DIAGNOSTIC ACCURACY OF A/A RATIO AND A/G RATIO FOR NONINVASIVE PREDICTION OF ESOPHAGEAL VARICES IN PATIENTS OF CIRRHOSIS WITH HEPATITIS B AND C

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ABSTRACT

Background: Non invasive marks of esophageal varices in cirrhotic patients of HBV and HCV infection would be of great importance. **Objective:** To determine diagnostic accuracy of Serum A/A ratio and A/G Ratio in detection of varices in Cirrhotic patients with Hepatitis B and C; taking endoscopic result as gold standard. **Methodology:** Study Design: Cross Sectional Study. Place and Duration of Study: Department of Medicine, Liaquat University of Medical & Health Sciences, Jamshoro and from 1st January to 30th June 2017. The source of data was patients of Cirrhosis due to HBV and/or HCV. Patients were admitted in Medical Unit-III, at LUMHS Hospital. Demographic data was collected, after informed consent of patient, vitals and relevant information about present complaint and presence of comorbidities was also recorded. Blood sample was collected to get Serum A/G ratio and AST/ALT and patients were shifted to Endoscopy unit at Medical Unit-I for invasive diagnosis of presence of Esophageal Varices. A/G ratio and A/A ratio was calculated as per operational definition and recorded in specifically designed performa for the study. Endoscopic results were compared with results of non-invasive predictors. **Results:** Out of 119 cases, 46.22% were female and 53.78% were male. Sensitivity, specificity, PPV, NPV and accuracy for AG ratio was found 79.1%, 28.6%, 78.3%, 29.6%, 67.2% respectively. Similarly, sensitivity, specificity, PPV, NPV and accuracy for AA Ratio was 81.3%, 17.9%, 76.3%, 22.7%, 66.3% respectively. **Conclusion:** Although, A/A Ratio and A/G Ratio were found to be sensitive to the presence of esophageal varices in cirrhotic patients with HBV and/ or HCV positive. Specificity of these markers is not qualifying to present these noninvasive markers as dependable markers to exclude the presence of esophageal varices in cirrhotic patients.

Key Words: Non-Invasive predictors, Esophageal Varices, Cirrhosis, AST/ALT, A/G RATIO.

INTRODUCTION

Esophageal variceal bleeding can lead to deadly complications in patients of Liver Cirrhosis with portal hypertension.[1] Early detection of esophageal varices (EV) is critical for the effective prevention and cure of variceal hemorrhage. Most of the patients with liver cirrhosis are being generally advised to undergo an evaluation of esophageal varices to assess the risk of bleeding through invasive endoscopies.[2,3]Endoscopy carries certain risks like cardio respiratory depression, aspiration pneumonia, perforation, bleeding, and infective endocarditis; thus endoscopy is contra indicated in severe shock, recent MI, unstable angina, cardiac arrhythmias, respiratory disorders, atlantoaxial sub luxation and visceral perforation.[4-6] On an average half of patients with cirrhosis have esophageal varices (EV), and only one third of patients with varices develop bleeding.[7-9] Acute upper GI bleeding is common medical emergency with 170/100,000 cases annually.[2] At least 50% patients who survive are at risk of bleeding during 1-2 years.[3] Esophageal varices is one of the most critical complications in liver cirrhosis with portal hypertension.[4] Timely detection of EV is very important and failure may lead to mortality up to 30-50%).[5] Previously endoscopy was only method to assess the presence of EV but with time and research non-invasive serological variable have been used like spleen size, thrombocytopenia, ascites, serum bilirubin, child pug class.[6] Serum AG Ratio and AST/ALT alter with liver insult and fibrosis, which is directly related to hepatic resistance and in turn results in portal hypertension that leads to the formation of esophageal varices.[7,8] People with history of early age Hepatitis B virus have an increased chance of protracted infection and are at highest risk of cirrhosis. Blood exposure using injections with non-sterile equipment, transfusion of contaminated blood, unsafe injection practices account for 21 million hepatitis B infections and 2 million Hepatitis C infections every year.[9-11] Liver cirrhosis is the end result of any injury that causes fibrosis followed by regenerative nodules may be reversible if cause is removed. Cirrhotic nodule may abnormally relate portal tracts with different veins may be preexisting or newly formed several mechanisms do take part in liver nodularity that are regrowth after necrosis, dissection of lobules by fibrosis, and remodeling associated with altered vascular relationships are probably all operative.[12] Most common causes of cirrhosis include hepatitis B and C and use of alcohol. Traditionally, liver cirrhosis and allied vascular disorders are termed as irreversible but topical research suggest regression and even reversal in cirrhosis is quite possible.[13,14] The objective of this study was to determine diagnostic accuracy of A/A ratio and Serum A/G ratio

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in detection of esophageal varices in cirrhotic patients with Hepatitis B and or C; taking endoscopic result as gold standard.

METHODOLOGY

This was cross sectional study, conducted from 1st January to 30th June 2017. Study subjects: Cirrhotic patients with Hepatitis B or and C with >6 months duration, between ages of 30-60 years, with child pug class A and B were included. Patients of cirrhosis, who have been previously suffered from attacks of hematemesis and have undergone screening endoscopy and cirrhosis due to other causes like alcohol, drug toxicity, auto immune and metabolic liver disease were excluded. The source of data was patients who reported suffering from cirrhosis due to HBV and/or HCV. Patients were admitted in Medical Unit-III, at Liaquat University of Medical and Health Sciences Hospital, Jamshoro. Demographic data was collected, after taking informed consent of patient; vitals and relevant information about present complaint, duration of diseases and presence of comorbidities was recorded. Every patient had undergone through general physical and abdominal examination to get findings of hepatic encephalopathy and ascites. Patients were also gone through abdominal ultrasonography to get confirmation for cirrhosis and ascites. Blood sample was collected to get Serum A/G ratio, AST/ALT ratio, bilirubin and, PT to get CTP class. Endoscopy was done to get the gold standard data for further comparison of results of study. AG ratio and AAR ratio was calculated. Data was entered in and analyzed by using SPSS version 20. Ethical approval was sought from Hospital Ethical Committee.

RESULTS

There were 119 cirrhotic patients with Hepatitis B 44 (37%) and C 72 (60.5%) and 3 (2.5%) both HBV and HCV and with Child-Pugh class A and B were included in this study. These patients had more than six months' duration of disease. The mean age of the patients was 44±8 years. Regarding Child-Pugh class, 55.46% patients were observed in class A and 44.54% were in class B and 76.5% patients were positive for presence of varices on endoscopy, while 23.5% reported with absence of varices. Grade II varices were most commonly observed i.e. 35.29%.

Table I: Diagnostic accuracy of serum A/G ratio in detection of esophageal varices

Parameter	Endoscopic findings		Total
	Varices +Ve	Varices -Ve	
A/G Ratio (≤1)	72 (TP)	**20 (FP)**	92 (77.3%)
A/A Ratio (≤1)	74 (TP)	**23 (FP)**	97 (81.5%)
A/G Ratio (>1)	19 (FN)	**8 (TN)**	27 (22.7%)
A/A Ratio (>1)	17 (FN)	**5 (TN)**	22 (18.5%)
A/G Ratio		**A/A Ratio**	
Sensitivity	79.1%	**Sensitivity**	81.3%
Specificity	28.6%	**Specificity**	17.9%
PPV	78.3%	**PPV**	76.3%
NPV	29.6%	**NPV**	22.7%
Accuracy	67.2%	**Accuracy**	66.3%

Table II: Diagnostic accuracy of Serum A/G And A/A Ratio in Detection of Varices in Cirrhotic Patients by Hepatitis B and C

Hepatitis	Parameters	Endoscopic findings		Total	P-Value
		Varices +Ve	Varices -Ve		
HBV	A/G Ratio (≤1) A/G	27 (TP)	5(FP)	32	0.045
	Ratio (>1)	6(FN)	6(TN)	12	
	Total	**33**	**11**	**44**	
	A/A Ratio (≤1)	28 (TP)	7(FP)	35	0.19
	A/A Ratio (>1)	5(FN)	4(TN)	9	
	Total	**33**	**11**	**44**	
HCV	A/G Ratio (≤1)	42 (TP)	15(FP)	57	0.49
	A/G Ratio (>1)	13(FN)	2(TN)	15	
	Total	**55**	**17**	**72**	
	A/A Ratio (≤1)	44 (TP)	16(FP)	60	0.27
	A/A Ratio (>1)	11(FN)	1(TN)	12	
	Total	**55**	**17**	**72**	
A/G Ratio	**For HBV**	**For HCV**	**A/A Ratio**	**For HBV**	**For HCV**
Sensitivity	81.8%	76.4%	**Sensitivity**	84.4%	80%
Specificity	54.5%	11.8%	**Specificity**	36.4%	5.9%
PPV	84.4%	73.7%	**PPV**	80%	73.3%
NPV	50%	13.3%	**NPV**	44.4%	8.3%
Accuracy	75%	61.1%	**Accuracy**	72.7%	62.5%

Out of 119 cases, 46.22% were female and 53.78% were male. Sensitivity, specificity, PPV, NPV and accuracy for AG ratio was found 79.1%, 28.6%, 78.3%, 29.6%, 67.2% respectively.

Similarly, sensitivity, specificity, PPV, NPV and accuracy for AA Ratio was 81.3%, 17.9%, 76.3%, 22.7%, 66.3% respectively. Diagnostic accuracy of AG ratio and AAR for HBV was above 70% and HCV was above 60%. All results are represented by Tables I, II and III.

Table III: Diagnostic Accuracy of Serum A/G and A/A Ratio in Detection of Child Pugh Classification In Cirrhotic Patients With Hepatitis B And C

Child Pugh Class	Parameter	Endoscopic findings		Sum	P-Value
		Esophageal Varices (+)	Esophageal Varices(-)		
Class A	A/G Ratio (≤1)	34(TP)	10(FP)	44	0.55
	A/G Ratio (>1)	15(FN)	7(TN)	22	
	Total	49	17	66	
	A/A Ratio (≤1)	35 (TP)	13(FP)	48	0.76
	A/A Ratio (>1)	14(FN)	4(TN)	18	
	Total	49	17	66	
Class B	A/G Ratio (≤1)	38 (TP)	10(FP)	48	0.99
	A/G Ratio (>1)	4(FN)	1(TN)	5	
	Total	42	11	53	
	A/A Ratio (≤1)	39 (TP)	10(FP)	49	0.99
	A/A Ratio (>1)	3(FN)	1(TN)	4	
	Total	42	11	53	
A/G Ratio	For Class A	For Class B	A/A Ratio	For Class A	For Class B
Sensitivity	69.4%	90.5%	Sensitivity	71.4%	92.9%
Specificity	41.2%	9.1%	Specificity	23.5%	9.1%
PPV	77.3%	79.2%	PPV	72.9%	79.6%
NPV	31.8%	20%	NPV	22.2%	25%
Accuracy	62.1%	73.5%	Accuracy	59.1%	75.4%

DISCUSSION

The research contributions in past provide the effectiveness of various parameters including ascites, serum albumin, Child's class, portal vein diameter, platelet count, spleen diameter ratio, spider naevi, splenomegaly, prothrombin time/activity, platelet count and serum bilirubin as important predictors to identify the presence of EV.[15,16,17] However, there are very few studies on diagnostic accuracy of AST/ALT ratio for presence of Varices. Treeprasertsuk et al[17] presented a reviewing study of patients developed varices with high AST/ALT ratio with patient with high AST/ALT ratios but have not developed varices (ratio: 1.8 versus 1.0, P < 0.0001). Nyblom et al,[16] used AST/ALT ratio to envisage chance of cirrhosis, he further had prospective studies to gauge the effectiveness of AST/ALT in envisaging the chance of EV. Studies have reached to conclusion that an AST/ALT ratio greater than 1.12 may be suggestively correlated with the presence of varices at initial endoscopy.[16-17] The limit is valid with Specificity=87%, Sensitivity = 47%, NPV=89.2%, PPV= 42.3% and AUROC=0.69. In a study,[18] authors have reached to a different cutoff i.e. AST/ALT>10 may be suggestively correlated with the presence of EV. This cutoff is valid with Specificity=89%, Sensitivity = 68%, NPV=83%, PPV= 77% and AUROC=0.83. Generally, AST/ALT ratio classify 81% patients with varices.

There are no published studies on diagnostic accuracy of A/G ratio for presence of Varices. In our study there were 119 cirrhotic patients having Hepatitis-B and Hepatitis-C with more than six months' duration with child pug class A and B were included in this study. There were 44 (37%) cases with hepatitis B, 72 (60.5%) were hepatitis C and 3 (2.52%) cases with both hepatitis B and C. Regarding Child-Pugh class, 55.46% patients were observed in class A and 44.54% were in class B. Endoscopic positive finding, 76.5% (91/119) cases were with esophageal varices while 23.5% (28/119) were showing negative sign of esophageal varices. Positive esophageal varices with respect to grade were found as 15.3%, 35.29%, 13.45% and 12.61% respectively for G-I, G-II, G-III and G-IV

CONCLUSION

A/A Ratio and A/G Ratio are reasonably sensitive to the presence of Esophageal Varices in Cirrhotic patients with HBV or HCV positive but the specificity of A/A Ratio and A/G Ratio is not qualifying to present these non-invasive markers as dependable markers to suggest the presence of Esophageal Varices in Cirrhotic patients.

REFERENCES

1. Kenneth RM. Gastrointestinal Disorder. CURRENT Medical Diagnosis and Treatment.50th ed. McGraw Hill. 2009: 487-581.
2. Blatchford O, Davidson LA, Murray WR, Blatchford M, Pell J. Acute upper gastrointestinal haemorrhage in west of Scotland: case ascertainment study. BMJ 1997; 315(7107):510-4.
3. Yu BAI, Zhao-shen LI. Management of variceal hemorrhage: current status, Chinese Medical Journal, 2009: 122(07): 763-5.
4. Tarzamni M K, Somi M H, Farhang S, Jalilvand M. Portal hemodynamic as predictors of high risk Esophageal Varices in cirrhotic patients, World J Gastroenterology. 2008; 14(12):1898-902.
5. Suzuki A, Mendes F, Lindor K. Diagnostic model of esophageal varices in alcoholic liver disease, Eur J Gastroenterol Hepatol. 2005; 17(3):307-9.
6. Fontana RJ, Lok ASF. Noninvasive monitoring of patients with Chronic Hepatitis C. International Journal of Hepatology. 2002; 36(5):S57-S64.
7. Nagula S, Jainc D, Groszmann RJ, Garcia TG. Histological Hemodynamic correlation in Cirrhosis- a histological classification of severity of cirrhosis.J Hepatol.2006; 44: 111-17.

8. WHO- Medical center; Hepatitis B, Fact sheets. URL:www.who.int/mediacentre/factsheets.
9. WHO: Best Practices for Injections and Related Procedures Toolkit. URL: www.who.int/injection_safety/9789241599252/en/.
10. WHO; Viral Hepatitis B; A62/22; URL: www apps.who.int/gb/ebwha/pdf_files/A62/A62_22-en.pdf
11. WHO; Viral Hepatitis B; A63/15; URL:www.who.int/gb/ebwha/pdf_files/WHA63/A63_R18-en.pdf.
12. P. P. Anthony et al. The morphology of cirrhosis' Recommendations on definition, nomenclature, and classification, Journal of Clinical Pathology, 1978:31: 395-414.
13. Desmet VJ, Roskams T. Cirrhosis reversal: A duel between dogma and myth. J Hepatol. 2004;40:860–7.
14. Wanless IR, Nakashima E, Sherman M. Regression of human cirrhosis. Morphologic features and the genesis of incomplete septal cirrhosis. Arch Pathol Lab Med. 2000;124:1599–607.
15. Kara R, Robert S, Gerri M, Adam L, Andrew A, Jan F. Towards Noninvasive Detection of OesophagealVarices. International Journal of Hepatology. 2012; 1-9.
16. H. Nyblom, E. Bj¨ornsson, M. Simr´en, F. Aldenborg, S. Almer, and R. Olsson, "The AST/ALT ratio as an indicator of cirrhosis in patients with PBC. Liver International 2006: 26:840–845.
17. S. Treeprasertsuk, K. V. Kowdley, V. A. C. Luketic et al. The predictors of the presence of varices in patients with primary sclerosing cholangitis. Hepatology, 2010: 51(4):1302–1310.
18. L. Cast´era, B. L. Bail, F. Roudot-Thoraval et al. Early detection in routine clinical practice of cirrhosis and oesophagealvarices in chronic hepatitis C: comparison of transient elastography (FibroScan) with standard laboratory tests and non-invasive scores," Journal of Hepatology, 2009,50:1: 59–68.

Article Citation: Jabeen S, Qadir A, Tufail B, Ahmed S. Diagnostic accuracy of A/A ratio and A/G ratio for noninvasive prediction of esophageal varices in patients of cirrhosis with hepatitis B and C. JSZMC 2018;9(3): 1476-1479