ORIGINAL ARTICLES

CAUSES OF ASCITES AND ITS CORRELATION WITH SERUM-ASCITES ALBUMIN GRADIENT IN PATIENTS ADMITTED AT MEDICAL WARDS IN A TERTIARY HOSPITAL IN GHANA.

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Abstract

Objective: Ascites can be classified depending on whether it results from portal hypertension (PH) or non-portal hypertension (NPH) causes. This classification is relevant because the modes of evaluation and management are different for these two groups. Serum-ascites albumin gradient (SAAG) has been proposed in many studies to categorise ascites better than ascetic fluid total protein. This has not been determined in Ghanaian patients with ascites. The aim of this study was to determine the aetiology of ascites and to assess the performance of SAAG in the classification of portal versus non-portal hypertension ascites among patients admitted to a tertiary hospital in Ghana.

Methodology: A cross-sectional study was conducted at the Korle-Bu Teaching hospital, where 140 patients with ascites were recruited within the study period. Data on socio-demography, clinical features, and results of relevant laboratory investigations and imaging studies were collected using pretested questionnaires

Results: The mean age of patients was 44.7±13.2 years. Chronic liver disease (CLD) was the major cause of ascites in this study representing 73.57%. SAAG had a sensitivity of 91.59%, positive predictive value of 95.15% and diagnostic accuracy of 90.0% in classifying ascites as due to a PH or NPH.

Conclusion: CLD was the major cause of ascites in Ghanaian patients. SAAG has satisfactory diagnostic accuracy in differentiating ascites related to PH from NPH causes. This could be used as a first line investigation in the aetiological diagnosis of ascites for initiation of prompt treatment.

Key words: *ascites, serum-ascites albumin gradient, portal hypertension, non-portal hypertension.*

Introduction

Ascites is defined as the pathological accumulation of fluid in the peritoneal cavity and may occur as a result of various causes.[1] Ascites can develop due to conditions which either directly involve the peritoneum (infection, malignancy), or occur remote from the peritoneum (liver disease, heart failure, hypoproteinaemia, kidney disease). Its causes have been well described in Western countries. Cirrhosis is the commonest cause of ascites in the Western world (75%), followed by peritoneal malignancy (12%), cardiac failure (5%) and peritoneal tuberculosis (2%).[2] In sub-Saharan Africa especially Ghana, ascites is a common symptom for which patients seek medical attention in internal medicine departments, however data pertaining to admissions as a result of ascites and its associated causes remains under documented.

Previous studies from sub-Saharan Africa countries described the prevalence of ascites in internal medicine departments to be between 3.6 to 10.8%.[3-5] Ascites causes significant discomfort for patients, particularly those with severe ascites due to difficulty in mobility and in carrying out activities of daily living, as well as social stigma associated with the condition. Successful treatment depends on accurate diagnosis of its cause, which may broadly be classified into PH and NPH causes. This is important because the mode of evaluation and management has some variation based on this classification. In the past, PH ascites was

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distinguished from the NPH causes by determining whether the ascitic fluid is a transudate or an exudate, by the estimation of the ascitic fluid total protein (AFTP). Ascites with AFTP of ≥25gm/L was considered to be exudative and <25gm/L as transudative.[6-8] This classification is however unable to correctly identify the aetiological factors responsible for its causation and has been challenged on various occasions in different clinical conditions especially in cirrhotic patients on prolonged diuretic therapy, cardiac ascites, patients of malignant ascites, spontaneous bacterial peritonitis, and sometimes even in patients with normal ascitic fluid parameters.[9] Moreover, it offers little insight to the pathophysiology of ascitic fluid formation.[9]

A more meaningful system has been developed, on the basis of the amount of albumin in the ascitic fluid in comparison to the serum albumin level. This system is called the serum-ascites albumin gradient or SAAG. Ascites due to PH has a SAAG value generally greater than 11gm/l. On the other hand, the SAAG value for ascites that is not related to portal hypertension has a value lower than 11gm/l. The SAAG is accurate in 96.7% cases even in the presence of diuretic and intravenous infusions of albumin.[8] However, it is inaccurate in cases of mixed ascites. There is a dearth of knowledge about the causes of ascites and its relation to SAAG in Ghana. This study was therefore to determine the causes of ascites among patients admitted to a tertiary hospital in Ghana, and to assess the performance of SAAG in the classification of portal versus non-portal hypertension ascites in the Ghanaian context.

Materials and Method

Study design

A formal approval of this study was obtained from the Ethical and Protocol Committee of the University of Ghana medical School. This study was conducted in accordance with the Helsinki Declaration. The research design was a cross-sectional hospital-based study, carried out at the Department of Medicine, Korle-Bu Teaching Hospital (KBTH), Accra, from 25th March 2016 to 25th November, 2016. One hundred and fourty (140) patients with ascites admitted to the medical block of KBTH were consecutively recruited. All adult patients above 18 years with ascites who provided informed consent were included. Diagnosis of ascites was made based on the clinical features of abdominal distension, the presence of shifting dullness and/or positive fluid thrill. This was subsequently confirmed by diagnostic paracentesis or an abdominal ultrasound scan**.**

Data Collection and Measurements

The study focused on socio-demographic data and clinical history by trained research personnel. Patients' medical records were additionally reviewed. Physical examination for clinical features of liver cirrhosis, congestive heart failure, nephrotic syndrome, lymphoma, abdominal tuberculosis, chronic kidney disease, and other causes of ascites prevalent in our setting was performed. Ascites was graded as mild (detectable only on ultrasound), moderate (visible moderate symmetrical abdominal distension), or severe (marked abdominal distension). A sample of 15mls of venous blood was taken for haematological, biochemical and serological investigations. Hematological and biochemical workup included full blood count, liver chemistry and function test blood urea and electrolyte and urine routine examination. All patients were tested for Hepatitis B surface antigen (HBsAg) and anti-bodies to hepatitis C virus (anti HCV-Ab) to determine the causes of liver cirrhosis. Abdominal paracentesis was performed using an aseptic technique at the right or left iliac fossa, 3cm above and 3cm medial to the anterior superior iliac spine. Approximately 10mls of ascitic fluid was collected using a sterile syringe and 5mls was inoculated into a sterile ethylenediaminetetraacetate (EDTA) bottle and sent to the laboratory for cell count and differentials, albumin and protein. Further tests were performed on the ascitic fluid if there was a need for further evidence of the cause of ascites including adenosine deaminase, lactate dehydrogenase, serum amylase, PH, acid fast bacilli and cytology. Ultrasound Scan: All patients underwent an abdominal ultrasound scan and the following details were recorded: maximum vertical span of the liver; nodularity of liver surface; spleen size (length of its longest axis); and presence of ascites. The size of the kidneys and the presence or absence of corticomedullary differentiation were also determined. Enlarged abdominal lymph nodes and any other masses seen were also noted. Additional investigations: Participants underwent further diagnostic investigations to ascertain the cause of ascites. These included but were not limited to chest x-ray (heart failure, lymphoma, TB), electrocardiography and echocardiography (heart failure), abdominal CT scan (malignancy), sputum for acid fast bacilli and Gene Xpert (TB).

Statistical Analysis

Data were entered, compiled, and analyzed using statistical package for the social sciences (SPSS) 16. Descriptive statistics were generated on patient demographics, clinical features and causes of ascites. Chi square was used to determine the level of association. A p-value less than 0.05 was considered significant. The diagnostic accuracy of the tests used in this study was calculated as the sum of true positive

plus true negative results divided by the total number of cases.[10]

Results

A total of 140 patients with ascites were recruited for the study with a mean age of 44.7±13.2 years (age range 18 to 74 years). Seventy-six (54.3%) patients were males, and 64 patients were females with a male to female ratio of 1.2:1 (Table 1).

Table 1: Demographic features

	Overall (n=140)	Portal (n=107)	Non-portal (n=32)
Age			
Mean	44.66±13.20	44.09±12.29	45.94±15.80
Median	45	45	47.5
Sex			
Male	76 (54.3%)	60 (56%)	16 (50%)

Abdominal distension (100%), weight loss (82.14%), pedal oedema (75.71%), abdominal pain (47.86%) and jaundice (42.86%) were the main clinical features (Table 2).

Table 2: Clinical presentation of the study participants

Clinical Features	Present (N, %)	Absent (N, %)
Abdominal distension	100(100)	0(0)
Jaundice	80(57.1)	60(42.9)
Abdominal pain	73(52.1)	67(47.9)
Fever	94(67.1)	46(32.9)
Chills	105(75.0)	35(25.0)
Weight loss	25(17.9)	115(82.1)
Pedal oedema	34(24.3)	106(75.7)
Hematemesis	126(90.0)	14(10.0)
Crepitations	118(84.3)	22(15.7)
Periorbital oedema	126(90.6)	14(9.4)
Hepatomegaly	108(77.1)	32(22.9)
Clubbing	122(87.1)	18(12.9)
Palmar erythema	110(78.6)	30(11.4)
Splenomegaly	128(91.4)	12(8.6)
Others	108(77.1)	32(22.9)

One hundred and three (73.57%) patients had a diagnosis of chronic liver disease and 18(12.86%) had a diagnosis of malignancy other than HCC as the cause of their ascites. Out of the 103 cases of ascites caused by chronic liver disease, liver cirrhosis accounted for 69 cases while hepatocellular carcinoma was 34. Other causes include heart failure, nephrotic syndrome, chronic kidney disease, abdominal tuberculosis and unknown cause constituted 0.71% (Table 3).

Table 3: Causes of ascites

Causes	Frequency	Percentage
Portal hypertension		
Chronic liver disease	103	73.57
Liver cirrhosis	*69*	*49.28*
Hepatocellular carcinoma	*34*	*24.29*
Heart failure	4	2.86
Non-Portal hypertension		
Abdominal tuberculosis	4	2.86
Chronic kidney disease	6	4.29
Nephrotic syndrome	4	2.86
Malignancy excluding HCC	18	12.86
Unclassified cause		
Unknown cause	1	0.71
Total	140	100.0

Note: Data are presented as frequencies and percentages.

Ascites was then classified as having either PH causes (chronic liver disease, congestive heart failure) and NPH causes (malignancy, nephrotic syndrome, chronic kidney disease, abdominal tuberculosis) (Table 4). After excluding 1 patient for whom the cause of ascites could not be clinically determined, 139 patients with ascites were included in sensitivity and specificity analysis. Of these, 107 patients had ascites clinically determined to be due to causes related to portal hypertension. SAAG rightly classified the causes of ascites into portal and non-portal hypertension at a cut-off value of ≥ 11 gm/L and < 11gm/L ($P < 0.0001$) (Table 4). SAAG at ≥11 gm/L had a sensitivity of 91.59%, specificity of 84.38%, positive predictive value of 95.15%, negative predictive value of 75.0% and diagnostic accuracy of 90.0% (Table 5). Total ascitic fluid protein correctly classified the causes of ascites with portal hypertension and without portal hypertension at a cut-off value of ≥ 25 g/l and <25g/l

(P < 0.0001) but with low diagnostic accuracy (Table 4 and 5).

Table 4: Ascitic fluid total protein (AFTP) and SAAG in patients with portal hypertension and non-portal hypertension causes of ascites.

	Portal hypertension causes	Non-Portal hypertension causes	Total	p-value
SAAG ≥11 g/L	98	5	103	
SAAG < 11 g/L	9	27	36	p < 0.0001
Total	107	32	139	
AFTP 25 ≥g/L	25	24	49	
AFTP < 25 g/L	82	8	90	p <0.0001
Total	107	32	139	

Table 5: Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy (DA) of SAAG and AFTP for separating portal hypertension and non-portal hypertension causes of ascites.

PARAMETER	SAAG	AFTP
Sensitivity	91.59	23.36
Specificity	84.38	25.00
PPV	95.15	51.02
NPV	75.0	8.89
DA	90.0	23.74

Discussion

Ascites can be a clinical feature of conditions with high morbidity and mortality such as abdominal tuberculosis, abdominal lymphoma, malignancy or liver cirrhosis. Ascites constitutes a recurrent indication for hospitalization of patients in internal medicine departments in Ghana, but its causes remain under reported in this country. Successful treatment of ascites depends upon an accurate diagnosis of its cause and a large number of patients with ascites have diseases that may be potentially curable. Classification of types of ascites according to the level of serum-ascites albumin gradient (SAAG) is the best single test for classifying ascites into portal hypertension (SAAG >11 gm/L) and non–portal hypertension (SAAG < 11 g/L) causes.[8] This study was therefore to determine the aetiology of ascites and the usefulness of SAAG in differentiating the causes of ascites in Ghanaian context, so that patients can be managed appropriately and effectively.

Chronic liver disease (liver cirrhosis and hepatocellular carcinoma) was the commonest cause of ascites accounting for 73.57% of cases, followed by malignancies excluding HCC; 12.86%. Collectively, other causes constituted 13.58% of the cases of ascites in this study. This is comparable with other studies conducted in Africa and in the Western world. [1, 2, 5, 11-12] For instance, these findings are similar to a study conducted in Nigeria which showed similar aetiologies of ascites.[11] However, patients in the Nigeria study had a lower prevalence of liver cirrhosis (44%), and high percentages of tuberculous peritonitis (23%) and malignant ascites (22%). This could be due to the fact that, the referral pattern of these patients may vary from country to country or institution to institution. In KBTH there is a separate unit for managing tuberculosis (TB) and those with suspected TB are not seen at the main medical ward and cancer cases are seen mainly by the surgeons. Also due to the availability of potent anti-tuberculous medication, it is possible that the prevalence of TB has fallen in Ghana and Africa as a whole. The similarities of the causes may be due to the common aetiologic factors that the patients are exposed to especially in sub-Saharan Africa.

The etiological spectrum of ascites is vast and practically includes pathology of all the systems. SAAG has been found to be effective in differentiating ascites into portal and non-portal hypertension causes. Narrowing the causes to portal and non-portal hypertension will limit the laboratory and imaging investigations needed to do to come out with the definitive aetiology especially in developing country like Ghana. The diagnostic accuracy of SAAG in the present study to classify ascites into portal hypertension and non-portal hypertension aetiology was 90.0%. These values are comparable to the results obtained by Goyal et al. (97%) and Runyon et al. 96.7%).[8, 13] Gupta R et al.[14] also found that SAAG at a cut-off level of 1.1 g/dL had an accuracy of 92% in distinguishing cirrhotic ascites from tuberculous and malignant ascites, which was similar to this study. The diagnostic accuracy of AFTP in this study was 23.74% which was far lower than SAAG in differentiating portal hypertension and non-portal hypertension as a cause of ascites. This is comparable to studies conducted by Akriviadis et al.,[15] and Gogoi et al, [16] they found out that the diagnostic accuracy of SAAG was high in differentiating the causes of ascites compared to AFTP.

The mean age of the respondents was 44.66±13.20 years. This is disturbing due to the fact that these

patients are in their economically productive years of life, and this has implications on productivity. This is similar to other studies conducted in other African countries [4,10] that looked at the causes of ascites that stated the mean age, but lower than a similar study done in Qatar.[17]

Similarities and differences in the mean age may be due to etiologies of ascites and especially prevalence of chronic viral hepatitis in the population, as well as the age of acquiring the viral infection since cirrhosis has been found to be the most common cause of ascites in all the studies.

Hepatitis C and alcoholic liver disease are more frequent causes of liver cirrhosis in Europe and the Americas, compared with sub-Saharan Africa, being caused mostly by viral hepatitis B acquired in infancy. The male: female ratio for this study was 1.2:1 which is similar to a ratio of 1.3:1 that was reported by Ouattara et al. in Côte d'Ivoire [5]. This may be due to the similarities in the causes of ascites and the fact that both countries are located in sub-Saharan Africa with exposure to similar aetiologic factors.

Limitations

Patients with malignant ascites from surgical ward and abdominal tuberculosis from TB ward could have been sampled to increase the numbers of non-portal hypertension causes of ascites, this could have given more insight into the clinical significance of SAAG. Another limitation is the fact that we could not specifically measure portal pressure and had to rely on clinical diagnosis of which cases were classified as PHT or NPHT based on disease pathophysiology.

Conclusion

In conclusion, the results of the present study show that SAAG is a test with satisfactory diagnostic accuracy in separating ascites related to portal hypertension from the forms of ascitic fluid collection caused by mechanisms unrelated to portal hypertension. This could be used as a first line investigation in the etiological diagnosis of ascites to better inform appropriate investigation requests in a resource limited setting.

Moreover, SAAG is a more readily accessible clinical test compared with other more sophisticated tests in most of the district hospitals in Ghana, therefore its application could be more widely utilized.

References

1. Shah R. "Ascites". Medscape 2016. [emedicine.medscape.com/article]
2. Runyon BA, "Ascites, In: Schiff L, Schiff ER, editors. Diseases of the Liver. Philadelphia: Lippincott Company, 1993, pp. 990 – 1015.
3. Dembele Y, "The etiology of ascites in the Internal Medicine Department of the University Hospital of Point G. About 67 cases," Thesis *Med Fac Med Pharm Odontol*, 2006. On www.keneya.net. [accessed 08/06/2013]
4. Baptiste OAJ, Dramane S, Stanislass D, Mamadou D, Amadou K, Fabrice A, Sroboua TA, N'guessan N. Interest of SAAG in etiological diagnosis of ascites in African Black. *Open J. Gastroenterol.* 2018; 8: 337-347.
5. Ouattara B, Kra O, Kouassi L, Kone S, Biekre R, Toure KH, Nzoue KS, Kadjo K, Niamkey EK. Aetiologies of ascites in a Department of Internal Medicine in Côte d'Ivoire (Sub-Saharan Africa). *Afr. J. Intern. Med.* 2014; 3: 056-059.
6. Witte MH, Witte CL, Dumont AE. Progress in liver disease: physiological factors involved in the causation of cirrhotic ascites. *Gastroenterolo*. 1971; 61: 742–750.
7. Rocco VK, Ware AJ. Cirrhotic ascites. pathophysiology, diagnosis, and management, *Ann Intern. Med.* 1986; 105: 573–585.
8. Runyon BA, Montano AA, Akriviadis EA, Antillon MR, Irving MA, McHutchison JG. The serum-ascites albumin gradient is superior to the exudate-transudate concept in the differential diagnosis of ascites. Ann. Intern. Med. 1992; 117: 215–220.
9. Beg M, Husain S, Ahmad N, Akhtar N. Serum/Ascites albumin gradient in differential diagnosis of ascites. *J. Indian Acad. Clin Med.* 2001; 2: 51-54.
10. Mew CE. Basic principles of ROC analysis. seminars in nuclear medicine. 1978; 8: 283-98.
11. Malabu UH, Olubuyide IO, Shaibu ME, Olawuyi F. Ascites in Ibadan, Nigeria- usefulness of albumin gradient in its etiologic diagnosis. *J. Biomed Res* 2006; 17: 105–109.
12. Tasneem H, Shahbaz H, Sherazi BA. Pharmacoepidemiology of ascites and associated complications in hospitalized patients: descriptive observational study. *Int. Curr. Pharm. J.* 2015; 4: 343–346.
13. Goyal AK. Differential diagnosis of ascetic fluid: evaluation and comparison of various biochemical criteria with a special reference to serum ascites albumin concentration gradient and its relation to portal pressure. *Trop. Gastroenterol.* 1989; 10: 51-55.

14. Gupta R, Misra SP, Dwivedi M, Misra V, Kumar S, Gupta SC. Diagnosing ascites: value of ascitic fluid total protein, albumin, cholesterol, their ratios, serum-ascites albumin and cholesterol gradient. *J. Gastroenterol. Hepatolo.* 1995; 10: 295–299.
15. Akriviadis EA, Wnias D**,** Hadjigavriel M, Mitsiou A Goulis J. Serum/ Ascites Albumin Gradient: Its value as a rational approach to the differential diagnosis of Ascites: *Scand. J. Gastroenterol.* 1996; 8(31): 814-817.
16. Gogoi P, Debnath E, Changkakati R. Serum/ascites albumin gradient (SAAG), a very cost effective and reliable first-line diagnostic parameter in the differential diagnosis of ascites - a study in a North-East Indian population. *Int. J. Res. Rev.* 2018; 5: 215–219.
17. Khan FY. Ascites in the state of Qatar: aetiology and diagnostic value of ascitic fluid analysis. *Singapore Med. J*. 2007; 48: 434–439.