the overall performance.

Machine learning and deep learning have evoked substantial interest among researchers and medical practitioners in detecting, classifying, and predicting the malignancy of lung nodules. Many methodologies are being explored and developed rigorously to augment the precision and dependability of lung nodule analysis and diagnosis. Numerous published academic papers suggested various methodological approaches to estimate the likelihood of malignancy in lung nodules.

Saied etal. explored and developed AI methods for classifying pulmonary nodules from CT scans. They

used texture Haralick and local binary pattern features in a machine learning approach, achieving an optimal AUC of 0.885 with random forest and a best accuracy of 0.819 with the support vector machine. [50]

Qiao etal. proposed a Fuse-Long Short-Term Memory-Convolutional Neural Network(F-LSTM-CNN)ensemble learning model to classify benign and malignant nodules by incorporating visual attributes and deep features to categorize benign and malignant nodules from the LIDC-IDRI dataset. They achieved accuracy, sensitivity, and specificity of 0.955, 1, and 0.937 with an AUC of 0.995 for lung nodule classification. [51]

Safta etal. classified nodules from the LIDC-IDRI dataset into malignant and benign categories based on GLCM features. In their study, the classification was performed with SVM for Multiple Instance Learning (MIL-SVM). They achieved AUC, Specificity, Sensitivity, and Accuracy of 0.9767, 0.9524, 0.9111 and 0.9310 respectively. [52]

Jena and George extracted the morphological features from the CT images of the LIDC-IDRI dataset and used a Kernel-based NonGaussian Convolutional Neural Network for classification. They achieved a classification accuracy of 87.3% [53]

Jiang et al. proposed a novel pixel value space statistics map (PVSSM) for accurately classifying pulmonary nodules in lung cancer diagnosis in the LIDC-IDRI dataset. This study used the singular value decomposition (SVD) method to extract features from the created feature matrixes. In their study, classification accuracies of 77.3%, 80.1%, and 84.2% for KNN, random forest, and SVM classifiers were obtained, respectively. [54]

Chen et al. utilized radiomic features as input, and for the classification algorithm, they used deep attentionbased MIL. They achieved a mean accuracy of 0.807 with a standard error of the mean (SEM) of 0.069, a recall of 0.870 (SEM 0.061), a positive predictive value of 0.928 (SEM 0.078), a negative predictive value of 0.591 (SEM 0.155), and AUC of 0.842 (SEM 0.074).[55]

Sahu et al. presented a computer-aided diagnosis system for risk stratification of pulmonary nodules in the CTimages of the LIDC-IDRI dataset by fusing shape and texture-based features in a machinelearning (ML) based paradigm. Using 30 dominant features from the pool of shape and texture-based features, the proposed system achieved classification accuracy, sensitivity, specificity, and AUC of 89%, 88%, 89 %, and 0.92, respectively. [56]

The results of the present study showed that the combination of different topologies combined with time-varying PSO for feature selection, with different supervised machine learning classification algorithms led to better classification performance in the context of accuracy, precision, sensitivity, specificity, and AUC score as compared to the studies as mentioned above [50-56]. Further exploration of the proposed method can help validate and enlighten the

effectiveness and adaptability of the parameters required to achieve the best result.

#### 6. Conclusion

Combining different topologies with time-varying inertia weights has yielded a practical framework for optimal feature selection. This foundational step improved the classification performance of the classifiers by selecting quality discriminative features and discarding the least important ones. Such techniques can assist medical professionals in accurate decision-making, reducing their workloads. Despite being trained on limited data, the classifiers showed promising results with the optimal number of features. Deep learning classifiers can be prone to overfitting if trained with a small dataset, such feature selection techniques combined with different traditional machine learning classifiers can reduce such problems, making more robust systems.

#### 7. ACKNOWLEDGMENT

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#### **Original Article**

# To study association of sleep quality and internet addiction among medical students

Rakesh Banal, Mala Bharti, Akhil Menia

#### Abstract:

**Background:** More than 30% of people suffer from sleep disorders. Medical students are at great risk to develop sleep disruption due to various reasons. Because of betteraccessibility and affordability the number of internet users has increased rapidly with over 2 billion global users. Indian users contributed to about 354 million internet users in 2015. Adolescents and young adults including medical students are especially at increased risk for internet addiction.Our study was a preliminary step towards understanding the effect of internet addiction on sleep quality among medical college students.

**Methods:** The study was conducted on 500 medical students, belonging to either sex and from all Profsof MBBS who were randomly enrolled in the study from Government Medical College, Jammu. Internet addiction was assessed by using the Internet Addiction Test while assessment of sleep quality was done by Pittsburgh Sleep Quality Index (PSQI).The information obtained was analysed by using appropriate Statistical methods.

**Results:** 15.4% of our study group had problematic internet use (possible addicts/addicts) 37.4% of our study group were having PSQI score of  $\geq$  5 indicating poor sleep quality. There was poor sleep quality in moderate user or addicts than in normal on average user and this relationship was statistically significant in our study.

**Conclusion:** There should be measures in the form of internet addiction awareness programs in Medical Colleges, which should be conducted to make students aware of the prevalence of internet addiction and its effect on their sleep and quality of life. Initiatives must be taken in order to create opportunities for relaxation, recreation and other extracurricular activities. It needs to be emphasized that students will have to be educated in safe and healthy practice for internet use.

#### Introduction:

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Sleep is usually the state of unconsciousness from which a subject can be aroused by appropriate sensory or other stimuli. It can also be defined as a normal, periodic, inhibition of the Reticular Activating System.[1] About one third of our life span is usually spent sleeping and a good sleep is necessary for optimal health and without enough sleep, both our body and mind become weak which can lead to changes in behaviour.[2] There are many benefits of good sleep which includes increased productivity at work, better coping skills, concentration and memory. Person having good eight hour sleep has better ability to make careful health decisions [3]More than 30% of people suffer from sleep disorders. Sleepiness during day time leads to mistakes, accidents and tragedies. Risk of death in people who sleep more than 8.5 hours or less than 3.5 hours a day is 15% higher than in those who sleep 7 hours a day.[1]

Taking into consideration a demanding and exhausting study and duty hours, medical students are at great risk to develop sleep disruption. In addition to hectic clinical and academic hours a change in living style such as poor accommodation and being away from family puts them at a greater risk of reduction in sleeping time to have extra time to cope up in studies and workload. [4]There is a known relationship between sleep and mental health. Various studies done in different countries shows that academic performance of medical students and health status were significantly affected by sleep deprivation.[5]

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Keywords Internet, Sleep, Medical students. Internet is no longer just used for educational and research purposes and because of accessibility and affordability the number of users has increased rapidly with over 2 billion global users. Indian users contributed to about 354 million internet users in 2015. Adolescents and young adults are especially at increased risk for internet addiction.[6] Internet addiction is defined as any online related compulsive behaviour which interferes with normal living and causes severe stress on family, friends, loved ones and one's work environment. Internet addiction has been called internet dependency and internet compulsivity.[7] Internet addiction is regarded as a kind of technological addiction, which is the result of the rapid development of science and technology. Based on how we use, it can be good or bad thing for human beings. [8]

In Asian countries, the prevalence of Internet addiction in adolescents was reported to be 13.8% in Taiwan, 10.7% in South Korea, ranging from 3.0% to 6.7% in Hong Kong and from 2.4% to 6.0% in China.[9]

Indian studies are still in their initial stages. In 2006 a mass study was done by I-Cube, which enrolled 65,000 individuals, it was seen in the study that 38% of individuals were heavy users (8.2 hours/week) mainly for the purpose of including email and instant messaging (98%), job search (51%), banking (32%), bill payment (18%), stock trading (15%), and matrimonial search (15%). The age group which was showing highest frequency of internet addiction was young males. In a study in school going adolescents, authors have reported after interviewing 603 adolescents that the prevalence of internet addiction was noted to be 3.96% in boys and 1.62% of girls. Over 15% of the total sample showed overuse of internet but below internet addiction criteria. Stress scores were significantly correlated with the internet use patterns in both sexes. The main use of the internet in either sex was for social networking.[10]

#### MATERIAL & METHODS

The present study was conducted in the Postgraduate Department of Physiology, Government Medical College, Jammu. The study was approved by Institutional Ethical Committee of GMC Jammu.

The study was conducted on 500 medical students, belonging to either sex and from all Profsof MBBS who were randomly enrolled in the study from Government Medical College, Jammu. A written informed consent was taken from all eligible subjects.

#### **INCLUSION CRITERIA:**

• Healthy male and female students of GMC, Jammu whohad given consent for participation in the study.

#### **EXCLUSION CRITERIA:**

Such students were excluded from the study, who:

- Were on Psycho-tropics like antipsychotics, antidepressants and sedatives.
- Suffered from Psychiatric illness.
- Had history of any chronic disease
- Did not give consent for the study.

After detailed discussion regarding the purpose and methodology of the study, all eligible subjects were requested to participate in the study. All the subjects included in the study were interviewed by the investigators and relevant information regarding the details of demographics (age, gender, place of living etc.), designation, purpose of using the internet (education, entertainment, news, gaming, social networking etc.) if the internet was used for all purposes mentioned, then the purpose for which it was used more frequently was be taken into consideration, the place of usage of internet, the time of day when the internet is accessed the most (morning, afternoon, evening, or night hours) and the average duration of use per day was noted down in the Performa.

All the subjects were provided with a questionnaire to measure the internet addiction and sleep quality.

Assessment of Internet Addiction - Internet addiction was assessed by using the Internet Addiction Test (IAT; Young, 1998) which is a 20item scale that measures the presence and severity of internet dependency among adults.

Assessment of Quality of Sleep - Assessment of sleep quality was done by Pittsburgh Sleep Quality Index (PSQI). It is a self-report instrument designed to evaluate sleep quality over the last month.

**Statistical Analysis:** The information obtained was compiled in the form of an excel sheet. Statistical analysis was performed by using SPSS statistical software, version 23 and graphs were prepared in XL windows. Descriptive statistics were calculated for summarizing quantitative variables (mean [ $\pm$  SD) or median (range). The significance of difference between quantitative variables was assessed by t-test. Pearson correlation was used to find the correlation between the internet addiction and sleep. For all statistical tests, a p value < 0.05 was taken to indicate a significant correlation among the variables.

#### **Results:**

Table 1, 2,3,4,5,6,7 and 8 shows the results of our study. Table 1 shows the distribution of study subjects according to the purpose of use of internet. It was observed from the table that most of the study subjects used internet for education purposes [45%] and social networking [37.8%] followed by entertainment [14.2%] and for other purposes like news and gaming [3.0%].

Purpose	Frequency (N)	Percent %
Education	225	45%
Social Networking	189	37.8%
News/Gaming	15	3.0%
Entertainment	71	14.2%
Total	500	100.0%

Table1. Distribution of study subjects accordingto purpose of internet usage.

 
 Table 2. Distribution of study subjects according to time of usage of internet

Time	Count	Percent (%)
Morning	6	1.2%
Afternoon	12	2.4%
Evening	166	33.2%
Night	316	63.2%
Total	500	100.0%

It was observed that most of the study subjects used internet during night hours (63.2%). Minimum number of study subjects used internet in the morning hours (6%). Table 2

Table 3. Distribution of subjects according to the average duration of use (In Hours) of use of internet

S.N	Average	Frequency	Percentage
0	duration	( <b>n</b> )	(%)
	of use		
	(in hours)		
1	1.00	54	10.8
2	2.00	229	45.8
3	3.00	130	26.0
4	4.00	51	10.2
5	5.00	22	4.4
6	6.00	13	2.6
7	7.00	1	0.2
Total		500	100.0

It was observed from the table 3 that average duration of internet use in most of the study subjects (45.8%) was 2 hours.

Table 6. PSQ	Score	distribution	of study	subjects.
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Table	4.	showing	frequency	distribution	of
interne	et us	age accord	ling to place	of usage.	

Place of usage	Frequency (N)	Column N %
Hostel	199	39.8%
Home	292	58.4%
Cyber café	1	0.2%
College	8	1.6%
Total	500	100.0%

It was observed from that most of the study subjects used internet at home (58.4%) and hostel (39.8%) and lesser number of subjects used internet in college (1.6%) and in cybercafé (0.2%).

Table 5. IAT Score distribution of studysubjects.

IAT group	Pattern	Males (n=245)	Females (n=255)	Total (N=5 00)	%
<20	Less than Average	14	31.00	45	9%
20-49	Average user	190	188	378	75.60%
50-79	Moderate user/Possi ble addict	38	33	71	14.20%
80-100	Addict	3	3	6	1.20%

The table 5 shows the distribution of study subjects according to their IAT scores.

Number of study subjects having IAT score < 20 was 45 (9%).

Number of study subjects having IAT score 20-49 was 378 (75.60%).

Number of study subjects having IAT score 50-79 was 71 (14.20%).

Number of study subjects having IAT score 80-100 was 6 (1.20%).

Mean IAT score was 35.85±15.41

	•	v 0			
PSQI group	Pattern	Males (n=245)	Females (n=255)	Total (N=500)	%
<5	Good quality sleep	154	159.00	313	62.6%
≥5	Poor quality sleep	91	96.00	187	37.4%

The study group was divided into two categories according to their sleep quality. Those having PSQI less than 5 (<5) are classified as good sleepers and those having PSQI equal to or more than  $5(\geq 5)$  are classified as poor sleepers. Table 6

The number of study subjects with PSQI Score <5(Good quality sleep) was 313 (62.6%). The number of study subjects with PSQI Score  $\ge 5$  (poor quality sleep) was 187 (37.4%). The mean PSQI Score of the study subjects was 4.55 ( $\pm 2.28$ ).

Table 7.	Association	of Internet	Addiction	(based o	on IAT	scores)	with S	Sleep	Quality	(PSQI so	cores)

IAT group	Ν	<b>PSQI</b> Mean scores	Std. Deviation	<i>p</i> -value
<50	423	3.78	1.31	-0.0001
≥50	77	8.77	1.75	<0.0001

The table 7 shows the association of internet addiction with sleep quality. The study subjects were categorized into two groups based on their IAT score: Non-addicted (IAT 50) and Addicted ( $\geq$ 50).

Non -addicts includes those who used internet less than average IAT score (<20) and those who were average users with IAT score between (20 -49).

Addicts include the study subjects who were moderate users or possible addicts with IAT score (50-79) and severe addicts with IAT score (80-100).

It was observed that study subjects with IAT score less than 50 had good quality of sleep with PSQI less than 5 (<5).

Study subjects with IAT score more than 50 had poor quality of sleep with PSQI equal to or more than 5 ( $\geq$ 5). A significant association was found between the internet addiction and sleep quality among the study subjects with (p-value <0.0001) which is statistically significant.

#### Table 8. Association of Sleep Quality (PSQI scores) with Internet use (IAT scores).

PSQI group	Ν	IAT Mean Scores	Std. Deviation	<i>p</i> -value
<5	313	27.52	7.94	<0.0001
≥5	187	49.80	14.78	

The table 8 shows the association of sleep quality with internet use [IAT scores]. The study groups were divided into 2 groups based on PSQI scores. with PSQI <5 good quality of sleep and PSQI  $\geq$  5 poor quality of sleep.

313 subjects in our study were having good quality of sleep and 187 subjects were having poor quality of sleep. The mean IAT score of the study subjects with good quality sleep was 27.52

The mean IAT scores of the study subjects with poor quality sleep was 49.80

It was observed that study subjects having poor quality of sleep were having high IAT scores in comparison to those having good quality of sleep.

There was a significant association found between sleep quality and internet addiction (p-value<0.0001) which was statistically significant.

# Table 9. Correlation between IAT and PSQIscores.

Correlations

		IAT	PSQI
IAT	Pearson Correlation	1	.862**
	Sig. (2-tailed)		.000
	Ν	500	500
	Pearson Correlation	.862**	1
PSQI	Sig. (2-tailed)	.000	
	Ν	500	500

\*\*. Correlation is significant at the 0.01 level (2-tailed).



Figure 1. Correlation graph between Sleep Quality (PSQI score) and Internet Use (IAT score). Taking IAT score on x-axis and PSQI score on y-axis.

#### Discussion

The severity of internet addiction is well established and in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), Internet Gaming Disorder is identified in Section III as a condition warranting more clinical research and experience before it might be considered for inclusion in the main book as a formal disorder. [11] Internet addiction is correlated with many Psychiatric and psychosocial disorder including poor sleep quality.[12] The COVID-19 pandemic has had a significant impact on everyday functioning, considerable measures being taken to reduce the spread of virus like prolonged lockdowns, physical distancing among others. Amidst all of this, studies report an increase in internet addiction especially among adolescents.[13]

Results of our study showed that there was no statistical significance between internet addiction and age, sex and residence of study group. There was no statistical significance between poor sleep quality and age, sex and residence of study group. Most of our study groups were using internet for education followed purposes, by social networking, entertainment and news/gaming. Most of the participants were using internet during night hours followed by evening, afternoon and least in the morning. Most of the participants were using internet at home followed by hostel, college and least at cyber café. 15.4% of our study group had problematic internet use (possible addicts/addicts) 37.4% of our study group were having PSQI score of  $\geq 5$ indicating poor sleep quality. There was poor sleep quality in moderate user or addicts than in normal on average user and this relationship was statistically significant in our study. Findings of our study were consistent with majority of such type of studies carried by various workers. Our study found that there is a significant relationship between internet addiction and quality of sleep among the medical students.

#### Conclusion

Detection of internet addiction therefore assumes a greater importance in professional institutions such as medical colleges. There should be measures in the form of internet addiction awareness programs which should be conducted to make students aware of the prevalence of internet addiction and its effect on their sleep and quality of life. Initiatives must be taken in order to create opportunities for relaxation, recreation and other extra-curricular activities. There is also a growing need to increase awareness of healthy sleep habits to improve the quality of life. It needs to be emphasized that students will have to be educated in safe and healthy practice for internet use.

#### Limitations

The present study was conducted in a single government tertiary care teaching hospital but the environment and educational resources may be different in private medical colleges as also in government degree colleges. Sample size of the study was less and was not carried out on large representative population. Both sleep quality and internet use was self reported.

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#### **Original Article**

## Gender Based Knowledge, Attitudes And Beliefs On Eye Donation Among Adult Population (18 Years And Above) In A Tertiary Care Hospital Of UT Of Jammu And Kashmir

Gupta Riya, Mahajan Richa, Langer Raja, Kumari Rashmi, Gupta K Rajiv,

#### Langer Bhavna

#### Abstract:

Introduction

**Background:** There is dearth of donor corneas available worldwide for transplantation since patients needing transplants far outnumber the cornea tissues available. Understanding, knowledge, attitude and beliefs about eye donation is key to address this shortage. It was with this aim that the present study was conducted in a tertiary care hospital among adult patients and accompanying attendants aged 18 years and above.

**Material and Methods:** This cross-sectional study was conducted among patients and attendants (aged 18 years and above) visiting OPD of PG Department of Ophthalmology in a tertiary care hospital. The questionnaire elicited information on sociodemographic characteristics, knowledge, attitude and beliefs about eye donation. Total number of respondents in the study was 340.

**Results:** 95% of the males were aware of eye donation and newspaper/ TV was the main source of information. Higher proportion of females knew that donated eyes cannot cure all types of blindness (pvalue<0.000). Majority of the respondents consider eye donation a service to mankind and about one-third believed that eye donation can lead to disfigurement. Belief that they would be born blind in the next birth if they donated eyes was higher among females (p-value<0.000).

**Conclusion:** Although majority of respondents had good awareness about eye donation, yet willingness to donate eyes was less than desired. Authors recommend educational media campaigns, collaborations with medical personnel, partnerships with religious leaders, use of social media and educational sessions with medical students and staff to promote awareness about eye donation as well as to counter the myths among general population

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As per WHO estimates, every five seconds, someone in the world goes blind [1] which is indeed a grim reminder that blindness still remains a major public health problem. Currently there are 45 million blind people in the world with addition of 1-2 million every year [2]. But crux of the problem is that 80% of this blindness is either preventable or treatable.

Corneal disease still remains a prominent reason as far as visual impairment and corneal blindness is concerned across the world but more so in the developing nations. Damage to cornea accounts for about 6-8 million of total blind cases in the world [2,3]. Majority of corneal damage is from trachoma followed by other causes like ocular trauma, ulceration, xerophthalmia, ophthalmia neonatorum, etc. [4]

During 2015-2016, only 59,810 eyes were donated against 62,67,685 registered deaths [5], thus implying a very low rate of eye donation in India. Apart from, this, utilization rates of tissues ranged from 33-49% [3] due to poor quality of tissue or clinical reasons. It translates into huge gap between demand versus availability of healthy corneas for transplantation [6].

To increase the procurement of cornea, raising the level of public education on eye donation is an important first step. Attention has been paid both to factors affecting procurement of cornea as well as public attitude towards eye donation in the developed world [7] but a lot remains to be done in the developing world. Also, various myths and

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Keywords

Eye donation, Knowledge, Attitude, Beliefs

beliefs in the developing world contribute to low eye donation rates [6,8].

A review of 55 research articles published in 13 countries reports that 52% of respondents endorsed willingness to donate their eyes after death but only a meagre 5% reported as pledged donors [8].So, despite high levels of awareness and willingness to donate , the actual conversion is low which is really a cause of great concern. Review of literature has revealed that there was a dearth of studies in north India about knowledge, attitude and beliefs about eye donation. It was in this context that the present gender based study was conducted among adult population aged 18 years and above in OPD of opthalmalogy department of a tertiary care hospital.

#### Materials and methods

The present cross-sectional study was conducted using a questionnaire that was developed by faculty members of community medicine department after extensive review of the existing literature. The questionnaire was meant to obtain information about knowledge, attitudes and beliefs about eye donation in adult population of Jammu region of India. The study population included patients and their attendants visiting OPD of ophthalmology department of Government Medical College Jammu. The questionnaire was assessed for clarity and ease of comprehension in a pilot group consisting of 30 subjects selected randomly from the general population. Necessary suggestions were incorporated prior to using the final version of the questionnaire. A single interview took 10-12 minutes as revealed in the pilot study.

The final version of questionnaire consisted of four parts. The first part ascertained the sociodemographic characteristics of the participants while second part elucidated knowledge of participants about eye donation. The third part and fourth part were concerned with attitudes and beliefs of participants about eye donation.

The study was conducted between 1<sup>st</sup> January 2021 and 28th February 2021. The study was duly approved by IEC, Government Medical College, Jammu. The study participants were selected randomly from the OPD of PG Department of Ophthalmology, Government Medical College, Jammu. The participants included either the patient him/herself or the accompanying attendant who must be above the age of 18 years. Informed written consent was obtained from the participants prior to their participation in the study and those who did not provide consent for participation in the study were excluded from the study. People with corneal scar and abnormal cognitive ability were also not included in the study. The interviews were conducted on alternate days of the week and around 12-15 participants were interviewed in a day.

Data was entered into Excel sheet and analyzed using SPSS version 21.0. Categorical data was represented by frequencies and percentages. Test of significance used was Chi-square test and p-value <0.05 was considered statistically significant.

#### Results

A total of 340 participants, 190(55.88%) males and 150(44.12%) females participated in the study as depicted in Table 1. 216(63.53%) respondents were in the age group of 18-45 years while 124(36.47%) were >45 years of age. Only 40 (11.76%) participants had a post graduate degree, 130(38.23%) were graduates while 40(11.76%) had received primary school education (Table 1).

males, 182(95.79%) and among Among the females, 108(72.0%) were well aware about eye donation which was found to be statistically significant (p-value of 0.000) as shown in Table 2. For 182 males and 108 females, source of information was recorded. Majority of the respondents (32.41%) reported newspaper/TV as the source of information. Respondents who replied negative about eye donation were informed that eye donation is possible and were further interviewed. 57.89% males and 68% females were aware of the fact that ideal time for collection is within 6 hours of death (p-value=0.072). 39.47% males and 25.33% females knew that a person with refractive error can donate (p value=0.008) [Table 2].

Higher proportion (73.33%) of females than males reported willingness to donate eyes and this difference was found to be statistically significant. (p-value=0.000). Majority of the participants (93.68% males and 94.67% females) consider eye donation a service to mankind. 31.58% males and 36.67% females believe that eye donation results in disfigurement (Table

Table 4 depicts the reasons for non-donation among the respondents. The main reason cited was the fear of other organs being taken than the one specified (37.5%).

Among the beliefs, only 10.53% males and 26.67% females believed that they will be born blind in the next birth if they donated the eye and this difference was statistically significant (p-value=0.000) as can be seen in Table 5.

#### Discussion

The results of the present study have revealed that 85.2% of the study subjects were aware about eye donation and the level of awareness was more among males than female respondents. These results are in agreement with high level of public awareness about eye donation in many studies around the world [8,9,10,11]. In contrast, low levels of awareness (30.7%) about eye donation were reported in a rural population of India [12] while a study in Northwest Ethiopia reported awareness levels of 56.4% [13]. In another study conducted in western India, 66.6% of the subjects were aware of eye donation and it was found to be equal among the male and female subjects [14]. This difference in awareness levels is probably due to different areas of study settings which has a bearing on the knowledge about eye donation in different regions. In the current study, despite 41.1% of the respondents belonging to rural areas, awareness levels about eye donation were quite high.

The main source of information about eye donation among the respondents in the present study was TV/ Newspaper (electronic and print media) followed by awareness camps. Similar results were reported by S.Krishnaiah[12], Maiya GR[15] and Bijapur VM [16]. However, Gupta AKR [14] in their study in western India reported awareness camps as the most common source of information about eye donation.

More males in the current study knew about the ideal time for eye donation which was within 6 hours after the death and overall 62.3% of the total respondents knew it correctly. Tata et al [17] reported it to be 76.3% while Gupta AKR [14] reported it to be 46.3%. On the other hand, Priyadarshini et al [18] reported a vary dismal rate of 4.34% thus denoting a low awareness.

Table 1: Distribution of respondents based onsocio-demographic characteristics (n= 340)

Socio-demographic	Male	Female
variables	( <b>n=190</b> )	(n=150)
Age Groups (in		
years)		
18-45	120	96
>45	70	54
Education		
Primary	25	15
Secondary	75	55
Graduate	70	60
Post Graduate	20	20
Place of Residence		
Urban	108	92
Rural	82	58
Occupation		
Business	52	02
Government service	28	10
Agriculture	62	40
Housemaker	00	48
Student	48	50
Religion		
Hindus	164	132
Muslims	26	18
Others	00	00
Marital Status		
Married	152	137
Single	18	08
Widow	12	05
Divorced	08	00

Only one-third of respondents replied that donor needs to be transported to hospital after death for eye

donation in contrast to 77.7% reported by Gupta AKR et al [14]. Only 56.7% of the respondents knew about the presence of eye bank in Government Medical College, Jammu. These results reflect that some parameters of knowledge are far from desired levels.

The results have further revealed that males were more willing to donate than their female counterparts and these results are in consonance with those reported by Gupta AKR et al [14]. Lack of willingness on the part of females may be due to male patriarchy. In a study conducted in Jordan, 67.2% respondents were willing to donate their corneas [19]. In the present study, 94.1% thought eye donation was a service to mankind and similar results were reported by Haddad FM in Jordan [19]. Only 38.2% of the respondents in the current study thought that eye donation would cause delay in funeral activities while Gupta AKR [14] reported this rate to be 85.5% in their study.

Among the beliefs of respondents, only 17.7% opined that they would be born blind if they donated eyes and only 16.7% were of the view that eye donation was against their religious beliefs. Hussen MS [13] reported that two-third of the respondents were of the view that eye donation is not against their religious doctrine. Gupta AKR [14] reported only 10.54% respondents answered that eye donation was against their religious beliefs. In the present study, majority of the respondents (86%) opined that religious persons were more likely to go for eye donation which is in conformity with the results of Singapore study [20].

#### Conclusion

The results have revealed that participants had good levels of knowledge about eye donation and many were willing to donate their corneas. Majority considered eye donation a service to mankind but one-third had a belief that it could lead to disfigurement. Public education programs involving healthcare workers, use of mass media, health campaigns in community and schools and religious talks need to be incorporated into the strategy to increase more awareness. Myths and misconceptions about eye donation which are still prevalent in some parts of the society need to be taken care of.

#### Limitations

The study population may not be entirely representative and small sample size are among the limitations of the present study. Results may be skewed due to non-participation bias as those who participated may have a higher level of awareness about corneal donation.

S.No		Yes	No	Yes	No		
1	Knows about eye donation	182	08	108	42	35.95	0.000
2	Source of information	Ma	ale (n=182)	Fema	ale (n=108)	$\gamma^2$ value	p-value
	Newspaper/ TV		57		37		
	Banners		35		23		0.73
	Doctors		40		18		
	Camps		50		30		
		Ma	ale (n=190)	Fema	ale (n=150)		
		Yes	No	Yes	No		
3	Can a living person pledge to donate eyes?	145	45	96	54	5.58	0.018
4	Knows that cornea is transplanted	85	105	56	94	1.60	0.205
5	Ideal time for collection is within 6 hours of death	110	80	102	48	3.23	0.072
6	Can a person with refractive error donate	75	115	38	112	6.93	0.008
7	Can donated eyes cure all types of blindness?	164	26	89	61	30.65	0.000
8	Is it permissible to sell or buy human eyes?	20	170	45	105	19.32	0.000
9	Donor needs to be transported to hospital after death for eye donation	70	120	49	101	0.47	0.492
10	Is there an eyebank in Jammu?	105	85	88	62	0.27	0.603
11	It is mandatory to obtain family permission before eye donation	62	128	42	108	0.64	0.422
12	Eyes can be removed at donor's house itself	35	155	25	125	0.08	0.780

 Table 2: Knowledge regarding eye donation (n=340)
 Image: Comparison of the second second

#### Table 3: Attitude regarding eye donation

S.No.	Ma		Male (n=190)		Female (n=150)		p-value
		Yes	No	Yes	No		
1	Willing to donate as and when required	102	88	110	40	12.96	0.000
2	Eye donation is a service to mankind	178	12	142	08	0.02	0.880
3	Eye donation causes delay in funeral activities	70	120	60	90	0.23	0.629
4	Eye donation results in disfigurement	60	130	55	95	0.75	0.384

S.No.	Reason	Yes	Percentage (%)
1.	Fear of other organs being taken than the one specified	48	37.50
2.	Lack of awareness of benefits of donation	8	6.25
3.	Fear of sanctity of human body after death	16	12.50
4.	Fear of misallocation of the donated organ	10	7.81
5.	Family objections	19	14.84
6.	Religious reasons	27	21.09

 Table 4: Reasons for unwillingness to donate (n=128)

#### Table 5: Beliefs regarding eye donation

S.No.		Male (n=190)		Female (n=150)		$\chi^2$ value	p-value
		Yes	No	Yes	No		
1.	Will be born blind in the	20	170	40	110	13.93	0.000
	next birth if donated the eye						
2.	Eye donation is against the	35	155	22	128	0.59	0.438
	religious beliefs						
3.	Eye donation after death will	110	80	98	52	1.65	0.198
	make you feel that you are						
	doing good						
4.	Idea of separating eye from	80	110	35	115	12.37	0.000
	body is unacceptable						
5.	Religious persons are more	158	32	136	54	6.63	0.010
	likely to donate					l I	

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#### **Original Article**

### Comparative Assessment Of Platelet Rich Fibrin Placed Through Tunnel And Pouch Technique With And Without The Use Of Enamel Matrix Derivatives For Recession Coverage – A 12 Month Randomized Control Trial

Ashish Bali, Sandeep Kumar Dubey, Pritish Chandra Pal, Iqbal Singh

#### Abstract:

**Introduction:** Apical migration of gingival margin i.e. gingival recession is one of the most common periodontal esthetic issues. Successful minimally invasive management of gingival tissue recession is still a concern in esthetic dentistry.

**Material & Method:** 50 sites in 50 patients with Miller' class I/II recessions were treated with tunnel and pouch technique (TPT) and platelet rich fibrin (PRF) with (Test group, n=25) or without (Control group, n=25) enamel matrix derivative (EMD) application. Subjects were followed for 12 months. Gingival recession depth (RD), Clinical attachment level (CAL), percentage of root coverage, Gingival Index, Plaque Index were measured at baseline and at 12 month. Data obtained were fed to IBM SPSS 22.0. Wilcoxon Sign Rank Test for Intragroup statistical analysis and Student't' test for intergroup statistical analysis were performed. The level of significance was fixed at  $p \le 0.05$ .

**Results:** CAL in control group was  $2.60\pm0.91$ mm and in test group it was  $3.33\pm1.05$ mm at  $12^{\text{th}}$  month. The mean difference of CAL gain was  $0.73\pm0.14$ mm, which was statistically significant (p=0.025). At  $12^{\text{th}}$  month the mean amount of RD coverage in control group was  $2.13\pm0.74$ mm and in the test group it was  $2.67\pm0.72$ mm. The mean RD difference of  $0.54\pm0.02$ mm was found to be statistically highly significant (p=0.012).

**Conclusion:** TPT technique when combined with PRF and root bio modification with EMD provides convincing results in miller's class I or II gingival soft tissue recession cases.

#### Introduction:

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Apically shifted marginal gingiva from its natural location i.e. cemento-enamel junction (CEJ) is termed as gingival tissue recession (GR).[1] Numerous developmental, anatomical or acquired etiological factors like abnormal tooth position, frenal pull, periodontal disease, bony fenestration or dehiscence, faulty tooth brushing, iatrogenic factors may lead to root exposure. Loss of gingival tissue and subsequent root exposure leads to unaesthetic appearance, dentinal hypersensitivity and root caries.[2] Successful root coverage has turned into a crucial therapeutic concern due to escalated cosmetic and functional demands in contemporary society. The desired hope of recession coverage intends to achieve complete root coverage (CRC) to provide a pleasing esthetic appearance. Periodontal plastic surgeons have assorted diverse surgical strategies to cover the pathologically denuded tooth surfaces. Conventional coronally displaced flap, rotational or advanced pedicle procedure, soft tissue grafting (free gingival or connective tissue) and modification of conventional methods such as with alternative soft tissue grafting, resorbable or non-resorbable membranes have been applied as evident from literature.[3] Reports have demonstrated that advancing the gingival flap through tunnel and pouch technique (TPT) has specific promising esthetic results and therefore classically employed. TPT is a reliable formulaic procedure in the treatment of Miller Class I or II GRs.[4,5] It has also been used with many regenerative materials like the guided tissue membranes, enamel protein derivatives, tissue engineered human fibroblast, alloderm material, dermal substitutes, platelet rich fibrin (PRF), placental

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#### Keywords

Gingival recession, root coverage, PRF, EMD

membranes with good reported clinical outcomes. Since the 1950s, several mucogingival surgical techniques aiming for CRC have been published with conflicting rates of success and predictability.[6] Concentrated growth factors are intricate in complex healing activity and PRF are assumed as key proponent of tissue regeneration. It contains platelet derived growth factors (PDGF), transforming growth factors (TGF) and diverse unidentified growth factors. Periodontalligament cells of human contain major mitogens PDGF. Type I collagen an obligatory element ofhealing is also stimulated by the PRF derived fibrin clot. Though autogenous soft tissue grafting is believed as a benchmark treatment for root coverage, alternate use of PRF eliminate the need for a donor site, minimize postsurgical hassle, and nurture expeditious gingival healing making minimally invasive approach.[7]

Heijl et al.[8] reported periodontal regeneration in an experimental recession defects with enamel matrix derivative (EMD). Former studies showed that EMD application on recessed root exterior imitate cementogenesis of nascent root development. Mellonig [9]histologically confirmed new cementum formation with EMD. Rasperini et al[10]explained a new attachment in GR treated with autogenous tissue graft and EMD. Hinged upon these former evidence, it seems equitable to use EMD for ameliorating the clinical outcomes of GR defects. As per our knowledge the literature is also scattered regarding this aspect. Hence, comparing the TPT and PRF combination with and without EMD application for the treatment of GR would be a minimally invasive and novel approach. Despite the availability of myriads of material and technique for treatment of GR, there is no authentic lucidity on the efficacy of these procedures.

Therefore this current research was done to clinically appraise and compare the efficacy of PRF placed through TPT with and without the use of EMD in the treatment of Miller's Class I or II GR sites and followed up for 12 months.

#### Material and methods:

Overall 50 patients with age group between 18-60 years (mean age 38.5) with Miller's class I /II GR present between  $2^{nd}$  premolars (upper/lower) teeth requiring surgical root coverage were selected from the outpatient department. 50 GR sites were randomly allocated into 2 groups by ablinded researcher. Group A (n=25) included – CAF with PRF and group B (n=25) included – EMD application in co-occurrence with TPT and PRF.

The Institutional Ethical Board approved the study protocol and consent form of the current randomized controlled trial. Each study participants were given a detailed verbal and written description of the proposed study, benefit and possible risk factors associated with the surgical intervention and anticipated outcome of the treatment. Those who agreed voluntarily and meet the inclusion criteria of the study signed a consent form. Study participants were in general good health. Inclusion criteria for the study were: patients exhibiting Miller's Class I/II GR defect<sup>5</sup> in maxillary or mandibular teeth (between 2<sup>nd</sup> premolars); age between 18-60 years; no relevant systemic disease; presence of identifiable CEJ; no radiographic evidence of interdental bone loss; no occlusal interferences, caries or restoration on the tooth of interest.

Exclusion criteria were – patient under medication known to interfere with gingival health or healing; habitual smoker or tobacco chewer; pregnant and lactating mothers; malposed/rotated teeth; history of periodontal surgery at investigation site within 6 months.

Initial Therapy: Preliminarily study participants received a complete scaling and root planing. If the teeth of interest had any distinguished root convexities that were planned to reduce. A punctilious plaque control programme was initiated for each study subjects 3 weeks before surgical procedure including stipulation in suitable brushing technique with soft tooth brush.

#### Surgical protocol:

Antiseptic solution (Betadine 10%, Skincare Surgi Pharma Pvt Ltd, Mumbai, Maharashtra, India) was applied on the field of operation with cotton swab. Surgical site was anesthetized using 2% xylocaine with 1:50,000 epinephrine (Lignox 2%, ICPA, Mumbai, India) on both the facial and lingual aspect.

Total of 25 sites in 25 patients were treated in the control group. The procedure started with a labial crevicular incision bard parker (BP) blade No.12 around the involved tooth except the interdental papilla region. This was followed by tunnel preparation by using tunneling instrument apically surpassing the mucogingival junction (MGJ) and proximally on both side of the defect extending around the abutting teeth. Adequate mobility of the flap was ensured to allow for flap advancement without tension. Root bio-modification of the exposed root surface was done by applying 24% EDTA gel (Prevest EDTA Gel 24%, Prevest Dentpro, Jammu, India) for 2 minutes and then washed with saline. 10 ml of venous blood was collected in 2 glass tubes from antecubital fossa using standardized protocol. Glass test tubes were then placed in a centrifugal machine (Labcare Ltd., Haryana, India) and centrifuged at 3000 revolutions/minute for 10 minutes. Blood settled into the following layers: red lower fraction containing red blood cells,

upper straw colored cellular plasma and the middle part containing the fibrin clot. The middle fraction was collected and membrane was made using PRF box (GDC Ltd., Punjab, India). PRF membrane was passed through the tunnel and sutured (Ethicon vicryl sutures USP 4-0, USA). Periodontal dressings were placed over it.

Total of 25 sites in 25 patients were treated in the test group. TPT design and PRF placement

was identical to the one described in the control group, except for the addition of Emdogain. After flap preparation the exposed root surfaces were conditioned with a 24% Prefgel for 2 minutes in order to remove the smear layer. The area was thoroughly rinsed with saline and dried. Commercially available EMD (Emdogain gel) was applied to the exposed root surface followed by PRF placement. Suturing was done as described in control group.

Sutures were removed at 14<sup>th</sup> day. Further evaluation was done at each month. Plaque control initiatives were followed till the study period.

#### Clinical measurements:

Following measurements were taken using CEJ as a fixed point at baseline and at 12<sup>th</sup> month

1. Recession depth (RD) - CEJ to gingival margin

2. Clinical attachment level (CAL) - CEJ to base of gingival sulcus

Additionally the percentage of root coverage was calculated after 12 months according to thefollowing formula: [(Preoperative RD – Postoperative RD) X 100] ÷ (Preoperative RD)

Also, gingival inflammation was monitored by using Gingival Index (Loe and Silness 1963).[11]Oral hygiene effectiveness was monitored by using Plaque Index (Silness and Loe 1964) [12]

Index (Silness and Loe 1964).[12]

**Statistical analysis:** Statistical analysis was done using IBM SPSS Software Package 22.0 (IBM Tech. Corp, New York, USA). Descriptive statistics were expressed as mean and standard deviation (SD). Data were analyzed using Wilcoxon Sign Rank Test for Intragroup statistical analysis (from baseline to  $12^{th}$  months in each group) and Student't' Test for intergroup statistical analysis (between test and control group). The level of significance was fixed at  $p \le 0.05$ .

#### **Results:**

#### **Control group:**

**CAL:** CAL was compared pre and post-operatively over 12 months period. The mean depth of CAL at baseline was  $4.67\pm0.72$  mm which was reduced to  $2.07\pm0.80$ mm at 12 month. The mean difference of  $2.60\pm0.91$ mm was found to be statistically highly significance (p=0.000). [Table 1]

**RD:** Mean RD at baseline was  $3.00\pm0.76$ mm which was reduced to  $0.87\pm0.64$ mm at 12 month. The mean RD difference compared to baseline was  $2.13\pm0.74$  mm which was found to be statistically highly significant (p=0.000). [Table 1]

**PI:** The mean and standard deviation value for PI at baseline and 12 months was  $0.16 (\pm 0.28)$  and  $0.26 (\pm 0.25)$  respectively & showed no significant difference in baseline to 12 month interval (F value = 1.068, p=0.349). [Table 1]

**GI:** The mean and standard deviation value for PI at baseline and 12 months was  $0.32 (\pm 0.47)$  and  $0.40 (\pm 0.50)$  respectively & showed no significant difference in baseline to 12 month interval (F value = 0.220, p =0.803). [Table 1]

#### Test group:

**CAL:** The mean depth of CAL at baseline was  $4.87\pm0.83$ mm which was reduced to  $1.53\pm0.74$ mm at  $12^{\text{th}}$  month. The mean difference of  $3.33\pm1.05$ mm was found to be statistically highly significant (p=0.000). [Table 1]

**RD:** The mean RD at baseline was  $3.02\pm0.76$ mm which was reduced to  $0.33\pm0.49$ mm at  $12^{th}$  month and mean difference compared to baseline was  $2.67\pm0.72$ mm which was found to be statistically highly significant (p=0.000). [Table 1]

**PI:** The mean and standard deviation value for PI at baseline and 12 months was  $0.16 (\pm 0.22)$  and  $0.16 (\pm 0.23)$  respectively & showed no significant difference in baseline to 12 month interval (F value = 0.000, p=1.00). [Table 1]

**GI:** The mean and standard deviation value for PI at baseline and 12 months was  $0.32 (\pm 0.47)$  and  $0.40 (\pm 0.57)$  respectively & showed no significant difference in baseline and 12 month interval (F value = 0.364, p= 0.696). [Table 1]

#### Inter group comparison:

CAL:

At  $12^{\text{th}}$  month the mean CAL gain in control group was  $2.60\pm0.91$ mm and in test group it was  $3.33\pm1.05$ mm. The mean difference of CAL gain was  $0.73\pm0.14$ mm, which was statistically significant (p=0.025). [Table 2]

#### RD:

At  $12^{\text{th}}$  month the mean amount of RD coverage i.e. root coverage in control group was  $2.13\pm0.74$ mm and in the test group it was  $2.67\pm0.72$ mm. The mean RD difference of  $0.54\pm0.02$ mm was found to be statistically highly significant (p=0.012). [Table 2]

#### **Discussion:**

Periodontal therapy has been directed primarily at elimination of periodontal disease and maintaining the function and health of the dentition. However it has become increasingly focusedon esthetics, which extends from hard and soft tissue management to tissue augmentation. Investigation of etiologic factors and consideration of therapeutic options directed at CRC aid in achieving an esthetic and natural appearance of the newly gained tissue. Patient's esthetic demands, progressive root surface exposure and dental hypersensitivity are the main indication for root coverage procedures. Among the various plastic procedures performed to relieve exposed root surfaces, TPT technique have shown more predictable recession coverage with apparently satisfactory esthetic results. Nevertheless, TPT when used alone is unstable on longterm, in spite of having the advantage of low morbidity. Furthermore, it does not always result in the regeneration of attachment apparatus which is a major risk factor in recurrence of GR. Therefore, TPT have been frequently combined with various regenerative materials aiming at attaining both regeneration of functional attachment apparatus and root coverage.[4,13]

Limitations like donor surgical site, technique

sensitivity, patient morbidity associated with procurement of autogenous gingival grafts led to the newer advancements as introduction of biomimetic agents such as platelet rich fibrin, bone morphogenic protein have given new promises for recession treatment. There has been an increasing interest in platelet concentrates in the field of periodontal regeneration. PRF developed by Choukroun et al. consists of a fibrin polymer matrix accumulate platelets and released cytokines in a fibrin clot.[14] Slow fibrin polymerization during PRF processing leads to the intrinsic incorporation of platelet cytokines, circulating stem cells and glycemic chains in the fibrin meshes. It is also found that PRF organizes as a dense fibrin scaffold with a high number of leukocytes release growth factors and concentrate. slow glycoproteins. The release of these growth factors like transforming growth factor beta (TGF-B), platelet derived growth factor, and vascular endothelial growth (VEGF) stimulates cell migration and factor proliferation within the fibrin matrix. VEGF functions to start angiogenesis and cell growth. TGF- $\beta$  is an inflammatory regulator can induce a massive synthesis of collagen and fibronectin.[15]

In our knowledge as per present literature none of the study has compared TPT+PRF combination with root bio modification using EMD and evaluated till 12 months long period. Therefore we can take reference of various closely similar studies to compare our result. Jankovic S et al. in 2012 in a 6 months randomized controlled trial found that PRF membrane provided clinically acceptable results and enhanced wound healing.[16] Present result is in accordance with the study performed by, Reddy S et al. in 2013[17 who also reported two cases where PRF membrane was used but in addition to coronally advanced flap technique and showed enhanced root coverage with increase in thickness of gingiva. Padma R et al. in 2013[18] found that addition of PRF to CAF technique provided superior root coverage. Eren G and Atilla G in 2014[19] reported that PRF can be an alternative to CTG membrane. Tunali M et al.[20] have shown CRC with both PRF and CTG membranes in 44 gingival recessions. Shiv Kumar et al.[21] obtained CRC at 73.86% of the sites treated with CAF + PRF procedure but 67.52% of root coverage at the CAF sites. These results might be due to the property of the PRF to progressively release cytokines and growth factors during fibrin matrix remodeling in the process of soft tissue healing. Salem S et al in 2020 evaluate the fouryear outcomes of the CAF versus the pouch and tunnel (POT) technique, both combined with connective tissue graft. The POT technique allows for long-term clinical coverage of gingival recessions.[22] Vatsala Chandra and colleagues in 2022 reported root coverage of 73.75% ± 7.80% and 70.83% ±8.26% by using TPT with PRF andCTG. He also reported less discomfort and better esthetics outcome with TPT.[23] Inasu S. and

Thomas B. in 2021 in a published case series showed goof clinical outcome while using TPT with PRF membrane.[24]

EMD mimics the function of enamel protein secreted by the inner layer of Hertwig's epithelial root sheath on the surface of new dentin. The material consists of matrix derived protein, primarily amelogenin, which is harvested from embryonic porcine teeth and studied in animals and humans providing evidence of tissue regeneration. Split mouth or controlled studies showed increased percentage of root coverage in defects treated with the TPT+EMD. The observed percentage of root coverage in test group is in accordance with the values in studies reported after the use of EMD. ranging from 80.8% to 93.8% at 6 months of follow up. This result is comparable to the results of studies done by Modica et al[25], Pizzo et al[26], Cueva et al[27], Castellanos et al[28]. Although EMD has been extensively used clinically but limited information is available regarding cell attachment or the mechanism of effect promoted by EMD. A recent study by Suzuki & Ohyama[29] provided the first evidence indicating that a bone sialoprotein like molecule in EMD and integrin on the surface of human periodontal ligament cell (HPDL) may mediate binding of EMD to the HPDL cell surface. The author also suggested that this might be crucial to the differentiation of these cells. This might explain why EMD was able to enhance the outcome of root coverage procedure utilizing TPT in the test group. [25,30] Role of root bio modification in success of root coverage has been found positive in our present study. Though root planning was performed in both the test and control group, additional EMD application was beneficial. Also patient compliance and participation was better as it was explained as minimally invasive method. TPT is less invasive than many conventional CAF procedure.

**Conclusion:** Though in recent years the role of root bio modification was questioned, this present study showed the use of EMD has significantly improved the root coverage percentage ascompared to control group. Also the use of TPT and PRF is proved to be a minimally invasive root coverage procedure. The degree of recession, root concavities, patients personal and oral hygiene habits may play a significant role in success or failure of root coverage.

Table - 1 : Intra group comparison from baseline to 12 <sup>th</sup> month of RD and CAL in control and test group										
Group	Parameters	Baseline		12 month after surgery						
		Mean	±SD	Mean	±SD	lean diff	±SD	't' value	ʻp' value	Sig/N S
Test	RD	3.02	0.76	0.33	0.49	2.67	0.72	11.47	0.000	HS
Test	CAL	4.87	0.83	1.53	0.74	3.33	1.05	11.55	0.000	HS
Control	RD	3.00	0.76	0.87	0.64	2.13	0.74	8.34	0.000	HS
Control	CAL	4.67	0.72	2.07	0.80	2.60	0.91	9.34	0.000	HS

 Table - 2 : Inter group comparison of RD coverage and CAL gain among control and test group at 12<sup>th</sup>

 month clinical measurement

S. No.	Parameters	N	Mean	SD	/lean Diff	SD	't' value	ʻp' value	Sig/NS
1	RD	Control	2.13	0.74	0.54	0.02	1.99	0.012	HS
	Coverage	Test	2.67	0.72					
		Control	2.60	0.91	0.73	0.14	2.04	0.025	Sig
2	CAL Gain	Test	3.33	1.05					

Control group	
Pre-operative view of gingival recession	Sulcular incision followed by tunnel preparation
	by using tunneling instrument
Adequate tunnel preparation to move the	Platelet rich fibrin membrane placement to the
gingival unit coronally	recession site through tunnel

Test group	
Suturing done and flap is coronally	12 month follow-up showing complete recession
Pre-operative view of gingival recession	Sulcular incision followed by tunnel preparation by using tunneling instrument
namel matrix derivatives to the recession site	h fibrin membrane placement to therecession site through tunnel



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## **Original Article**

# Effectiveness of two commercially available herbal toothpastes on oral hygiene parameters in diabetic population- a randomized clinical crossover study

Ashutosh Nirola, Megha Sharma, Shivian Chhabra

## Abstract:

**Background:** Diabetes mellitus is a group of metabolic disorders that causes high blood sugar levels. The susceptibility and severity of periodontal diseases increases in diabetic patients, with the impact on the disease process inversely proportional to the level of glycemic control. Maintenance of oral hygiene therefore becomes utmost important in these patients.

**Aim**: The aim of this study is to evaluate the effectiveness of two commercially available herbal toothpastes on oral hygiene parameters in diabetic population.

**Material and methods:** The 6 week randomized clinical crossover trial included 50 diabetic patients of 35 years old and above who were randomly assigned to either the Colgate Diabetics Advanced Ayurvedic Solution toothpaste (Test group A) or Complete Care Herbal Toothpaste (Test group B). Bleeding on probing, gingival index and plaque indices were assessed on day 0, 7 and 14. In addition a questionnaire was given to all the patients in both the groups evaluating their experiences after using the toothpastes.

## **Results and Conclusion:**

Both the herbal toothpastes significantly reduced plaque levels, gingival inflammation and bleeding on probing but Colgate Diabetics Advanced Ayurvedic Solution toothpaste demonstrated comparatively better results.

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#### Introduction:

A chronic metabolic disorder called diabetes mellitus is characterized by a rise in blood sugar levels linked to impaired insulin action and/or reduced insulin production[1]. Long term hyperglycemia being the immediate consequence of diabetes mellitus ultimately leads to multiorgan damage ranging from micro to macro vascular complications[2]. Except for cardiovascular diseases, the American Diabetic Association states that hemoglobin A1C (HbA1C) levels should be less than 7% to prevent the majority of diabetic complications.[3]

A recent study by the International Diabetic Foundation found that 463 million people worldwide have diabetes, and that number is projected to rise to 578 million by 2030. They also reported that India has the second largest diabetic population after China, estimated to be at 77 million in 2019, expected to rise to 101 million by 2030 and to 134 million in 2045 [4].

Dehydration, inadequate wound healing, diabetic ketoacidosis, and illnesses like MI, stroke, kidney failure, retinopathy, which causes blindness, neuropathy, and foot infections that may require amputation are just a few of the complications of diabetes [5]. Another complication of diabetes mellitus is periodontal disease, which affects the majority of diabetic adults [6]. Oral symptoms were found in more than 90% of diabetic patients. The oral tissues are known to be severely harmed by DM, which has been linked to periodontal disease, tooth loss, xerostomia, caries, dysfunctional salivary glands, sluggish wound healing, lichen planus, geographic tongue, and candidiasis. Diabetic neuropathy may contribute to trigeminal nerve pain and temporomandibular joint disorders as well as burning mouth syndrome (glossodynia), dysgeusia, and taste impairment.

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**Keywords** Herbal Toothpaste, diabetes, oral

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Compared to the general population, diabetic patients have a higher incidence of periodontal issues. Periodontal disease and diabetes have a strong reciprocal and negative impact on one another. Periodontal disease has a negative impact on a patient's glycemic control, which makes diabetes more severe and complicated. Diabetes increases the risk of gingival and periodontal problems in the population.

The inflammatory response to dental plaque is affected by hyperglycemia, which worsens gingivitis and periodontitis. As long as chronic infection and inflammation persist in the jaw bone, it can also contribute to the slower healing of lesions near the apex of the teeth. Extraction of teeth that suffer from chronic periodontitis or periapical periodontitis leads to decreased levels of inflammatory biomarkers. Moreover, diabetes and the use of diabetes medication can lead to dry mouth, which contributes to development of caries, periodontitis, and thrush (candidiasis). Both periodontitis and diabetes, together can lead to potentially severely diminished quality of life.

Instances of periodontal disease are more common in diabetic patients. The most effective method of mechanical oral hygiene, including proper tooth brushing with dentifrices, appears to be the maintenance of oral health. It is the most widely used and convenient oral health prevention tool. Toothpastes act as a delivery system for therapeutic agents, preventing plaque formation and gingival and periodontal disease by limiting the growth of microorganisms. Additionally, it was discovered that individuals who were more effective at brushing their teeth had lower HbA1C levels and plaque scores [7]. Studies have shown that some chemicals, such as triclosan and chlorhexidine, when added to toothpastes. inhibit the growth of plaque. However, long-term use of these chemicals can result in tooth discoloration, altered flavour, and the development of antimicrobial resistance[8].

Due to their fewer side effects, natural medicines are becoming more and more popular today. Many people believe that herbal toothpastes are safer than those made with chemicals. Several ingredients in them that have anti-inflammatory, anti-plaque, anti-oxidant, and antiseptic properties are responsible for their effectiveness. When it comes to preventing plaque and gingivitis, herbal toothpastes are just as effective as conventional or fluoride toothpastes [9]. Herbal toothpastes have been shown to reduce plaque accumulation, gingival bleeding, and salivary anaerobic bacterial counts [10].

There are many clinical studies in which oral healthcare products, such as toothpastes and mouthwashes have been evaluated for their efficacy in various health conditions, but only a few were conducted in diabetic patients. Therefore, the current randomized clinical control study aimed to assess the effectiveness of two commercially available herbal toothpastes on oral hygiene parameters in diabetic population.

## Materials and Method

The study included a total of 50 diabetic patients with the age group of 35 years and above visiting the Department of Periodontology, LuxmiBaiDental College and Hospital, Patiala, Punjab. Patients were informed about the study and informed consent was taken. All the procedures in the present study were done by the main investigator to eliminate inter operator variability.

## Inclusion criteria:

- Subjects in the age group of 35 years and above.
- Subjects with diabetes mellitus with HbA1c > 6.5 suffering from generalized chronic periodontitis.
- Subjects having minimum 20 functional teeth in the oral cavity.
- Cooperative patients willing to participate in the study.

# **Exclusion criteria:**

- Subjects suffering from other systemic diseases other than DM.
- Subjects who are on active treatment of antibiotics and corticosteroids
- Pregnant and lactating females.
- Smoking and alcohol consumption
- History of periodontal treatment within the past 3 months.
- Subjects who have been using herbal products and dentifrices.
- Subjects with history or present condition of allergic response to any pharmaceutical products, toiletries or its components or ingredients in the test product.

The study was approved by the institutional ethical committee and review board. The following two herbal toothpastes were used in the randomized crossover clinical study Colgate Diabetics Advanced AvurvedicSolution( Colgate Palmolive, India) containing YashadaBhasma, Surya Kshar and extracts of Madhunashini, Amalaki, Nimba and Jamun. The second paste was Complete Care Herbal Toothpaste (Himalaya, India) containing Pomegranate extract, Neem extract, Miswak extract, Babool extract, Triphala, Five-leaved Chaste Tree, Bishop's weed, Black pepper.

## Patient selection

The sample size for the present study was estimated to be minimum of 25 subjects in each group using formula

 $n=(r+1)/r SD^2(Z\beta-Z\alpha)^2/(d)^2$ 

Where n= number of samples

```
r=1
(r+1)/r=2
SD=0.1
```

 $Z\beta=0.84$  $Z\alpha=1.96$ d=0.25

A ratio of 1:1 of sample size was selected for the present study.

Study design

This crossover randomized single- blinded study was conducted for a period of 6 weeks. A sample size of 50 diabetic patients meeting the inclusion criteria were selected. Randomization was done by drawing lots into either Test group A Colgate Diabetics Advanced Ayurvedic Solution toothpaste( Colgate Palmolive, India) or Test group B Complete Care Herbal Toothpaste (Himalava, India). After being assigned to their respective groups, the participants were blinded. On the first (baseline) day of the study, all the individuals were subjected to an oral examination. No prophylaxis was undertaken prior to commencement of the study, and no attempt was made to modify the participant's oral hygiene habits. Patients were advised to get their HbA1C levels checked and those fulfilling the inclusion criteria were selected. Then they were given a dentifrice that had been labeled and tagged with a number. They were asked to brush twice daily with a 1 cm line of paste in respective brushes for two minutes, using modified bass technique. The participants were given soft toothbrushes and the brushing technique was demonstrated and an image of the technique was provided to the participants.

Patients were divided into two groups:

#### In Phase 1,

**Test Group A**- those intervened with Colgate Diabetics Advanced Ayurvedic Solution toothpaste(Colgate Palmolive, India) for 2 weeks

**Test Group B**- those intervened with Complete Care Herbal Toothpaste(Himalaya, India) for 2 weeks.

- Plaque Index (Silness J and Loe H, 1964)
- Gingival Index (Loe H and Silness J, 1963) and
- Bleeding on Probing by Sulcus bleeding Index (Muhlemann HR and Son. S, 1971)

were recorded on day 0( baseline), Day 7 and Day 14. On Day 14, all the subjects in both the test groups were given a questionnaire form, evaluating patient satisfaction and experience after using herbal toothpastes.

After the end of Phase 1, the toothpastes were switched over between the groups after a washout period of 15 days to reduce the possibility of a "carry- over impact". During the washout period subjects were advised to brush with water alone. No changes in their brushing habits were made.

## In phase 2,

**Test Group A**- those intervened with Complete Care Herbal Toothpaste (Himalaya, India) for another 2 weeks.

**Test Group B**- those intervened with Colgate Diabetics Advanced Ayurvedic Solution toothpaste(Colgate Palmolive, India) for another 2 weeks

• Plaque Index (Silness J and Loe H, 1964)

- Gingival Index (Loe H and Silness J, 1963) and
- Bleeding on Probing by Sulcus bleeding Index (Muhlemann HR and Son. S, 1971)

were recorded on day 0( baseline), Day 7 and Day 14.

On Day 14, all the subjects in both the test groups were given a questionnaire form, evaluating patient satisfaction and experience after using herbal toothpastes.

## Questionnaire

- Q1- Did the toothpaste give a feeling of freshness of breath?
  - A. Yes
  - B. No

Q2- Did the toothpaste produce foam?

- A. Yes
- B. No

Q3- Did you like the flavor of the toothpaste?

- A. Yes
- B. No

Q4- After how long does the flavor of toothpaste recede from your mouth?

- A. Less than 5 minutes
- B. More than 5 minutes
- C. After having food/water
- D. After gargling

Q5- Did the toothpaste delay bad breath?

- A. Yes
- B. No

Q6- Did the toothpaste reduce gum swelling, redness and gum bleeding?

- A. Yes
- B. No

Q7- Did the toothpaste reduce gum swelling, dry mouth and ulcers?

- A. Yes
- B. No

Q8- Are you satisfied using the given toothpaste?

- A. Yes
- B. No

# STATISTICAL ANALYSIS

The raw data collected was then typed in Microsoft Excel in the form of tables. SPSS software was used for statistical analysis (Version 22, IBM Corp, Armonk, NY, USA). The normality of the data was evaluated using statistical tests. Paired t test was used for intragroup analysis (from baseline, day 7 and day 14) and unpaired t test for intergroup comparison. Intergroup comparison was done between-

Phase 1 group A and Phase 2 group A

Phase 1 group B and phase 2 group B

# Results

Intragroup comparison

Mean values of PI, GI and BOP index recorded from baseline to day 7 and day 14 when compared for group A and group B in both the phase 1 and phase 2 showed statistically significant reductions(p<0.05) in scores of plaque index, gingival index and BOP index. Both the herbal toothpastes resulted in improvements of oral hygiene parameters.

Intergroup comparison

Comparison done betweenrefPhase 1 group A and Phase 2 group AIfPhase 1 group B and phase 2 group BsWas found to be statistically non-significant for all the<br/>oral hygiene parameters ie., PI, GI and BOP.s

PLAQUE INDEX

Percentage reductions in scores of plaque index in phase 1 group A was 14.5% (baseline till day 14) as compared to phase 2 group A which showed a reduction of 16.7% (baseline till day 14)

Percentage reductions in scores of plaque index in phase 1 group B was 11.3% (baseline till day 14) as compared to phase 2 group B which showed a reduction of 13.7% (baseline till day 14)

INGIVAL INDEX

Percentage reductions in scores of gingival index in phase 1 group A was 15.5% (baseline till day 14) as compared to phase 2 group A which showed a reduction of 14.1% (baseline till day 14)

Percentage reductions in scores of gingival index in phase 1 group B was 15.5% (baseline till day 14) as compared to phase 2 group B which showed a reduction of 16% (baseline till day 14)

• BLEEDING ON PROBING INDEX

Percentage reductions in scores of bleeding on probing index in phase 1 group A was 11.5% (baseline till day 14) as compared to phase 2 group A which showed a reduction of 13.1% (baseline till day 14)

Percentage reductions in scores of bleeding on probing index in phase 1 group B was 9.7% (baseline till day 14) as compared to phase 2 group B which showed a reduction of 19.1% (baseline till day 14)

All the 50 participants completed the questionnaire and submitted the forms. On evaluation the results revealed, 70% of diabetic patients using Colgate Advanced Ayurvedic Solution experienced long lasting freshness of breath, refreshing flavors and improvements in problems like dry mouth and oral ulcers as compared to Himalaya Complete Care Herbal Toothpaste in which 50% of the patients experienced overall satisfaction using the toothpaste.

The results revealed that Colgate Advanced Ayurvedic Solution led to overall improvement in "well being" of the patients after using the toothpaste.

## Discussion

Gram negative bacteria found in dental plaque cause the chronic infection known as periodontal disease. The degree of tissue damage is significantly influenced by the balance between a localised infection and an excessive host inflammatory response. According to recent research, periodontal disease may not only affect the oral cavity but may also have systemic effects, resulting in a mild inflammatory response[11].

It has been demonstrated that diabetics have significantly higher rates of periodontal disease than do non-diabetics in terms of incidence, prevalence, severity, and progression. According to the theory, both conditions have a "two-way relationship" in which patients with periodontitis are more likely to develop diabetes mellitus and people with diabetes are more likely to have both conditions.

As a result, it's critical to be aware of the potential coexistence of hyperglycemia and periodontitis since both conditions adversely affect one another. As a result, maintaining good oral hygiene in diabetic patients becomes absolutely essential. Effective periodontal therapy has been shown in numerous studies to lower hyperglycemia and lower the risk of many of the complications associated with uncontrolled diabetes in patients [12].

The most popular type of dental care done at home is brushing your teeth with dentifrices. The use of therapeutic ingredients in toothpastes aids in the reduction of biofilm, thereby enhancing gingival health. Nowadays, herbal toothpastes provide a useful substitution for regular dentifrice formulations. The trend of "going natural" has fueled an increase in consumer demand for these goods, with many people reportedly choosing them because they are not tested on animals, have no side effects, don't use animal products, are vegan-friendly, don't contain any additional artificial colors or flavors, and are preferred for cultural reasons. Herbal products sometimes outsell toothpastes with fluoride in some areas. By using in vitro, in vivo, and animal studies, many herbal or plant extracts have been touted as having anti-inflammatory, antipyretic, analgesic, antibacterial, antiviral, anticarcinogenic, and antioxidant activities [13,14].

The goal of the current study was to compare how well two commercially available herbal toothpastes performed on various oral hygiene measures in a diabetic population. According to the study's findings, both herbal dentifrices helped diabetic patients with plaque accumulation, gingival inflammation, and bleeding upon probing. [15,16]

This could be attributed to the effects of various ingredients present in both of the herbal toothpastes-

Colgate Diabetics Advanced Ayurvedic Solution toothpaste

Gymnemasylvestre (Madhunashini): wound healing herb, possessing antidiabetic, antiiflammatory, antimicrobial and antioxidant properties

Emblicaofficinalis (Amalaki): antioxidant properties Azadirachtaindica (Neem): anti-germ action Eugenia jambolana (Jamun): well known astringent Hiora Complete Care Herbal Toothpaste

Punicagranatum (Pomegranate): Topical applications have been found to be particularly effective for controlling oral inflammation, as well as bacterial and fungal counts in periodontal disease. Numerous in vitro studies demonstrate the antimicrobial activity of pomegranate extracts.

Terminaliachebula (Triphala): has potent antioxidant and antimicrobial activity

Vitexnegundo (Chastetree): Anti- microbial and antiinflammatory activity.

Azadirachtaindica (Neem): antimicrobial property, which may be used in oral care preparations.

When compared to Complete Care Herbal Toothpaste. Colgate Diabetics Advanced Ayurvedic Solution toothpaste showed overall greater reductions in plaque index, gingival index, and bleeding on probing index. The study also showed that using Colgate Diabetics Advanced Ayurvedic Solution toothpaste helped patients feel more "well-being" overall. After using the toothpaste, the majority of them reported that it left their mouths feeling fresh and tasting good. Additionally, it helped diabetic patients with their xerostomia and oral stomatitis. This might be because the toothpaste contains the Madhunashini herb (G. sylvestre), which has been clinically proven to treat diabetes. Its traditional antidiabetic formulation also demonstrated hypoglycemic potential by increasing insulin secretion, which in turn promotes islet cell regeneration and increases glucose utilisation. Gymnemic acid molecules saturate the receptor site in the absorptive upper coverings of the bowels, inhibiting the absorption of sugars by the intestine and lowering blood sugar levels as a result. This action demonstrates the enormous anti-diabetic potential of gymnemic acid. [17]

G. Gymnemic acid molecules share an atomic structure with glucose molecules. These molecules block the taste buds' receptor sites from being activated by sugar molecules in food, which reduces the desire for sweets[18]. Gymnema leaf extract, particularly the peptide "Gurmarin," has been found to obstruct the tongue's ability to taste sweet and bitterflavours. The same effect is produced by gymnemic acid. It is thought that by inhibiting the sweet tastesensation, those who take it will consume fewer sweet foods, which may account for some of its hypoglycemic effect [19].

Sylvestre leaves have been used in herbal medicine to treat adult-onset diabetes mellitus and have been shown to cause hypoglycemia in laboratory animals (NIDDM). When a diabetic patient takes gymnema leaf extract, the pancreas is stimulated, which results in an increase in insulin release [20].

In a randomized control clinical trial with two different herbal toothpaste formulations, Hosadurga R et al. enrolled 50 patients with established gingivitis and instructed them to use the pastes for 30 days. Both herbal-based dentifrices were discovered to lessen plaque accumulation and gingival inflammation. This is further supported by our study, which found that both herbal toothpastes enhanced certain aspects of oral hygiene[21].

In a study comparing three toothpastes—regular fluoride toothpaste, ayurvedic toothpaste, and a positive control toothpaste—Utgikar J et al evaluated ayurvedic toothpastes in a diabetic population. The findings showed that diabetic subjects who used ayurvedic toothpaste had lower plaque and gingival indices[4].

In a 12-week randomised double-blind placebocontrolled study, Jayashankar S et al. found that using ayurvedic toothpaste significantly reduced plaque and bleeding on probing[10].

Complete Care Herbal Toothpaste was tested for effectiveness by Mazumdar M et al, who found that it significantly improved oral health overall and decreased GI, PI, and BOP indexes[22].

In our study, it was found that using both herbal toothpastes improved oral hygiene metrics like the plaque index, gingival index, and bleeding on probing index. Colgate Diabetics Advanced Ayurvedic Solution toothpaste, however, demonstrated greater improvements in the diabetic patients' general health, periodontal health, and gingival health. Improved oral hygiene standards following use of the herbal toothpastes may have improved the patients' diabetic status because diabetes mellitus and periodontitis have a "two-way" relationship.

Our study has some restrictions, including a small sample size and a brief study period. Since our focus was on how plaque index, gingival index, and bleeding on probing scores were affected in diabetic patients with generalised chronic periodontitis, we also did not use control groups to determine overall efficacy because it would be difficult. Furthermore, the only factor used to determine whether subjects used the herbal toothpastes given to them was their responses. In order to assess how well diabetic patients were controlled after receiving the toothpastes, we also neglected to check their HbA1C levels. Nevertheless, from the present study, both the herbal toothpastes are promising in their use in diabetic patients and could be considered as a potential adjunct alongwith nonsurgical periodontal therapy.

## Conclusion

According to the study's findings, both herbal toothpastes significantly reduced plaque levels as well as gingival inflammation and bleeding upon probing. To assess the systemic and local effects of the study's toothpastes, extensive follow-up is needed. To support the findings of this study, additional research is needed to assess the treatment retention over the long term and to compare it to other commercially available dentifrices.

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#### **OBITUARY**



#### Dr. Parveen Kaur (1945-2023)

Dr. Parveen Kaur D/o Sardar Basawa Singh and Sardarni Parmeshwar Kaur was born in the month of June 1945. Her family originally hailed from village chowki then Tehsil Bagh (P.O.K) and was settled in the city of Poonch. She along with her family got migrated to Jammu city when she was just 2 years old. Her father was a highly respected man, a Head Superintendent in the office of then Raja of Poonch state and both her parents had inculcated high moral values and greatest virtues in her. She was the youngest among five brothers and three sisters.

She passed her matriculation from Gurmat Kanya Pathshala in year 1960 and did her intermediary from Govt. College for Women Jammu. She passed her MBBS degree in the year 1968 from Govt. Medical College Srinagar. In the year 1969, she got married to Dr. Surinder Singh Soodan, an eye specialist and the eldest son in his family. Just one day after marriage she received interview calls for her post-graduation from Delhi, Chandigarh and Amritsar. She decided to pursue her post - graduation in Govt. Medical College Amritsar where she completed her double MD in both Microbiology and Pathology. She joined Govt. services in Govt. hospital Gandhi Nagar and had a vast teaching experience of more than 35 years, more than 22 years as Professor. She had many publications in national and international journals. Besides being a teacher for undergraduate and post graduate students, she had been post graduate Guide and Examiner in Pathology and Microbiology for many universities in India and Abroad.

She was also assigned foreign assignment and deputed by Ministry of External Affairs as Assistant Professor to faculty of medicine University of Al-Fateh Tripoli, Libya for 5 years and was also assigned charge as Director of Laboratories to various hospitals attached there.

After coming back to India, she later become Head of Combined Departments of Pathology, Microbiology and Blood Bank in Govt. Medical College, Jammu and later when Departments bifurcated for many years she worked as Head of Microbiology Department GMC Jammu. During her tenure as HOD Microbiology she was the first to start AIDS surveillance work in Jammu Province in the year 1986.

She got promoted as Principal and Dean, Govt. Medical College Srinagar in 2002 and was the first female Principal

of Govt. Medical College Srinagar from Jammu region. She remained as the most respected Principal there and as Dean she got immense appreciation on record for the work done by her at Lal Ded Memorial and SMHS Hospital, Srinagar.

Her other professional responsibilities included Dean faculty of Medicine Kashmir University, Member Governing Body J&K State Medical Faculty, Coordinating member Water Pollution Committee Jammu District, Member standing investigative Committee J&K state, Member secretary Hospital infection Control Committee GMC Jammu, Incharge AIDS reference centre Jammu province and member Indian Medical Association.

Due to her professional excellence, sincerity and hard work, she got two years further extension in her service and served as member board of professional entrance examinations J&K. After retiring from Govt. services she served as Professor and Head Microbiology Department ASCOMS and also was member of Indian Doctors for peace and development and kept continuing with her other social and family responsibilities with utmost commitment.

She was an inspirational figure .and highly honest and Her personality was highly positive and she remained an epitome of grace, determination, great willpower, immense love and wisdom.beloved vibrant sister, a very respectful dutiful daughter.

As in her own words quoted from the book "Quest of life" she said,

"One thing that has remained my principal of life, I have always been empathetic. Empathy is to see and feel through the eyes of the other. I have always been like that whether it was dealing with people professionally or in my personal life. To be truthful and hardworking was my way. To be helpful and dutiful is how I have lived.

My father was a great man and he had nurtured us since childhood to be always prepared to face harsh realities of life, to be respectful, truthful and never hurt anyone. My mother was a pious lady, she always taught us to remain modest. My parents always taught us to remain humble yet to be bold.

Let me tell you I follow the teachings of Guru Gobind Singh Ji and according to him we should never hurt others but if some injustice is done then we must also know how not to stay quiet. So I suppose that was the teaching imbibed in us, we were soft but had immense strength to face the hardships of life. I knew I would never do wrong to others and so nothing bad would happen to me.

With God's blessings I was married to a family where I was always loved and respected. The affection and regard I have received by each one of them has been a marvellous journey for me. This was a blessing. Being the youngest child in family, I was loved a lot by all much beyond the expression of words. When I got married I become the eldest daughter in law, my husband's brothers and sisters were young. They have literally stayed with me and I always considered them to be my own children. Even today if you ask me his brothers and sisters come first and then my own children. This is the sort of bond we share. The respect and love that I had received from one and all is beyond any comparison. I am immensely grateful for I have received the motherly love from each one of them throughout my life.

My husband has remained a caring husband and always been like a shield for me. He has been an ideal father. We have always taken decisions of life together. My children, their husbands who are also like my children and my grand children are extremely loving ones, I feel blessed that I have got such a life and family. I am a totally contented lady, most grateful to God. There is nothing more that I could ask for in life."

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