Original Article

A Insight to Hepatobiliary Disease: Comparative Study of De Ritis Ratio and R-Value.

Gobardhan Kathariya, Alka Singh, Rohit Gondwal, Vijay Chaudhary

Abstract

Background

The present study was aimed to compare De ritis ratio with the R value to establish a better marker for the assessment of hepatobiliary disease.

Methods

Fifty patients freshly diagnosed patients of Hepatobiliary disease (aged 20-55 years) were taken for the study along with thirty age and sex matched healthy controls. Serum AST, ALT and ALP were estimated by Simens Dimensions RxL De ritis ratio was calculated as AST/ALT and R-value was calculated as ALT / upper limit of normal (ULN) divided by ALP / upper limit of normal (ULN). The comparison of De ritis ratio and R- value were made in terms of independent 't' test, area under receiver operating characteristic curve.

Result & Conclusion

On comparing these both parameters on the basis of independent student "t" test it was found that the R-value is more significant that De ritis ratio. Further, the AUROC analysis, revealed that R-value covered a greater area than De ritis ratio. Altogether, these findings infer that R-value is a better parameter in assessment of hepatobiliary disease. Additionally, the R-value being a calculated parameter incurs no additional cost to the patients and health care system. Hence, the authors suggest the incorporation of the R-value in the routine liver profile panel for the better diagnosis of hepatobiliary disease.

JK-Practitioner2024;29(1):56-58

Introduction

The hepatobiliary tract is the target for a wide variety of infections. Hepatobiliary disease is defined as any disorder of the hepatobiliary system that impairs its normal function. According to World Health Organization (WHO), around 46% of the total global diseases and 59% of the mortality is due to chronic liver diseases[1]. In the Indian scenario, the liver diseases accounts as the tenth most common cause of death according to WHO [2].

The measurement of serum transaminase levels, such as alanine transaminase (ALT) and aspartate transaminase (AST) are an effective modality to detect the hepatic dysfunction, and their values can also be useful in the differential diagnosis of the hepatobiliary diseases [3]. ALT is mainly present in the cytosol of the liver and is more specific for liver disease whereas AST can be fractionated into both cytosolic as well as mitochondrial forms and thus, it is less specific for liver disease [4]. Generally, mitochondrial AST activity in the serum shows a marked increase in case of extensive liver cell degeneration and necrosis [5]. The ratio of the serum activities of AST and ALT was first described by Fernando De Ritis in 1957 and has been ever since known as the de Ritis ratio [6]. De Ritis described the AST/ALT ratio as a useful indicator of the aetiology of hepatitis. Increased value of the de Ritis ratio can be a vital biochemical clue in the alcoholic patients and for diagnosing alcoholic hepatitis; also, it can be a sensitive indicator of hepatobiliary disease [7].

The R-value; as per the American College of Gastroenterology guidelines is defined as serum alanine aminotransferase (ALT) / upper limit of normal (ULN) divided by serum alkaline phosphatase (ALP) / ULN and is helpful to discern the pattern of liver injury [8]. The scoring system of R- value is given as:

R > 5 indicates hepatocellular liver injury

R < 2 indicates cholestatic liver injury

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Indexed

EMBASE ,SCOPUS , IndMED ,ESBCO, Google Scholar besides other national and international databases

Cite this article as

Chaudhary V, Kathariya G, Singh A , Gondwal R. A Insight to Hepatobiliary Disease: Comparative Study of De Ritis Ratio and R-Value. Pract2024;29(1):56-58.

Full length article available at **Jkpractitioner.com** one month after publication

Keywords

Hepatobiliary disease, De ritis ratio, R value.

R 2-5 indicates mixed liver injury

In view of this, the present study was aimed to assess the usage of both De Ritis ratio as well as R-value in the evaluation of hepatobiliary disease risk.

Table 1: AST/ALT Ratio (de Ritis Ratio) in Liver Diseases

CONDITION	AST/ALT RATIO
Alcoholic liver disease	2.0-> 6.0
Organic toxic hepatitis	>2.0
Cirrhosis	1.4-2.0
Intrahepatic cholestasis	>1.5
Extra hepatic cholestasis	<1.4
Normal individuals	1.15
Chronic active hepatitis	1.3
Extra hepatic biliary obstruction	0.8
Acute viral hepatitis	0.5-0.8

Method

This is a case-control study conducted in the department of Biochemistry in MM Medical College & Hospital, Kumarhatti, Solan. Fifty consecutive patients were taken for the study.

Inclusion criteria:

Freshly diagnosed patients of Hepatobiliary disease (aged 20-55 years) who presented for the first time in the OPD

Exclusion criteria:

i. Patients of Diabetes mellitus as well as other metabolic syndrome.

ii. Kidney disorders and patients on follow up/ on extensive medical treatment.

Thirty age and sex matched healthy individuals were selected as controls. The study was duly approved by institutional ethical committee and informed consent was taken from all participants involved in the study.

Detailed history of the patients was recorded.

5 ml blood was collected in plain vial and serum was separated using standard protocol. After the collection of blood sample, Serum AST, ALT and ALP were estimated by Simens Dimensions RxL in the clinical biochemistry lab, Department of biochemistry, MMMCH, Solan. De ritis ratio was calculated as AST/ALT and R-value was calculated as ALT / upper limit of normal (ULN) divided by ALP / upper limit of normal (ULN).

Two levels (low and high) of internal quality control was run with every batch of patients' sample. External quality control with CMC, Vellore is being done.

Statistical Analysis

The significance between the groups was determined using independent student't' test. Significance is considered only at $p < 0.05$. To compare the predictive values of De ritis Ratio and R-value, ROC analysis was done. The area under ROC (AUROC) is considered a global performance indicator for a prognostic factor [9]. Greater area under curve of the ROC curve indicates better marker of the study.

Result

Among the 80 individuals who had participated in the study, females outnumbered males. De ritis ratio and R- value were calculated for all the subjects. The result (mean ± S.D) of De ritis ratio and R- value is illustrated in Table 2.

Table 2: Mean and S.D values of De ritis ratio and R-value

One-Sample Statistics

	N	Mean	Std. Deviation	Std. Error Mean
De-ritis ratio	80	.8556	.44260	.04948
R-value	80	3.09694	3.124826	.349366

One-Sample Test

	Test Value = 1					
	T	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
De ritis ratio	-2.918	79	.005	-.14438	-.2429	-.0459
R-value	6.002	79	.000	2.096937	1.40154	2.79233

**The significance of the parameter was determined by independent student 't' test using SPSS 23 version. P < 0.05 was considered statistically significant.*

To compare the predictive values of De ritis ratio and R-value, AUROC analysis was done and on comparison area under Receiver Operating Characteristic curve (AUROC) for R-value was found to be significantly higher (0.849 at 95% Confidence Interval; 0.761,0.936) than for De ritis ratio (0.547 at 95% Confidence Interval; 0.422,0.672) ***(Figure 1).***

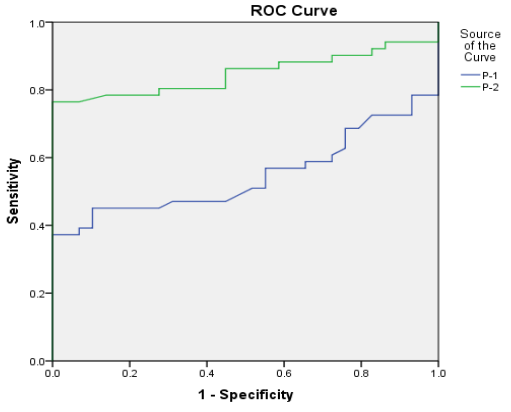
Figure 1: *Receiver Operating Characteristic curve for De ritis ratio and R value. P-1 denotes De ritis ratio and P-2 denotes R-value.*

Case Processing Summary

Group	Valid N (listwise)
Positive[a]	51
Negative	29

Larger values of the test result variable(s) indicate stronger evidence for a positive actual state.

a. The positive actual state is Control.



Discussion & Conclusion

The diagnosis of hepatobiliary disease relies on the parameters included in the liver function tests. Apparently, the AST/ALT (De Ritis) ratio as well as R- value has emerged as a useful indicator for the management of the hepatobiliary disease.

ALT and AST are usually requested when there is suspicion of liver disease and their release from liver cells to the circulation may indicate hepatocellular damage or death. In several researches it has been found that as the AST/ALT ratio elevates, the severity of underlying liver disease also increases [10- 13.] Gurung et al. [14] found in their study that the AST/ALT ratio increases in progressive impairment of the hepatic function and the findings of the study are also supported by the study conducted by Deb et al.[15].There are several studies which show that AST/ALT ratio over 1.5 to 2.0 strongly indicates alcoholic hepatitis state [16-18]. The R-value allows differentiation of the hepatocellular injury from the cholestatic/mixed liver injury and the best time to assess the ratio R is at the start of the liver injury[19].

In our study, on comparing these both parameters on the basis of independent student "t" test it was found that the R-value is more significant that De ritis ratio. Further, the AUROC analysis, revealed that R-value covered a greater area i.e. 0.849 (95% Confidence Interval; 0.761, 0.936) than De ritis ratio i.e. 0.547(95% Confidence Interval; 0.422, 0.672). This study has demonstrated the superiority of R-value over De ritis ratio in patients of hepatobiliary disease. Moreover, R-value being a calculated parameter incurs no additional cost to the patients and the health care system. Hence, it is necessary to consider R-value in the diagnosis as well as management of hepatobiliary disease.

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