CORRELATION BETWEEN SERUM ASCITES ALBUMIN GRADIENT (SAAG) AND ESOPHAGEAL VARICES IN PATIENTS HAVING CHRONIC LIVER DISEASE

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ABSTRACT

Objective: To determine the correlation between level of serum-ascites albumin gradient (SAAG) grading of esophageal varices (EV), in patients having chronic liver disease.

Study Design: Prospective, observational and a cross sectional study.

Place and Duration of Study: Medical Unit III, Sandeman Provincial Hospital Quetta, form Oct 2015 to Apr 2016.

Material and Methods: Patients with diagnosis of cirrhosis were enrolled. Detailed history, physical examination and biochemical measurements were recorded. Patients underwent upper GI endoscopy for grading of esophageal varices.

Results: Eighty patients fulfilling the inclusion criteria were included in this study. There were 56 (70%) males and 24 (30%) females. The mean ± standard deviation age of study population was 44.86 ± 12.319 years. On analysis of age group it was observed that 40 (50%) patients were less than 40 years of age, 73 (91.25%) patients had SAAG value above 1.1 mg/dl. On analysis of correlation of SAAG with the grade of varices, a strong association was observed (r=0.631).

Conclusion: An association, in the patients having ascites, between the level of SAAG and the development of esophageal varices is present. Patients having a high SAAG were found with more commonly present Esophageal varices thus establishing a high probability of finding EV in patients with higher values SAAG.

Keywords: Chronic liver disease, Esophageal varices, SAAG, Upper GI endoscopy.

INTRODUCTION

Chronic liver disease is one of the common diseases prevailing in South Asia. The increasing prevalence needs to be evaluated and updated for hepatitis B and C, the main causative agents for chronic liver disease, as increasing number people are being affected by this dangerous disease. The overall burden of Hepatitis B and C associated chronic liver disease has also increased in Pakistan[1].

HBV and HCV are the most important etiologies of chronic liver disease leading to cirrhosis. Patients with cirrhosis are eventually confronted with the development of esophageal varices due to portal hypertension and esophageal variceal bleeding is the most common and potentially lethal complication of liver cirrhosis, occurring at an incidence of 30-40% and carrying a mortality of rate of 30-50%. Two third of survivors will bleed again within a period of six months if not treated with prophylactic beta blockers or endoscopic therapy. Those receiving such therapy are less likely to bleed and that is why screening such patientsfor esophageal varices by periodic endoscopy is recommended, which can have cost implications[2,3].

Several retrospective studies have shownthat SAAG and serum albumin as probable non-invasive biochemical markers of esophageal varices in cirrhotic patients and SAAG has been concluded an indirect biochemical marker in detecting the occurrence and grades of esophageal varices as a n endoscopic parameter of portal hypertension. The SAAG is simple and minimally invasive technique which has a validity rate of 90% in detecting ascites due to portal hypertension[1,4].

SAAG is an excellent biochemical parameter in differentiating ascites due to portal hypertension from other causes of ascites and ascites with high SAAG is indirectly associated with the

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presence of esophageal varices in cirrhotic patients[2,5].

A serum ascites albumin gradient (SAAG) value >1.1g/dl, means that the cause of ascites is most likely to be portal hypertension; this is usually in the setting of cirrhosis. When the gradient <1.1g/dl,the work up for infectious or malignant causes of ascites should be done[6].

Patients with cirrhosis often are subjected to screening endoscopy for varices so that prophylactic therapy and/or follow up can be planned. Routine endoscopic screening of all cirrhotic patients with or without varices carries health service cost implications. In a province like Baluchistan it might be cost effective to identify those patients who would benefit most from routine screening. In order to reduce the increasing burden that endoscopy units will have to bear, the present study is not only going to help in improving cost effectiveness of routine endoscopy but also optimizing prophylactic therapy in the form of beta blockers by the clinicians. The study will allowthe use of SAAG as a prior indicator, although indirect, which would help in estimating the complications of portal hypertension in the form of esophageal varices. Thus keeping away from needless interference and avoiding the risk of bleeding, infections and other complications during screening endoscopy.

PATIENTS AND METHODS

This cross sectional study was conducted in the medical unit 3 of Sandeman Provincial Hospital Quetta from October 2015 to April 2016. In this study 80 cirrhotic patients were included. The subjects were chosen by non-probability consecutive sampling, all having chronic liver disease with ascites visiting Medical OPD and emergency department of SPH Quetta fulfilling the inclusion criteria which included classical findings of chronic liver disease on clinical examination, deranged liver biochemistry and ultrasonography findings consistent with cirrhosis of liver. Exclusion criteria incorporated all those patients having ascites due to etiologies other than cirrhosis like congestive heart failure, abdominal tuberculosis, hepatocellular carcinoma, renal failure, intra-abdominal malignancy. The criteria were strictly followed to control the confounder and bias in the study. Informed consent was taken from the patients before including them in the study. The study was conducted after taking approval from ethical review committee of the institute. The whole study protocol was described to the patient so that confidence could be gained. The attendant of the patient accompanied him/her at all times in regard with ethical issue. Female patients were provided full privacy during the procedure. The information of the patient was kept confidential. Patients were subjected to laboratory investigations i.e, complete blood count, liver function tests, serum albumin, prothrombin time and viral profile (HBsAg, anti HCV), diagnostic tap of the ascitic fluid under aseptic measures, ascitic fluid analysis: cell type, cell count, sugar and ascitic albumin. Serum ascitic-albumin gradient was calculated. Abdominal ultrasound was done to look for altered echo texture of liver parenchyma, ascites, size of the portal vein and splenomegaly. Upper GI endoscopy of all patients was performed in med unit III SPH Quetta, by a consultant gastroenterologist, again after a written consent by the patient. Patients werepre medicated with

Table-I: Analysis of age of study population.

	Minimum	Maximum	Mean	Std. Deviation
Age	20	75	44.86	12.319

Table-II: Analysis of various variables of study population.

	Minimum	Maximum	Mean	Std. Deviation
SAAG	0.60	4.60	1.905	0.7955
Variceal grade	1	4	3.075	1.040

intravenous Hyoscine and Xylocain spray as a topical anesthetic and evaluated for the occurrence and grades of esophageal varices.

Observer was blinded to SAAG value at the time of endoscopy to avoid bias of the results. The correlation between SAAG value and esophageal varices (occurrence and grades) was examined to determine the applicability of the

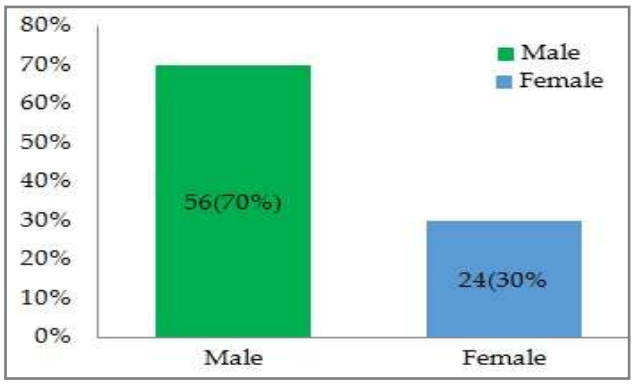

Figure-I: Gender wise distribution.

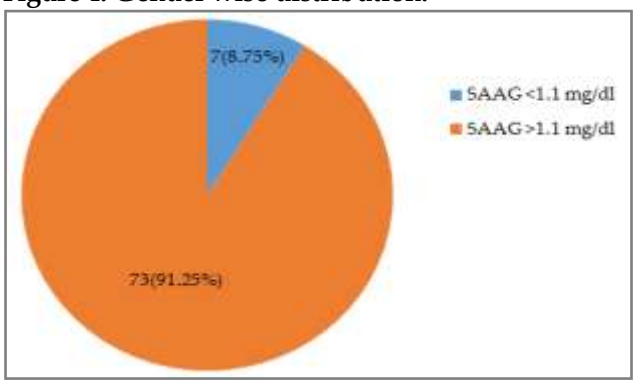

Figure-II: Frequency of saag value.

method to Baluchistan population. Basic demographic information, SAAG value and endoscopic findings were recorded on a predesigned proforma (Annex-I).

Statistical Package for the Social Sciences (SPSS) for Windows version 17.0 was used for the purpose of statistical testing of data. Descriptive statistics: frequencies and percentages were computed for categorical variables like gender, level of SAAG and grade of esophageal varices. Mean and standard deviation were used to estimate quantitative variables like age. Pearson Correlation Coefficient was used to measure the linear correlation between SAAG and grade of esophageal varices. It gave a result of -1 to +1, where +1 is total positive correlation, 0 is no correlation, -1 is total negative correlation. Effect modifier was controlled through stratification of age & gender to see the effect of these variables on outcome variable.

RESULTS

Eighty patients fulfilling the inclusion criteria were enrolled in this study.

There were 56 (70%) males and 24 (30%) females (fig-1). The mean ± standard deviation age of study population was 44.86 ± 12.319 years (table-I).

On analysis of age group it was observed that 40 (50%) patients were less than 40 years of age, 73 (91.25%) patients had SAAG value above 1.1 mg/dl (table-II).

Positive correlation of SAAG with variceal grade was observed (table-III).

Stratification of age and gender is mentioned in tables III through X.

DISCUSSION

Ascites, defined as accumulation of fluid in the peritoneal cavity, might be an association of several diseases. Ascites in patients, due to any disease, poses issues in diagnosis and therapy[7-9]. Biochemical, microbiological and cytological analysis of ascitic fluid is very important and mainstay for differential diagnosis among the diseases causing ascites. Conservatively, ascites has been categorized as being either transudative or exudative, based upon the ascitic fluid total protein concentration[10,11], the ascitic fluid to serum ratio of total protein[12,13], or the ascitic fluid to serum ratio of lactic dehydrogenase[14].Despite the presence of these mentioned parameters, none are effective in distinguishing the types of ascitic fluid but the serum-ascites albumin concentration gradient (SAAG) has been declared superior, in comparison with the exudatetransudate concept in distinguishing by several studies. The classification has a validity rate of 90% or more in detecting the ascites as a complication of portal hypertension[15-17]. The

classification of ascitic fluids according to the absence or presence of portal hypertension (PHTN) has been made possible owing to the high precision and minimal invasiveness of SAAG[7,16-23]. It is repeatedly highlighted in the literature that the SAAG is an indirect indicator of PHTN[1,16,17,19-23] and that a direct relationship probably exists between SAAG and different PHTN measurements such as the portal pressure gradient[1], net portal pressure[19,20] or corrected portal pressure[17]. These quantifications can be procured only by invasive measures, which are associated with cost implications and hence not feasible in most centers in the resources strained countries. Esophageal varices have proven to be an endoscopic parameter of portal hypertension in cirrhotic patients. The indirect way to assess the presence PHTN is by detection of esophageal varices (EV). A number of potential modalities exist to assess the status of EV including barium

Table-III: Analysis of corelation of saag with variceal grade.

		SAAG	Variceal Grade
SAAG	Pearson Correlation	1	0.631**
	Sig. (2-tailed)		0.000
	N	80	80
Variceal Grade	Pearson Correlation	0.631**	1
	Sig. (2-tailed)	0.000	
	N	80	80

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

Table-IV: Analysis of data with age stratification.

Age Group			SAAG	Variceal Grade
Less than 30	**SAAG**	Pearson Correlation	1	0.665**
		Sig. (2-tailed)		0.000
		N	40	40
	Variceal Grade	Pearson Correlation	0.065**	1
		Sig. (2-tailed)	0.000	
		N	40	40
30 and Above	**SAAG**	Pearson Correlation	1	0.605**
		Sig. (2-tailed)		0.000
		N	40	40
	Variceal Grade	Pearson Correlation	0.605**	1
		Sig. (2-tailed)	0.000	
		N	40	40

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

Table-V: Analysis of data with gender stratification.

Gender			SAAG	Variceal Grade
Male	SAAG	Pearson Correlation	1	0.592**
		Sig. (2-tailed)		0.000
		N	56	56
	Variceal Grade	Pearson Correlation	0.592**	1
		Sig. (2-tailed)	0.000	
		N	56	56
Female	SAAG	Pearson Correlation	1	0.731**
		Sig. (2-tailed)		0.000
		N	24	24
	Variceal Grade	Pearson Correlation	0.731*	1
		Sig. (2-tailed)	0.000	
		N	24	24

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

radiography, ultrasonography and upper gastro-intestinal endoscopy. The upper gastrointestinal endoscopy is currently the best reliable procedure available to diagnose presence of EV and hence, PHTN[24]. The quantification of the portal pressure gradient (PP-GRAD) and the portal pressure (PP), as demonstrated by previous research, have been deemed most appropriate hemodynamic variables for assessing the growth of PHTN and its complications in the form of esophageal varices[20-24]. The SAAG has been found having correlation with different PHTN measurements, such as PP-GRAD, net portal pressure[19-20], or corrected portal pressure. In 1990, Kajani *et al*[24] investigated the correlation in patients with alcoholic liver disease and with cirrhosis due to other causes seperately[16]. In this study, a correlation was found between SAAG and either portal pressure or esophageal varices in patients with cirrhosis due to alcohol abuse. But in the patients with non-alcoholic cirrhosis, no correlation was found between SAAG and portal pressure, while the correlation between SAAG and the grade of varices was found to be weaker. Despite these controversial results and discrepancies, the SAAG owes an ability to indicate the existence or absence of PHTN with an accuracy of 96.7%[7-9,16,23]. This test possess an accuracy despite of ascitic fluid infection, diuresis, therapeutic paracentesis, albumin infusion, and etiology of liver diseases[7-9]. In a study performed by Hoefs *et al*. in 1983, which showed that an excellent correlation exists between portal hypertension and SAAG[25]. In this study, a numeric formula was established for the first time between portal hypertension and SAAG. While it was established in this formula that $p<0.05$, the numeric formula was as follows: PP-GRAD=7.08 X (SAAG+3.62).

In this study a clear cut correlation between SAAG levels and the growth of esophageal varices in patients having cirrhosis due to chronic liver disease was found. Patients having a high SAAG were the ones only found with esophageal varices thus establishing a high probability of finding EV in patients with higher values SAAG.

Further more our study shows that grades of esophageal varices were significantly related with the degree ($p<0.01$) of SAAG with a Pearson relationship of r=0.55 ($p<0.01$) so as the size (grade) of esophageal varices increases, the degree of SAAG also increases. This suggests that the size of esophageal varices has a strong association with the degree of SAAG. This is in contrast to the study conducted by Torres *et al* which concluded that size of esophageal varices in patents with ascites and degree of SAAG not related with high SAAG. This conflict may be due to variations in different populations and due to deference in the prevalence of cirrhosis and extent of liver damage as the studies of Demirel *et al*[20] & Torres *et al*[21] were conducted on Western population where the main causative factor of liver cirrhosis is alcoholism while our study included Pakistani patients in whom the chronic viral hepatitis B and C were the main etiological factors for the development of liver cirrhosis. Poor nutritional status of Pakistani patients may be another contributing factor.

This fact is supported by similar results of study by Masroor *et al*[22] conducted on Pakistani population. In addition, Torres *et al*[21] detected a range of SAAG ≥1.435 ± 0.015 g/dl as a requir-able mean to predict the occurrence of EV. This value is very much similar to our study which gives the value of SAAG ≥1.905 ± 0.7955g/dl as accurate perfect markers of occurrence of EV.

To summarize if we take into account the association between SAAG and PP-GRAD, it can be reasonably stated that the measurement of SAAG, owing to it being a minimally invasive technique, is a significant indirect indicator in assessing PHTN and its complication such as EV. However, since the variance in the correlations of and the limitations of SAAG and PHTN measurements afore mentioned cannot be ignored, the SAAG should be considered as a preliminary and indirect quantification of PHTN. Our findings help us conclude that the presence of EV in patients with ascites is only associated with patients with High SAAG. Similarly, the presence but not the size of the EV in patients

with ascites and High SAAG is directly related to the degree of SAAG.

CONCLUSION

There exists a significant relationship between the level of SAAG and the development of esophageal varices in patients with chronic liver disease. There was a higher probability of finding higher grades of EV in patients with higher values of SAAG.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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