CAUSES OF ASCITES AMONG ADULT PATIENTS ADMITTED IN MEDICAL WARDS AT MUHIMBILI NATIONAL HOSPITAL IN DARESSALAAM, TANZANIA

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By

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled **Causes of ascites among adult patients admitted in Medical wards at Muhimbili National Hospital in Dar Es Salaam, Tanzania** in fulfillment of requirements for the degree of Master of Medicine (Internal Medicine) of Muhimbili University of Health and Allied Sciences.

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Dr. Ewaldo V. Komba

(Supervisor)

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Date

DECLARATION AND COPYRIGHT

I, **Masolwa D. P. Ng'wanasayi**, declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other university for a similar or any other degree award.

Signature……..... Date……

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ABSTRACT

Introduction: Ascites is a common cause of admission in Africa, especially among patients with liver cirrhosis[23], and schistosomal periportal fibrosis, both of which are associated with significant morbidity and mortality[21]. However, other causes of ascites are also prevalent in Africa. Tuberculosis account for 23% of all patients with ascites, but contributes up to 50% among those with HIV. Malignant ascites is also a significant morbidity and mortality, and has been reported in up to 25% of ascites in Africa[14,15]. Renal and cardiac causes of ascites are also significant. However, much is not known about the causes of ascites, and the clinical, socio-demographic characteristics of these patients in out settings.

Objectives: To determine the causes of ascites and describe the characteristics of adult patients with ascites admitted in medical wards at Muhimbili National Hospital.

Methodology: Hospital Based Descriptive Cross-Sectional Study.

Results:A total of 103 participants, mean age 40.9±1.51 years were included in this study, with equal sexual distribution. The mean duration of symptoms was 3 months, and majority of the participants reported history of abdominal distension, generalized body malaise, lower limb swelling, loss of appetite, and difficulty in breathing. Only a few patients had history of fever (34%), or weight loss (38%). Common causes of ascites were liver cirrhosis 34%, malignant ascites 24.2%, heart failure 17.5%, chronic kidney disease 12.6%, and TB Peritonitis 8.7%. Less common causes werenephrotic syndrome 1.9%, and chronic pancreatitis 1%.Of the 25 participants with malignant ascites, Hepatocellular carcinoma 60% was the most common malignancy. However, the primary tumor site could not be identified in nine participants.

Conclusions: Ascites commonly affect the younger age group with mean age 41 years. And the common causes of ascites were liver cirrhosis, malignant ascites, heart failure, chronic kidney disease, and tuberculous peritonitis.

Recommendations: We recommend another study tofurther describe patientswith malignant ascites in our settings. Another study is also needed to determine the prevalence and risk factors of Spontaneous Bacterial Peritonitis among patients with ascites in our settings.

ABBREVIATIONS

AASLD	-	American Association for the Study of Liver Disease
AD	-	Adenosine Deaminase
AF LDH	-	Ascitic fluid lactate dehydrogenase
AF TP	-	Ascitic fluid lactate dehydrogenase
AF/S LDH	-	Ascitic fluid serum lactate dehydrogenase ratio
AF/S TP	-	Ascitic fluid serum total protein ratio
CCF	-	Congestive Cardiac Failure
CKD	-	Chronic Kidney Disease
CLD	-	Chronic Liver Disease
CML	-	Chronic Myeloid Leukemia
CP	-	Chronic Pancreatitis
GFR	-	Glomerular Filtration Rate
GIT	-	Gastrointestinal Tract
HAART	-	Highly Active Anti-retroviral Therapy
HCC	-	Hepatocellular Carcinoma
HF	-	Heart Failure
HIV	-	Human Immunodeficiency Virus
HRS	-	Hepatorenal syndrome
KS	-	Kaposi Sarcoma
LC	-	Liver Cirrhosis
LDH	-	Lactate Dehydrogenase
MA	-	Malignant Ascites
MNH	-	Muhimbili National Hospital

MOI	-	Muhimbili Orthopaedic Institute
NS	-	Nephrotic Syndrome
PCM	-	Peripartum Cardiomyopathy
PHT	-	Portal Hypertension
PTB	-	Pulmonary tuberculosis
RHD	-	Rheumatic Heart Disease
SAAG	-	serum ascites albumin gradient
SBP	-	Spontaneous Bacterial Peritonitis
TB	-	Tuberculosis
TBP	-	Tuberculous Peritonitis
TP	-	Total Protein

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CHAPTER ONE

1.0 INTRODUCTION

Ascites refers to pathologic fluid collection within the abdominal cavity[1, 2]. Healthy men have little or no intra-peritoneal fluid, but women may normally have as much as 20 mls, depending on the phase of their menstrual cycle[1].

In England ascites contributes only 0.048% of hospital consultant episodes, but 77% of these patients require hospital admission, while 68% require emergency admission. 51% are males, with mean length of hospital stay of 9.6 days. Mean age for hospital admission is 60 years, but 47% of them are aged 15-59 years[24].

In the United States of America common causes include liver cirrhosis (81%), cancer (10%), heart failure (3%), Tuberculosis (2%), Dialysis (1%), pancreatic disease (1%), and other causes (2%) [4]. However, Tuberculosis is very common in most parts of Africa and must always be considered in all cases of chronic ill-health of an obscure nature[7]. It may account for 20-50% of all cases of ascites, especially due to the HIV epidemic[10, 11].

1.1 PATHOGENESIS OF ASCITES

The pathogenesis of ascites is varied depending on the cause, but it may either be due to increased ascitic fluid secretion in the peritoneum, or decreased clearance of the ascitic fluid by the lymphatic system due to either blockage, or stasis as in malignancy.

Transudative Ascites

This is by far the most common type, especially among patients with liver cirrhosis, and schistosomal periportal fibrosis. Similar type is seen in patients with congestive heart failure, or chronic kidney disease, and is characterized by low ascitic fluid protein. It is usually either due to a raised pressure across the portal vein, or changes in the hydrostatic pressure and oncotic pressure gradient across the portal vein.

The primary event that leads to portal hypertension is caused by the abnormalities in hepatic microcirculation as manifested by elevated hepatic resistance to portal flow. Reduced endothelial nitric oxide (NO) production and vasodilatory response to NO are both considered as important pathogenic mechanisms. As portal hypertension develops, it results into increased production of endothelial Nitric Oxide by the arteries of the splanchnic and systemic circulation, and leads to vasodilatation the so-called "hyperdynamic circulatory state" [60]. When both portal hypertension and splanchnic arterial vasodilatation occur, capillary permeability and lymph formation in the splanchnic organs markedly increase and exceed the ability to return the lymph to the circulation by the thoracic duct, thus causing its accumulation in the peritoneal cavity[61].

Exudative Ascites

This is typically due to active secretion of proteins into the peritoneal space, as a result of localized inflammatory process due to infection of the parietal or visceral peritoneum, such as in tuberculosis[37], pancreatitis, or malignancy. It is generally characterized by high ascitic fluid protein, and low serum ascitic fluid albumin gradient[27].

Malignant ascites is commonly due to the peritoneal seedling of malignant cells, commonly due to ovarian, endometrial, and cervical neoplasms in females, and gastrointestinal cancer in males[61].

1.2 LITERATURE REVIEW

1.2.1CAUSES OF ASCITES

1.2.2Liver cirrhosis

Cirrhosis is defined by World health Organization (WHO) as diffuse process characterized by fibrosis and conversion of normal hepatic architecture into structurally abnormal nodules[46]. Cell death, fibrosis, and regeneration are thus combined to create cirrhosis[47] which is classified as micro nodular (nodular size ranging between 0.1 to 1cm, alcohol consumption being the commonest cause) and macro nodular (nodules of variable sizes up to 5cm, with chronic viral hepatitis as the commonest cause) [9, 48].

While the disease has been associated with alcohol in Europe and North America; in Africa up to 59% of patients are infected with Hepatitis B viral infection, and 17% of these patients are found with TP_{53} mutation due to Aflatoxin exposure [92]. The disease typically affect majority of males; with a mean age of 58 years in Asia[74, 91], and 42.5 years in Africa[92].

Nearly 50% of patients with liver cirrhosis develop ascites within 10 years of diagnosis[3], and once the diagnosis is made 5-7% of these patients develop ascites annually[5], and it is a predictor of early mortality. Survival at 1 year is 60%, while the 5- year survival rate is between 25-50% among patients with ascites secondary to chronic liver disease[19, 20]. Prognosis is particularly poor for patients with refractory ascites and for those developing complications, including spontaneous bacterial peritonitis (SBP) and hepatorenal syndrome (HRS) [20]. However, roughly 15% of patients with liver cirrhosis develop ascites of non-hepatic origin[3].

1.2.3Abdominal Tuberculosis

Peritoneal tuberculosis can involve any part of the gastrointestinal tract, and occurs in three forms: 1) wet type with ascites, 2) dry type with adhesions, and 3) fibrotic type with omental thickening and loculated ascites[36]. Individuals with HIV infection, cirrhosis, diabetes, malignancy, and those receiving continuous ambulatory peritoneal dialysis are at

high risk for tuberculous peritonitis[37]. The most common site of involvement of the gastrointestinal tuberculosis is the ileocaecal region. And may presents with a palpable mass in the right lower quadrant and/or complications of obstruction, perforation or malabsorption especially in the presence of stricture[36]. Chest X-ray may be diagnostic in less than 25% of the cases. But laparoscopy is useful in doubtful situations[36]acute or chronic. Patients often have fever (40–70%), weight loss (40–90%), abdominal pain (80–95%), abdominal distension, diarrhea (11–20%), and constipation. Fatigue, malaise, and anorexia are also seen[37].

Useful modalities for investigating a suspected case include small bowel barium meal, barium enema, ultrasonography, computed tomographic scan and colonoscopy. Ascitic fluid examination reveals straw colored fluid with high protein, serum ascites albumin gradient less than 1.1 g/dl[8, 36], predominantly lymphocytic cells, and adenosine deaminase levels above 36 U/l. Laparoscopy is a very useful investigation in doubtful cases.

Another diagnostic modality involves measurement of ascitic fluid Adenosine deaminase, an enzyme involved in the conversion of adenosine to inosine, and is active in T than B cells. Its activity is proportional to T cell activation, as it occurs in Tuberculosis[36]. ADA levels are high in tuberculous ascites than malignant ascites, or liver cirrhosis. Taking a cut off level of > 33U/l has sensitivity, specificity, and diagnostic accuracy of 100%, 97%, 98% respectively[58]. In co-infection with HIV the ADA values can be normal or low. Falsely high values can occur in malignant ascites[59].

Malabu, U.H, et al[8], in a 2-year prospective study, which involved 90 adult patients with ascites at the University College Hospital Ibadan, Nigeria, it was reported that 44% had liver cirrhosis, 23% had tuberculous peritonitis, 22% had malignant ascites, 5 (6%) had heart diseases and 5% had nephrotic syndrome. Among the 21 patients who had Malignant ascites 7 had ovarian carcinoma, 5 had gastric carcinoma, 4 had breast carcinoma, and one each for colon carcinoma, prostate carcinoma, Bronchogenic carcinoma and Burkitt's lymphoma. Three patients had intestinal metastasis.

1.2.4Schistosomiasis

However, schistosomiasis is also a common cause of ascites in tropical Africa. In a cross-sectional study done in North Eastern Zaire by Wood PhB, and Crofts. JW[9], involving 75 cases with gross ascites, schistosomal periportal hypertension was found in 19 (25.3%) of the patients. While 10 (13.3%) had hepatoma, 12 (16%) had alcoholic (micronodular) cirrhosis, 13 (17.3%) had post hepatitic (macronodular) cirrhosis. Other causes were biliary cirrhosis 1, cancer of stomach 1, cancer of pancrease 2, lymphoma 1, sickle cell anemia 1, nephrosis 5, TB peritonitis 2, Heart failure 2, and Pancreatic pseudocyst.

Schistosmiasis is an endemic disease in tropical countries, according to WHO 600 million people live in risk areas, and 200 million people are infected in 75 countries[20]. Deposition of eggs and dead worms in various tissues result in formation of immune complexes. They obliterate small vessels and forms granulomas in the portal tract which obstruct the portal vein[21].

About 5-10% of patients with chronic hepato-intestinal schistosomiasis, commonly due to *Schistosomamansoni,* eventually develop portal hypertension, and are considered to have severe form of the disease. The main manifestation is gastrointestinal bleeding, leading to high morbidity and mortality. However, these patients do not usually present with features of hepatic dysfunction such as jaundice, spider nevi, or palmar erytherma, but may present with ascites. Epidemiologic data is very important for its diagnosis, since other causes of pre-sinusoidal causes may present similarly. Stool examination may be repeatedly negative, but abdominal ultrasound, histology of the liver, or its angiographic study is usually conclusive of Schistosomiasis[21].

1.2.5Malignant Ascites

Malignancies are a common cause of ascites both in the developed and in developing countries. Studies in US have shown that malignancies account for up to 10% of all causes of ascites. Studies in Asia have shown a prevalence ranging from 13% to 25%[14, 15]. Most of the malignancies were due to metastatic colon carcinoma. In Africa, one previous study done in the late 1970's in Eastern Zaire[9] reported malignancy in 22.7% of the patients with

ascites, and most of them had hepatocellular carcinoma. In recent study in Nigeria, 22% of the patients with ascites had malignancy, with the commonest being ovarian cancer, gastric carcinoma, and breast cancer. However, this could be due to the fact that this study involved mostly (78.4%) females[8].

In general, the presence of ascites portends a poor prognosis. The mean survival in patients with malignant ascites is generally less than 4 months. However, with ascites due to a malignancy that is relatively sensitive to chemotherapy (e.g., newly diagnosed ovarian cancer), the mean survival may be significantly better (i.e. 6-12 months) [63].
Complex mechanisms are responsible for malignant ascites. Liver metastases can cause hepatic venous obstruction and result in portal hypertension. Increased portal pressure leads to transudation of fluid across the splanchnic bed into the abdominal cavity.

The ascites of peritoneal carcinomatosis accumulates via a different mechanism. Tumor cells on the peritoneal surface directly interfere with normal venous and lymphatic drainage, causing fluid to 'leak' into the abdomen. A humoral vascular permeability factor that allows exudation of fluid from the peritoneal vessels has also been identified[64]. Chylous ascites can result from the lymphatic obstruction commonly seen in lymphoma.

1.2.6Cardiac Causes

The estimated crude incidence of heart failure in Sub-Saharan Africa is 3-20 per 1000 per year. It has great social and economic impact, since it typically affects those who are young and economically active individuals[82]. Studies indicate that heart diseases contribute 7-10% of all medical admissions, and heart failure account for 3-7% of them[69]. Ninety eight percent of patients with heart failure are due to non-ischemic causes. Hypertensive heart disease, rheumatic heart disease, and cardiomyopathy account for up to 65% of the cases. However, the true prevalence of coronary artery disease is underestimated due to diagnostic limitations[70].

Endomyocardial fibrosis (EMF) is common in most parts of tropical Africa and has been estimated to account for between 25 and 40%, of heart disease[7]. Most patients present with gross ascites and minimal peripheral edema. It has been suggested that EMF is both a cardiac and systemic disease. A study in Uganda histopathologically examined peritoneal biopsy specimens from 30 patients with EMF. Of these, 25 biopsy specimens showed peritoneal fibrosis with inflammatory infiltrates. Five specimens were unsatisfactory, but among them two samples showed striated muscle fibrosis. In addition 60% of the patients had eosinophilia and investigators proposed that EMF includes a systemic inflammatory process that may contribute to ascites in these patients[108]. In another series of EMF patients in Uganda, the ascitic fluid protein content was described as consistent with an exudate in 35 of 47 patients. However, the serum ascites albumin gradient was not reported[109].

Rheumatic heart disease (RHD) is also a significant cause of ascites in tropical Africa, with a prevalence rate of up to 30.4 cases per 1000 population among children in Mozambique[12,13]. Both of these together with Peripartum cardiomyopathy (PCM) usually present before middle age, unlike in the developed world where the average age of patients with heart failure is 76 years[71]. Up to 68% of female are affected by RHD as found by Sliwa, K. et al[83] in a prospective register in Soweto, South Africa.

Pericarditis and cor-pulmonale contribute about 10% of cases of heart failure. Cor-pulmonale is largely reflecting on the role of chronic post-tuberculous lung disease, while pericarditis is due to the effect of HIV on tuberculosis[72].

1.2.7Nephrotic Syndrome

The term nephrotic syndrome refers to a distinct constellation of clinical and laboratory features of renal disease. It is specifically defined by the presence of heavy proteinuria (albuminuria greater than 3.5 g/24 hours), hypoalbuminemia (less than 3.0 g/dL), and peripheral edema. Hyperlipidemia and thrombotic disease are also frequently observed. In most adults with nephrotic syndrome ascites can be attributed to both hypoalbuminemia, and presence of liver disease or congestive heart failure with increased hepatic sinusoidal pressure[73].

Ackermen Z, studied 52 adults and 21 children with nephrotic syndrome. He found that the prevalence of ascites among adult patients was 23%, significantly lower than children whose prevalence was 52%[73]. Other studies reported the prevalence of nephrotic syndrome among patients with ascites ranging from 3% to 7%[8, 9, 74].

1.2.8Chronic Kidney Disease

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function, and a progressive decline in glomerular filtration rate (GFR). And typically corresponds to CKD stage 3-5, when the GFR is below 60ml/min/m^3 [75].The incidence of ascites in advanced kidney disease (CKD) varies from 0.7% to 20%[76]. And up to 3% of all medical admissions in tropical countries are due to renal related complains[93]. Interestingly, however CKD may also be a complication of liver cirrhosis[77]. Depending on the etiology and stage of the disease CKD may present with signs of hypertension, edema, anemia, and associated easy fatigability; decreasing appetite with progressive malnutrition, abnormalities in calcium, phosphorus, and mineral-regulating hormones, such as 1,25(OH)2D3 (calcitriol) and parathyroid hormone (PTH); and abnormalities in sodium, potassium, water, and acid-base homeostasis; and finally uremic syndrome which usually require renal replacement therapy[75].

The association of chronic renal failure and ascites was first described in 1970[89]. The reported incidence of ascites varies from 0.7 to 26% with male predominance and affect wide range of age from 11 to 71 years (mean age 41 years)[87, 88].Ascites has also been associated with dialysis among patients with chronic kidney disease[90].

1.2.9Pancreatic Diseases

Acute pancreatitis is frequently associated with ascites, and together with pleural effusion has been identified as independent predictors of severity. Ascites has also been reported in chronic pancreatitis[78]. Acute pancreatitis typically presents with acute abdominal pain and distension, nausea, and vomiting[79].

Maringhini A, et al studied the incidence, natural history, and prognostic role of ascites among patients with acute pancreatitis. Among 100 patients, 18 had ascites. And the presence of ascites was associated with pseudocyst during follow up[67].

The pathogenesis of pancreatic ascites is uncertain, but there are three possible mechanisms; the first is pancreatic duct obstruction, with leakage of pancreatic fluid into the peritoneal cavity causing diffuse peritoneal infiltration and ascites; second is the obstruction of the pancreatoduodenal lymphatics by enlarged lymph nodes, peripancreatitis, pancreatic cysts, and fibrosis. This results in retrograde lymphatic flow with formation of chylous ascites; and third is the hyponatremia due to malabsorption from pancreatic disease. This augments ascitic collection by physical influence, and loss of protein into the ascitic fluid establishes a vicious cycle[78, 79].

HIV infected patients experience increased incidenceof pancreatitis as the CD4 counts decrease[41]. In addition to non-HIV related causes, patients with HIV tend to have more drug induced and idiopathic pancreatitis[38]. Though opportunistic agents are noticed in the pancreas at autopsy, their role in acute pancreatitis is unclear[38,40]. Clinical features and management are similar to non-HIV patients; non-HIV related causes should be considered in the differential.

Didanosin (ddI), a NRTI can cause pancreatitis in up to 25% of patients treated with this agent[42]. CD4 counts less than 100 and prior pancreatitis increases the risk of didanosine induced pancreatitis[38]. Pentamidine induced pancreatitis has been reported with both intravenous as well as long term aerosolized therapy[39]. Other causes of drug induced pancreatitis include Zalcitabine, Lamivudine, Sulfonamides and Steroids. Discontinuation of the offending agent is required when identified.

1.2.10Neoplasms

The increased occurrence of gastrointestinal malignancies in HIV infected individuals has been raised in the past[43]. A study of 14,986 HIV infected patients demonstrated increased risk of both HIV related (KS and lymphoma) and non-HIV related malignancies

(Hodgkin's disease, skin cancer in males and colon cancer in females)[45]. There is inadequate data on incidence of GI malignancies in older HIV patients; it is unclear if HIV infection increases the occurrence of colon cancer in the elderly.

Kaposi's sarcoma (KS) is the most common HIV related GI malignancy accounting for about 60% of cases. Gastrointestinal KS is generally asymptomatic, unless extensively involved. Kaposi sarcoma has also been associated with onset of ascites in AIDS patients, with purplish nodules observed on the parietal and serosal peritoneum at laparoscopy or laparatomy, and characterized by increases red cells and high serum ascites albumin gradient[95, 95]. Treatment with HAART has clearly reduced the rate of new cases of KS and improved prognosis[38,45]. Non-Hodgkin's lymphoma of the gastrointestinal tract is usually high grade, with short survival; presentation includes abdominal pain, altered bowel habits, intestinal obstruction and weight loss[45].

1.2.11 HIV and Ascites

HIV related Ascites occurs from a myriad of causes ranging from Kaposi's sarcoma, lymphomas, nephrosis, pericarditis to cirrhosis contracted through hepatitis B or C infections or alcoholism. It is for this reason that ascites in an HIV infected patient requires consideration of almost every known cause of ascites[2].

1.2.12 Mixed causes of ascites

Although cirrhosis is the cause of ascites in most patients with ascites evaluated by the internist, a cause other than liver disease is found in approximately 15% of patients in the developed world[4]. The proportion may be higher in Africa. Approximately 5% of these patients have two causes of ascites[4, 110]. This is referred to as mixed ascites.

In the developed world usually these patients have cirrhosis plus one other cause, such as peritoneal carcinomatosis, or tuberculous peritonitis. Interpretation of ascitic fluid in these patients is difficult, and they pose a diagnostic challenge. However, in Africa due to differences in distribution of causes of ascites such patients may have a combination of different causes of ascites other than liver cirrhosis[8].

1.3 COMPLICATIONS OF ASCITES

Mechanical, bacterial and metabolic complications occur in ascites[101]. Mechanical complications result in respiratory impairment, physical immobility, and compression of great vessels, hernias, promotion of gastroesophageal reflux, impaired gastric motility and obstructive sleep apnea syndrome. Disturbances of electrolyte, altered drug pharmacokinetics, hepatic encephalopathy and hepatorenal syndrome are known metabolic complications of ascites[101]. However, the most important complication of ascites is spontaneous bacterial peritonitis.

Spontaneous Bacterial Peritonitis (SBP)

SBP frequently affect patients with liver cirrhosis and ascites. It has been reported in up to 25% of adults with alcoholic liver cirrhosis, but has also been reported in various other conditions including post necrotic cirrhosis, chronic active hepatitis, active viral hepatitis, congestive heart failure, metastatic malignant disease, systemic lupus erythematosus, lymphedema, and rarely without any underlying illness[80].

It is defined as an infection of previously sterile ascitic fluid without any demonstrable abdominal source of infection. Polymorphonuclear cell count of over 250 cells/mm^3 is diagnostic of this condition ascitic fluid culture is positive in 50-70% of cases. Common isolated organisms are usually gram negatives E.Coli, Klebsiella, but sometimes gram positives such as Streptococci, and Staphylococci[81]. And patients with ascitic fluid total protein concentration lower than 15g/l have an increased risk of spontaneous bacterial peritonitis[100].

Various routes of infection have been postulated. A hematogenous, or lymphogenous route through an episode of bacteremia is a widely accepted mode of infection. Also an overgrowth of bacteria in the gut is common in cirrhosis, and may result in transmural migration of bacteria through an intact gut wall. Furthermore, portosystemic shunting also diminishes hepatic clearance of bacteria enhancing metastatic infection at susceptible sites such as ascites collection. The skin, respiratory tract, and urinary tract can also be sources of primary infection.

Clinically SBP may be asymptomatic. Where symptomatic, abdominal pain, and fever are the most characteristic symptoms. Generalized tenderness occasionally with rebound may be elicited. Vomiting, ileus and diarrhea due to altered gastric motility, hepatic encephalopathy, GIT bleeding, renal impairment, septic shock and hypothermia may be present in a high number of patients but are rather non-specific[80,81].

1.4 SOCIO-DEMOGRAPHIC CHARACTERISTICS OF PATIENTS WITH ASCITES

The incidence and prevalence of ascites in the general population is largely unknown, due to lack of large epidemiological studies, both in Africa and elsewhere. Only small descriptive studies exist in literature. However, in Africa ascites is associated with many factors including poverty, overcrowding, malnutrition, and Human Immunodeficiency Virus (HIV) [2]. And many individuals do not attend hospitals at all, while a few especially in rural areas seek medical advice only after consulting traditional herbalists [7, 8].

1.4.1 Age distribution of ascites

Ascites affect individuals of all age groups, but due to the distribution and pathogenesis of the various causes associated with ascites, certain age groups are more likely to have one disease than the other.

Ascites in Infants and Children

In children ascites is usually due to liver or renal disease. Cirrhosis from chronic liver disease is the most common hepatic cause of ascites in infants and children[103]. Risk factors may include neonatal or infantile cholestatic symptoms, chronic viral hepatitis or jaundice, injections, transfusion of blood or blood products and family history of liver diseases. In adolescents history of intravenous drug use, sexual promiscuity and tattoos may give clue to liver disease[102]. Other causes of ascites include inflammatory conditions of the bowel such as eosinophilic enteropathy[104], Crohns disease[105], tuberculous peritonitis[106, 107], pancreatic ascites, chylous ascites, andvitamin A intoxication.

Children with ascites may have history of increasing abdominal girth or inappropriate weight gain. Infants may also have history of periorbital edema.

Ascites in Adults and the elderly

Liver cirrhosis is the most common cause of ascites in adults. It is found at much higher proportions, in the developed than in the developing world. However, in Africa other causes of ascites such as tuberculous peritonitis and malignant ascites are also common. Cardiac and renal causes of ascites are less common[8]. Abdominal tuberculosis is common among young adults. Two third of these patients are aged 21- 40 years old[36].

Wood Ph. B, and J.W Crofts studied 75 patients with ascites in Zaire. They found that a young person with ascites is more likely to have schistosomal periportal fibrosis or micro nodular (post-hepatitis) cirrhosis than macro nodular (alcoholic) cirrhosis or hepatocellular carcinoma (HCC). Hepatocellular carcinoma and other malignancies were more common with advancing age[9, 14].

The mean age of adult patients with ascites is probably lower in Africa than in Asia, and Europe. The mean age of participants was 58.8 years in Saudi Arabia[74],55.6 years in Iran[112],and63.4 years in Turkey[113].While in two studies in Africa, one in Gambia, and another in Ivory Coast, the mean age of ascitic patients was 42.5 years and 48.9 years respectively[92,111].

1.4.2 Sex distribution of ascites

In a recent study in Nigeria among 90 adult patients with ascites, 78.4% of them were females. And in studies done in Asia among patients with exudative ascites, majority of the patients were females, reported at 62.2%, and 71.4% respectively[14, 15].

However, all of these studies were hospital based, and are therefore prone to sampling bias, but may suggest that ascites is more common in females than males regardless of its nature.

Malabu UH, et alin Nigeria reported that the commonest malignant tumors in patients above the age of15 years were primary carcinoma of the liver andstomach in males, and carcinoma of the cervix, breast, and ovaries in females[7].

Wood Ph.B, et al made an attempt to report sex ratio for the various causes of ascites among 75 patients with ascites in Zaire. Hepatic ascites had a male female ratio of 1.8:1, schistosomal fibrosis 1:1.2, hepatocellular carcinoma 1:1.5, macro nodular cirrhosis 1:1.6, micro nodular cirrhosis 1:4.7, and non-hepatic ascites 1:3 respectively[8]. Tuberculosis has been reported to have equal sex incidence[36], while others have reported a female predominance [14, 37].

However, these ratios are not consistent across different studies and geographical locations, and probably there is a shift of trend with time.

1.5 CLINICAL CHARACTERISTICS OF PATIENTS WITH ASCITES

Ascites is widely recognized as a condition with poor prognosis, of which prompt treatment is sought. However, most patients present to hospital several months after onset. This can be partly explained by the fact that most patients seek the help of traditional herbalists before finally considering a hospital[7]. However, Mamdani M and BangserM, have described the challenges of accessing health care in Tanzania, especially among the poor. They identified several factors limiting access including long distance to health facilities, lack of reliable roads and transport, health care charges, bribes, and poor quality of care[84].

A history of dyspnea, fatigue, anorexia, early satiety, nausea, vomiting, pain, or diminished exercise tolerance in the setting of weight gain, increases in abdominal girth (with or without protrusion of the umbilicus), a sensation of fullness or bloating suggest the presence of ascites. Some people simply describe a vague generalized abdominal discomfort or a feeling of heaviness with ambulation. Increased intra-abdominal pressure

can produce esophageal reflux symptoms. Delayed gastric emptying may prompt complaints of indigestion, nausea, and vomiting[65].

Luck NH, and his colleagues studied the role of diagnostic laparoscopy among 33 patients with low serum ascitic fluid albumin gradient in Lahore, India. 45% of them were males, with mean age of 48 years, and mean duration of presenting complains of 3.3 months[66]. 66% of these patients had tuberculous peritonitis, 15.2% had peritoneal carcinomatosis, 3% had Budd-Chiari syndrome, 21.2% malignancies, and 12% had liver cirrhosis. Co-morbid conditions were liver cirrhosis, hypertension, diabetes mellitus, and chronic renal failure.

The most common presenting complains were fever (72.7%), abdominal distension (66.7%), abdominal pain (18.2%), weight loss (36.4%), and generalized weakness (15.2%). On physical examination 66.7% had pallor, 24,4% had Hepatomegally, 1% each had jaundice, lymphadenopathy, and splenomegally[66].

Mahmood K, et al studied a total of 45 patients with exudative ascites (17 male and 28 female) with age range from 20 to 65 years. The commonest presentation of these patients was abdominal distension (93.3%), abdominal pain (46.67%), fever (44.4%) and weight loss (33.3%) [15]. While Anjun A, found that among 30 patients with exudative ascites, all of them complained of abdominal distension, and only 30% complained of abdominal pain[14].

Wood Ph.B, et al in Zaire found that majority of cases with schistosomal periportal fibrosis and macro nodular cirrhosis had a palpable spleen, while only a minority of cases with hepatocellular carcinoma (HCC), and micro nodular cirrhosis had a palpable spleen. It was also reported that only 8 of 59 cases of hepatic ascites had history of hematemesis, but only 5 of them had a palpable spleen. Majority of patients with ascites didn't have a palpable liver. But a majority (9 out of 10) of patients with hepatoma had a palpable liver[9].

1.6 DIFFERENTIAL DIAGNOSIS OF ASCITES

1.6.1 Serum Ascitic Fluid Albumin Gradient (SAAG)

Classification of ascites based on the serum albumin ascites gradient (SAAG) is superior and has replaced the exudate–transudate concept with characterizations that are based solely on ascitic fluid protein concentrations, and it provides a reliable tool to determine whether ascites can be attributed to portal hypertension or has another etiology[20].

The SAAG is calculated by subtracting the ascitic fluid albumin concentration from the serum albumin concentration[16]. The serum and ascites samples should be obtained at approximately the same time.

Patients with a SAAG of 1.1 g/dl or more have ascites that is due, at least in part, to portal hypertensive cause, but is also found when ascites is caused by right-sided cardiac failure or constrictive pericarditis[20]. Patients with a SAAG of less than 1.1 g/dl do not have portal hypertension. These correlations are accurate to 97% [17].

According to Runyon BA, et al[26] the following are some causes of high albumin gradient: Liver cirrhosis, Alcoholic hepatitis, Congestive heart failure, Massive hepatic metastases, Vascular occlusion, Fatty liver disease of pregnancy, and Myxedema. Causes of low albumin gradient are: peritoneal carcinomatosis, Peritoneal TB, Pancreatitis, Serositis, Nephrotic syndrome, Bowel obstruction/perforation/infarction.

In general, a high SAAG predicts diuretic responsiveness. One exception is nephrotic syndrome, in which the SAAG is low but there is typically a response to diuretics[17].

1.6.2 SAAG versus Exudate-Transudate Methods

The level of ascitic fluid total protein classifies ascitic fluid as either an exudate (if AF TP > 25g/dl) or transudate (if AF TP < 25g/dl) [15]. But some studies have used a higher cut off value of 30g/dl[28]. Ascitic fluid serum protein (AF/S TP) ratio is also another method used to classify ascites into either an exudate or transudate. Ascitic fluid is as an exudate if AF/S TP ratio is > 0.5, and it is a transudate if AF/S TP ratio is < 0.5.

Levels of the enzyme Lactate dehydrogenase (LDH) which is present in various organs and tissues (red blood cells, myocardium, lungs, kidneys) have been used as a marker of exudative, and transudative pleural effusion, and ascitic fluid. Ascitic fluid-serum lactate dehydrogenase ratio of > 0.6 is an exudate, and vice versa for a transudate[34,35].

Several studies have questioned this concept, due to several observations: 1) Normal peritoneal fluid total protein concentration is sometimes 4g/dl[29]; 2) Ascitic fluid protein concentration increases in cirrhotic patients with diuresis and albumin infusion; 3) some transudative ascites like cardiac ascites have high protein concentration, while some traditionally exudative ascites like malignant ascites, or tuberculosis have low concentrations of protein[30]; and surprisingly 4) Liver cirrhosis may be the most common cause of high protein ascites[31]. These observations have led into confusion while interpreting AF TP results and resulted in missed diagnoses.

The serum-ascites albumin gradient (SAAG) has been proved in prospective studies to categorize ascites better than the total-protein-based exudate/transudate concept and better than modified pleural fluid exudate/transudate criteria. In a prospective study involving 901 patients, Runyon BA, et al[26] found that albumin gradient (SAAG) correctly differentiated causes of ascites due to portal hypertension from those that were not due to portal hypertension 96.7% of the time. The AF TP, when used as defined in the old exudate-transudate concept, classified the causes of ascites correctly only 55.6% of the time. This resulted in part because the AF TP of most spontaneously infected samples (traditionally expected to be exudates) was low, and the AF TP of most cardiac ascites samples (traditionally expected to be transudates) was high.

In a study to evaluate the causes of ascites in Saudi Arabia, involving 132 participants, 69% had liver cirrhosis, 10.6% had tuberculous peritonitis, 9.1% had malignant ascites, 7.6% had congestive heart failure, 3.0% had nephrotic syndrome. And the positive predictive values of AF TP, A/S TP ratio, A/S LDH ratio, and SAAG were 68%, 76%, 67%, and 80% respectively; while the negative predictive values were 96%, 96%, 84%, and 98% respectively. SAAG had a diagnostic efficiency of 91% in separating ascites due to liver disease from other causes of ascites[74].

In a recent prospective study in Nigeria by Malabu U.H, et alalso evaluated the causes of ascites among 90 adult patients with ascites, 44% had liver cirrhosis, 23% had tuberculous peritonitis, 22% had malignant ascites, 6% nephrotic syndrome, and 5% heart disease. It was found that SAAG was lower among patients with Liver cirrhosis (LC), and was high among patients with TB peritonitis and malignant ascites (TBP/MA). There were no differences in the biochemical parameters of patients with TBP/MA[8].

In this study, the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic efficiency of SAAG was 95%, 98%, 98%, 95%, and 96% at cut off value of 1.1g/dl; AF LDH was 83%, 70%, 74%, 80%, and 77% at cut off vale of 180 IU/L; AF TP was 63%, 83%, 80%, 69%, and 73% at cut off value > 3g/dl; AF/S LDH was 71%, 70%, 71%, 70%, and 70% at cut off value > 0.6; and AF/S TP was 61%, 65%, 64%, 62%, and 63% at cut off value >0.5; respectively[8].

1.6.3 Usefulness of SAAG in Children

Similar observations were reported in another study by Das B, et al[32], which involved 40 children aged between 0 to 4 years of age, 65% had Chronic liver disease, and 35% had nephrotic syndrome. AF TP correctly diagnosed 53.8% of chronic liver Disease (CLD) cases and 92% of Nephrotic syndrome (NS) cases as transudative type. The misclassification rate was high in CLD group in comparison to NS group ($p< 0.001$). While SAAG value correctly classified CLD as high gradient in 85% of cases, and classified NS as low gradient in 85% of cases. The misclassification rate for both groups was 15% and less than AF TP.

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic efficacy of SAAG (71%, 92%, 83%, 85%, 80%), AF TP (95%, 46%, 48%, 92%, 63%), AF/S TP (71%, 35%, 37%, 69%, 48%), and AF/S LDH (79%, 23%, 35%, 67%, 43%) respectively[32]. These results shows that SAAG had similar sensitivity to the rest of the criteria used, but had far higher specificity, and diagnostic efficacy.

Generally, these studies demonstrate the superiority of SAAG against the other criteria used. And SAAG is now recommended by the American Association for the Study of Liver Diseases (AASLD) as a standard tool in the differential diagnosis of ascites[33]. However, only one study has been done in West Africa and none has been done in East Africa to compare the utility of SAAG against other traditional criteria, most of which are still in use in many parts of the continent.

1.6.4SAAG in the Diagnosis of Malignant Ascites

In a study by Shen-Jyn Chen, et al [18], to determine the clinical value of tumor markers in the diagnosis of malignancy-related ascites (not including hepatocellular carcinoma), serum and ascitic fluid levels of carcinoembryonic antigen, cancer antigen 125, carbohydrate antigen 19–9, tissue polypeptide antigen and serum-ascites albumin gradient were determined in 66 patients with cirrhotic ascites, 28 patients with hepatocellular carcinoma and ascites, and 29 patients with malignancy-related ascites.

In this study, three tumor markers and serum-ascites albumin gradient showed significant difference between patients with malignancy-related ascites and those without. At the best cut-off levels chosen from near 95% of the data in those without malignancy-related ascites, the sensitivity, specificity and accuracy to diagnose malignancy-related ascites were, respectively, 65.5%, 93.6%, 87.0% using serum carcinoembryonic antigen 10 ng/mL; 69.0%, 94.7%, 88.6% using ascitic fluid carcinoembryonic antigen 5 ng/mL; 65.5%, 93.6%, 87.0% using ascitic fluid carbohydrate antigen 19–9 50 U/mL; 62.1%, 98.9%, 90.2% using serum-ascites albumin gradient < 1.1 g/dL.

It was concluded that although serum-ascites albumin gradient (SAAG) offered the best diagnostic accuracy and specificity, its sensitivity was not good enough. This study demonstrated that SAAG and tumor markers are not sensitive parameters in the diagnosis of malignancy-related ascites. Nonetheless, SAAG had demonstrated higher diagnostic efficacy than the rest of the tumor markers.

1.6.5 Ascitic Fluid Cytology

Cytologic analysis is the most specific test to demonstrate malignant ascites. It is about 97-100% sensitive with peritoneal carcinomatosis[26], but is poor in detecting other types of malignant ascites. And it is usually negative in patients with Hepatocellular carcinoma, or lymphoma with chylous ascites[26].

JhaR, and colleagues investigated the sensitivity and specificity of ascitic fluid cytology among 65 patients with ascites (37 with malignancies, and 28 non-malignant ascites). They found that the sensitivity and specificity of ascitic fluid cytology was 56.7%, and 100% respectively[85].

JunaidTA, and colleagues[86] also analyzed ascitic fluid cytology specimens from 859 patients in Nigeria, but malignant cells were identified in only 24.4% of the samples[86].

Cell counts with a differential are useful in the presumptive diagnosis of bacterial peritonitis, particularly if the neutrophil count is greater than 250 cells per ml. If infection is suspected, a Gram stain and culture should be performed. Direct inoculation of the ascitic fluid into blood culture bottles increases the sensitivity of detecting infection up to 85%[17].

1.6.6 Peritoneal Biopsy

In a study by Anjun, A and Khan, MN[14], which assessed the role of laparoscopic peritoneal biopsy involving 30 consecutive admissions with high albumin gradient (>1.1g/dl) aged 14 to 65 in Pakistan, 16 patients had a suggestive biopsy, while in 14 patients biopsy revealed chronic nonspecific inflammation. Of the 16 patients with suggestive diagnosis, tuberculous peritonitis was the most common confirmed diagnosis with 9 patients (32%), followed by malignant ascites in 7 patients (25%), two patients had chronic renal failure (6.6%), and four patients had chronic liver disease (13.3%). Among those who had tuberculosis, one patient had chest x-ray features of pulmonary TB, and another patient had exudative pleural effusion [14]. In this study most of the patients were females (71.4%), as compared to males (28.6%). The most common symptoms among these patients were

abdominal distension (30%), abdominal discomfort (36%), difficulty in breathing (40%), weight loss (63%), anorexia (66%), and low grade evening fever (46%)[14].

In another descriptive case study by Khalid Mahmood, at al[15], evaluating the usefulness of percutaneous peritoneal biopsy using the Abraham's needle among patients with exudative ascites (ascitic fluid total protein > 25g/gl), involving 45 patients (17 males, and 28 females) aged 20 to 65 years. The commonest presentation was abdominal distension (93.3%), abdominal pain (46.67%), fever (44.4%), and weight loss (33.3%). 40% of the patients had nonspecific chronic inflammation, 10 (22.2%) showed caseating chronic granulomatous inflammation suggestive of tuberculosis, and 6 (13.3%) revealed metastatic adenocarcinoma. In one patient peritoneal mesothelioma was reported. In the remaining 10 (22.2%) patients biopsies were inconclusive. Of interest here is that ascitic fluid cytology showed predominantly lymphocytes in 86.6% of the cases. Only three patients had atypical cells on cytology reflecting its low sensitivity[15].

These two studies demonstrate the superiority of peritoneal biopsy in the diagnosis of exudative ascites, although they both used different classification criteria for ascites. All of the biopsies taken laparoscopically had a positive yield, and was able to confirm diagnosis in 53.3% of the 30 enrolled patients[14]; while 22.2% of the percutaneous biopsies were inconclusive, and was able to confirm diagnosis in only 37.78% of the 45 enrolled patients[15]. This highlights the limitations inherent of the percutaneous peritoneal biopsy, due to the blind nature of the procedure.

A study in Uganda assessed the usefulness of peritoneal biopsy among thirty ascitic patients with Endomyocardial fibrosis (EMF). Eighty three percent of biopsy samples showed variable degrees of peritoneal fibrosis with inflammatory infiltrates, indicating that EMF is both a cardiac and systemic disease[108].

Nonetheless, percutaneous peritoneal biopsy with an Abraham's needle was shown to be safe and inexpensive diagnostic tool that can be utilized in resource poor settings. It provide a means to confirm of the diagnosis, while saving patients from more traumatic diagnostic procedures such as open laparotomy for biopsy. The commonest side effects

were pain (91.1%) and mild swelling (53.3%) at the biopsy site[15]. Only one patient had intra-abdominal bleeding, as evidenced by pallor and falling hematocrit, and was treated conservatively with blood transfusion.

1.7 PROBLEM STATEMENT

Prevalence of ascites in the general population is not documented. But it is known that only patients with moderate to severe ascites seek medical attention[2], and it is also important to note that most poor villagers in Africa consult several native herbalists before seeking medical help[7]. Therefore cases seen in hospitals do not usually reflect the true incidence.

Liver cirrhosis is the most common cause of ascites both in Africa and elsewhere. And ascites is the most common cause of admission for patients with liver cirrhosis[8, 9, 23]. Liver cirrhosis contributes for up to 44% of admitted patients with ascites in Africa[8]. Schistosomiasis is another common cause of chronic liver disease, second only to liver cirrhosis[9]. Tuberculosis is also an important cause of ascites in Africa and Asia. Previous studies have shown that it accounts for up to 23% of all patients with ascites[8, 14]. Malignant Ascites also accounts for 13-25% of all patients with ascites in Africa[14, 15].

Other causes of ascites, such as nephrotic syndrome, chronic kidney disease, and heart diseases are also prevalent both in Africa and Asia. Nephrotic syndrome has been reported to affect 3 to 6% of adult patients with ascites, while heart failure has been reported to affect 5 to 8% of such patients [8, 74]. Chronic kidney disease was reported as a co-morbid condition in patients with ascites [66], but ascites has been reported in up to 26% of patients with chronic kidney disease [87].

However, the clinical, and socio-demographic characteristics; together with the distribution of the most common causes of ascites in our setting is not known.

1.8 RATIONALE

Since most causes of ascites especially in the African setting, are treatable if diagnosed early, it is important therefore for the practicing physician to be aware of the common causes of ascites among adult patients, and the characteristics of these patients in our locality.

This study therefore determined the causes, and characteristics of adult patients with ascites admitted in medical wards at Muhimbili National Hospital in Dar es Salaam, Tanzania

1.9 OBJECTIVES

1.9.1 Broad Objective

To determine the causes of ascites and describe the characteristics of adult patients with ascites admitted in medical wards at Muhimbili National Hospital

1.9.2 Specific Objectives

1. To describe the socio-demographic characteristics of adult patients with ascites admitted in medical wards at Muhimbili National Hospital

2. To describe the clinical characteristics of adult patients with ascites admitted in Medical wards at Muhimbili National Hospital

3. To describe the laboratory characteristics of adult patients with ascites admitted in Medical wards at Muhimbili National Hospital

4. To determine the causes of ascites among adult patients with ascites admitted in Medical wards at Muhimbili National Hospital

CHAPTER TWO

2.0 METHODOLOGY

2.1. Study Design

Hospital Based Descriptive Cross-Sectional Study

2.2. Study Setting

All Medical wards, in Mwaisela Block, at Muhimbili National Hospital, in Dar-Es-salaam, Tanzania

Muhimbili National Hospital is Tanzania's national referral, and university teaching hospital. It receives patients from all over the country. On average, daily attendance to the various outpatient clinics is about 1000 patients, and has a 1500 bed capacity.

The department of Internal Medicine is housed in Mwaisela Block, which has 3 male wards, 3 female wards, and one high dependent unit. The inpatient bed capacity is about 220. These wards are further divided into super-specialty units such as Dermatology, Hematology, Cardiology, Endocrinology, Nephrology, Neurology, Gastroenterology and Hepatology, Pulmonology, and Infectious Diseases.

About 25 patients are admitted daily. All of them are initially clerked by an Intern Doctor, and a Resident student; and are later on reviewed by a Specialist Physician.

2.3 Target Population

All adults with ascites admitted in Medical wards at Muhimbili National Hospital, Dar-Es-salaam, Tanzania

2.4 Study Duration

From August, 2012 to February, 2013

2.5 Sample Size Estimation

Sample size was calculated using formula for Prevalence studies with Finite Population Correction*

$$n' = \frac{NZ^2P(1-P)}{d^2(N-1) + Z^2(1-P)}$$

Whereas:

n'= Sample size with finite population correction

N= Population size = 200

Z = statistic for a level of confidence = 1.96

d = Level of precision (which is variable) = 0.07

P = Proportion of liver Cirrhosis among patients with ascites in Nigeria by Malabu, et al [8]= 44%

Therefore, Sample size (n) = 99

*Naing L, Winn T, and Rusli BN. Practical issues in calculating the sample size for prevalence studies. Archieves of Orofacial Sciences 2006; 1: 9-14

2.6 Inclusion Criteria

Consenting adult patients with the following features:-

- Aged 18 years and older
- Evidence of ascites on abdominal examination

2.7 Exclusion Criteria

None

2.8 Sampling Technique

All adult patients admitted in medical wards at MNH wereconsecutively screened for presence of ascites.

2.9 Recruitment Method

Abdominal examination was done to all adult patients admitted in Medical wards daily. All adult patients diagnosed to have ascites clinically, by either positive shifting dullness or fluid thrill were included into the study

2.10 Grading of Ascites

All patients with ascites were graded according to the grading system proposed by the International Ascites Club [6].

1. Grade 1 — mild ascites detectable only by ultrasound examination
2. Grade 2 — moderate ascites manifested by moderate symmetrical distension of the abdomen
3. Grade 3 — large or gross ascites with marked abdominal distension

2.11 Data Collection Tools

A structured questionnaire was used to collect information from each patient. The information obtained included demographic data, age, occupation, marital status, educational level, and relevant history on ascites/abdominal distension (duration, onset, progression, aggravating, and relieving factors), any associated factors/symptoms, physical findings, lab and imaging investigation results, and final diagnosis reached.

Pre testing of the data collection tool for its validity and readability was conducted among patients admitted in Medical wards at the MNH one month prior to onset of data collection, and the patients involved during the pretesting exercise were not included in the study. Thereafter, pretested tools were revised and restructured according to observed errors.

2.12 Investigations

The following Investigations were done to all study participants ascitic Fluid (LDH, Total Protein, Albumin, Cytology, Aerobic and Anaerobic Bacterial Culture & Sensitivity), Serum Lactate Dehydrogenase, Total Protein, Albumin, Full Blood Count, Erythrocyte Sedimentation Rate, Liver Function Tests (Aspartate aminotransferase, Alanine aminotrasferase, Alkaline Phosphatase, Direct Bilirubin and Total Bilirubin), Renal Function Tests (Serum Creatinine, Uric Acid, and Urea), HIV ELISA, Serum electrolytes

(Sodium, Calcium, Potassium) , Abdominal Ultrasound , Peritoneal biopsy,and Chest x ray.

The following Investigations were done only where indicated

1. Sputum for AFB, and Ascitic fluid for Mycobacterial Culture and Sensitivity
   - In a patient with any combination of symptoms of fever, cough, weight loss, excessive night sweating, abdominal pain, or distension, for at least 2 weeks.
   - With or without features suggestive of pulmonary tuberculosis on Chest x ray.
   - Exudative ascites (AF TP > 30g/dl, AF/S TP > 0.5), or low gradient (SAAG < 11g/l) ascites.
2. Serum Amylase
   - History of acute severe upper abdominal pain, with or without nausea and vomiting
3. Urinalysis
   - History of any of the following: reduced urine output; frothy urine; hematuria; lower limb, facial, or generalized body swelling.

2.13 Description of Bedside Procedures

2.13.1 Venopuncture

1. The patient was informed about the procedure, and the possible risks involved
2. The following supplies were collected before the procedure
   a. Venopuncture tray with Alcohol cotton swabs (70%), two dry clean gauzes, Tourniquet, At least two 10cc Syringes, Two sets of clean gloves, and Plaster
   b. Three Collection tubes
      i. 1 purple top tube (with EDTA) for Full Blood Picture and Erythrocyte Sedimentation rate
      ii. 1 green top (with Sodium Heparin) for biochemistry analysis
      iii. 1 red top (vacuum) tube for HIV testing
   c. Safety box for disposal of syringes and needles
3. Then the tubes were labelled with the patient name and identification number

4. The patient was advised to lie supine with the forearm extended in a downward position to prevent backflow, then the following steps were followed
    a. Tourniquet was applied on the patient arm 3-4 inches above the puncture site
    b. The patient was asked to make a fist to make the veins easily visible
    c. The most suitable vein was selected by palpating the vein path
    d. Either the cephalic, median cubital, or the basilica vein was selected
    e. The venopuncture site was cleaned with alcohol in a circular motion and allowed to dry
    f. The syringe and needle were assembled
    g. The needle was inserted, bevel side up, into the vein
    h. About 10 mls of blood was collected
5. The tourniquet was released, and the following steps were followed to remove the needle
    a. Pressure was applied at the puncture site with a dry cotton gauze
    b. The needle was removed, and pressure was continued to be applied until bleeding had stopped
6. Then about 3mls of blood was transferred from the collection syringe into the collection tubes, and then the samples were sent to the lab within 30minutes.
7. All contaminated supplies were properly disposed

2.13.2. Abdominal Paracentesis

The purposes of examining the ascitic fluid were to exclude subacute bacterial peritoneal peritonitis (SBP), and to distinguish whether or not portal hypertension is the cause of the ascites [2].

Paracentesis were performed using a standard 1.5 inch 22 gauge needle, either in the midline, midway between the umbilicus & the symphisis pubis or laterally, about 1.5 inches above and medial to the anterior superior iliac spine.

Three sterile vacuum tubes were each filled with 3 cc of ascitic fluid, and were sent to the lab for Gram stain, aerobic and anaerobic culture and sensitivity, Cytology, Biochemistry

(i.e. Albumin, Total protein, and Lactate dehydrogenase, and Glucose) determinations. A fourth tube with 3cc of ascitic fluid was collected for Mycobacterium culture (if exudative). Additional 10mls of ascitic fluid were collected and transported to the laboratory in two Bact/ALERT blood culture bottles; one for Anaerobic and Aerobic culture and sensitivity testing.

2.13.3 Peritoneal Biopsy

The following procedure was followed

a. Verbal consent was obtained, detailing all the risks and benefits of the procedure.
b. The patient was asked to lie supine with one pillow under the head.
c. The right lower quadrant of the abdomen was selected for biopsy
    i. It wasdraped, and injected with 2% Xylocain, which was infiltrated as deep as the peritoneum
    ii. A small incision (0.5cm) was made with a disposable surgical blade.
    iii. Abraham's needle was pushed into the peritoneum, with rotatory movement
    iv. Ascitic fluid was aspirated after reaching the peritoneal cavity

- Then the needle was withdrawn as far as the abdominal wall, so as to engage the peritoneal surface.
    v. An assistant would sometimes push the abdominal wall against the needle tip to facilitate engagement of the peritoneum
- After this maneuver, the same steps were follow as during pleural biopsy, and 2-3 pieces of peritoneum were obtained in multiple steps
- Skin incision was closed with silk 2/0 and dressing wasbe done.
- Patient was be advised to lie on the left side, and observed in the ward for 24 hours.
- Pieces of biopsies were put in 10% formalin bottle, labeled, and sent to histopathology laboratory.
- Patient was advised to have the stitch removed after 5-7 days.

2.14 Laboratory Procedures

2.14.1. Ascitic Fluid Culture and sensitivity

Upon receipt of the BacT/ALERT blood culture bottles they were incubated for a maximum of 5 days at 37^{o}C. During those five days, daily monitoring was done for development of turbidity, gas formation, and batty change to yellow color which indicate bacterial growth.

If any of those signs was positive at any time then the sample was sub-cultured into Chocolate Agar, Blood Agar, Cled agar, and Mackonkey Agar. These agars were also incubated for a maximum of 72 hours, and monitored for any signs of bacterial growth.

Then the bacterial colonies were identified appropriately. Both *E.coli* and *Klebsiella spp* formed yellow colonies on Cled agar; while *Klebsiella spp* also formed pinkish colonies on Mackconkey agar, and had positive quelling reaction.

These colonies were then tested for sensitivity with various antibiotics including Ciprofloxacin, Cotrimoxazole, Augumentin, and Gentamycin.

2.14.2 Ascitic Fluid Cytology Technique

The following procedure was followed for each sample of ascitic fluid sent for cytology analysis

i. Ascitic fluid samples were received in cytology laboratory filled in sterile vacuum (Red top) containers.
ii. Macroscopic examination of the samples was done and recorded.
iii. After which the sample was centrifuged to obtain deposits and the supernatant was discarded.
iv. The deposits obtained were used to make at least 2-3 slides for each sample of ascitic fluid.
    a. The slides were then immediately fixed with 50-50% Ether Alcohol, and 95% Alcohol. Then wait for 15 minutes.

b. After 15 minutes, the slides were stained with Papanicolaus stain
c. Then they were subsequently rehydrated with 90%, 80%, and 70% alcohol. After which they were washed on a stream of tap water.

v. The slides were then dipped into Hematoxylin for 4 minutes. This is a basic dye which stains nuclei with higher affinity.
   a. Then, cleaned with tap water, and rinsed with 1% acid alcohol in order to decolorize the tissues.
   b. Then the slide was again washed on running water for blueing
   c. After 3 minutes the specimen were dehydrated on a series of 70%, 80%, and 95% alcohol respectively.

vi. Then the specimen was stained with orange G dye which stains premature cells. Then rinsed on 95% alcohol

vii. Then they were counter stained on Eosin Azua (EA 36) for 3 minutes. Then rinse on 95% alcohol ×2, and absolute alcohol ×2.

viii. Then slides were left on Xylene, which is aa clearing agent; for 5 minutes.

ix. And finally, the slides were mounted with DPX, or cover slipped.

x. Then they were sent to the Pathologist for microscopy

2.14.3 Tissue Histology Technique

The following procedure was followed for all tissues which were received in the Histology Laboratory.

i. All the tissues were in formalin containers. Once received they were put on a fume chamber for sectioning. However, since almost all specimens in this study were small pieces the whole submitted piece was taken as a whole block, and put in a tissue cassette and clip.

ii. Then the tissue cassette was put on a tissue processor machine for 24 hours; which process the tissues through formalin, 70%, 80%, and 95% alcohol respectively, xylene, and finally dipped in paraffin wax

iii. Then the tissue was transferred from the tissue cassette into a mold, and then freezed. After which the tissue was removed from the mold

iv. From here the tissue while still cold, was taken in block for sectioning into thin sections by the microtone machine. Then the thin slides were put on a hot plate at a temperature of 60-70 ^{o}C, in order to melt the wax

v. Then the slides were arranged in a rack for staining, where the following steps were followed
    a. First dipped 10× into two Xylene solutions, for 3 minutes each
    b. The rehydrated by dipping 10 times on one solution of Absolute alcohol, two solutions of 95% alcohol, one solution of 80% alcohol, and one solution of 70% alcohol.
    c. Then the slides were washed with tap water.

vi. Following this, the slides the nucleus was stained with a basic dye, Hematoxylenefor 5 minutes.
    a. Then rinsed with water.
    b. The slides were then differentiated on a solution with 1% acid (HCl)-70% alcohol
    c. And then the tissues were blueing with water for 10 minutes

vii. The cytoplasm was stained with 1% Acqueous Eosin solution for 5 minutes
    a. Then rinsed with water

b. And dehydrated by dipping 10 times into one solution of 70% alcohol, one solution of 80% alcohol, two solutions of 95% alcohol, and two solutions of absolute alcohol.

viii. Then the slides were cleaned in two solutions of Xylene for 3 minutes each

ix. Finally the slides were mounted with DPX and cover slip

x. Then sent to the Pathologist for microscopy

2.14.4 Serum and Ascitic Fluid Biochemistry and Serology Analysis

This was done by using ABBOT ARCHTECH C 8000 Biochemistry Analyser

Serum HIV Serology was assessed by ELISA method (ABORT AxSYM)

2.15 Radiological Procedures

Philips Mode HD 3 machine, with a 3.5Hertz transducer was used for abdominal ultrasound.

Philips Villa (Italy) Conventional X ray machine was used for chest X rays, with Kilovolts (Kv) ranging from 70-120 Kv, and milliamps-second (MAs) varying 16 to 360 MAs.

2.16 Data Management

All filled questionnaires were coded before entering data into the computer using EPI data Software version 3. Data cleaning was done by using consistence checks, and SPSS (Statistical Package for Social Sciences) version 18.0 statistical software was used for data analysis. Frequency distribution tables were used to summarize the data. Data was presented as means, +/- standard deviation, percentages and 95% Confidence Interval. P value of < 0.05 was considered statistically significant.

2.17. Operational Definitions

1. Liver Cirrhosis

Liver cirrhosis was defined by the presence of the following;-

i. Shrunken liver on physical examination, as evidenced by liver span of less than 10cm

ii. Plus any combination of three of the following Ultrasound features [49,50]

   a. A coarsened or heterogeneous echo pattern

   b. Increased parenchymal echogenicity

   c. Nodularity of liver surface [micro nodules (diameter 0.1 to 1cm), or macro nodules (varying diameter)]

iii. With or without ultrasound features of portal hypertension, characterized by Portal and splenic veins greater than 10mm in diameter (sensitivity and specificity of 82%.) [51]

2. Tuberculous peritonitis (TBP)

Was defined by the presence of ascites with any of the following

i. Peritoneal biopsy showing evidence of chronic caseous necrosis

ii. Peritoneal biopsy showing evidence of chronic inflammation, plus evidence of tuberculosis elsewhere

   a. TB of the Pleura as evidenced by presence of pleural effusion, and pleural biopsy showing chronic caseous necrosis, or Pleural fluid Adenine Deaminase > 33 IU/l

   b. Pulmonary TB as evidenced by typical symptoms of TB (fever, cough, weight loss, and excessive night sweating), plus suggestive Chest x-ray findings (lung cavities, perihilar lymphadenopathy, or lung infiltrates), with or without positive sputum for AFB.

c. TB Lymphadenitis, as evidenced by presence of chronic caseous necrosis on lymph node FineNeedle Aspiration Cytology, or biopsy.

3. **Malignant Ascites (MA)**

Was defined as ascites that is associated with cancer at different sites, characterized by

i. Ascitic fluid cytology with evidence of malignant cells

ii. Evidence of Primary malignancy by imaging or biopsy (of the peritoneum or any other tissue) in any of the following organs: ovaries, endometrium, breast, lungs, colon, stomach, pancreas, prostate, or any other organ

4. **Heart Failure**

This was diagnosed according to the Framingham Criteria (Appendix VI) which has a sensitivity of 100% and specificity of 78% [57]. Diagnosis of congestive heart failure required the presence of

i. At least two major criteria, or

ii. 1 major criterion plus 2 minor criteria

All participants with suspected heart failure had an echocardiography done to define the underlying etiology.

5. **Nephrotic Syndrome**

Nephrotic syndrome was defined to be present in any patient had all of the following clinical features:-

i. Generalized edema

ii. Hypoalbuminemia, as evidenced by serum albumin < 30mg/dl

iii. Heavy proteinuria, as evidenced by >3g of protein in 24 hours Urine collection

iv. Hyperlipidemia, as evidenced by serum total cholesterol > 5.12mmol/l

6. **Chronic Kidney Disease (CKD)**

Was defined by the presence of the following combination of features

i. At least three months history of any of the following

   a. Reduced urine output

   b. Hematuria

   c. Frank pain

   d. Edema

   e. Hypertension

ii. Signs of uremia (such as upper GI bleeding, pericarditis, skin itching or rashes, encephalopathy)

iii. GFR below 60ml/min/1.73m3 as defined by the Cockcroft-Gault equation

2.18 Ethical Considerations

Prior to data collection, ethical clearance was sought from the MUHAS Ethical Committee. And permission to conduct the study was obtained from MNH administration.

Each patient was asked to sign a written consent for the purpose of participating in this study, which included details of HIV testing, all invasive procedures (i.e. veno-puncture, abdominal paracentesis, and peritoneal biopsy), detailing the procedure, benefits and potential complications.

All information obtained from study participants was kept confidential, and shared only with the attending health care personnel involved.

All patients enrolled in the study received all routine services while admitted in the medical ward, and upon discharge follow-up care was continued through the various specialty clinics within the hospital.

All HIV positive patients were screened for presence of any opportunistic infections, eligibility for HAART, and were treated according to the current guidelines for the management of HIV patients in Tanzania.

CHAPTER THREE

3.0 RESULTS

3.1 Socio-demographic characteristics of the study sample

A total of 125 adult patients admitted with ascites in Medical wards at MNH during the study period, were selected for inclusion into the study. Among them, 7 denied consent to participate, and 15 had incomplete data.

Therefore, a total of 103 participants were included in this analysis. Among them 53 (51.5%) came from Dar-Es-Salaam, while the rest came from other regions upcountry.

Of the 103 participants, 52 (50.4%) were females, with mean age of 40.9 ± 1.51 years. Majority 59 (57.3%) of them were in the age group 18-39; and 61 (59.2%) of them were either married or cohabiting, but the difference between sexes was not statistically different (p 0.31).

Majority 77 (74.8%) of the study participants had primary education and below, and the remainder had secondary education and above. Males had higher education compared to females, but the difference noted was not statistically significant (p 0.32).

Most 65 (63.1%) of the participants were involved in income generating activity, of which 23 (22.3%) were peasants, 24 (23.3%) were petty traders, 10 (9.7%) were private sector employees, and 8 (7.8%) were government employees. More males were involved in income generating activity compared to females, with a statistically significant difference (p 0.01).

Table 1: Socio-demographic Characteristics of Adult patients with ascites admitted in medical wards at Muhimbili National Hospital (N= 103)

Character	Females (N= 52)		Males (N=51)		Total (N=103)		p-value
	n	%	n	%	N	%	
Age Group (years)							
18-39	35	67.3	24	47.1	59	57.3	0.78
40-59	9	17.3	18	35.3	27	26.2	
60+	8	15.4	9	17.6	17	16.5	
Marital Status							
Single	19	36.5	11	21.6	29	28.2	0.31
Married/cohabiting	25	48.1	36	70.6	61	59.2	
Divorced/Widowed	8	15.4	4	7.8	12	11.6	
Education							
Primary Education & below	40	76.9	37	52.9	77	74.8	0.32
Secondary Education	10	19.2	5	9.8	15	14.6	
Post-Secondary Education	2	3.8	9	17.6	11	10.7	
Occupation							
Government employee	1	1.9	7	13.7	8	7.8	0.01
Private sector employee	4	7.7	6	11.8	10	9.7	
Petty trader	10	19.2	14	27.5	24	23.3	
Not employed	24	46.2	14	27.5	38	36.9	
Peasant	13	25.0	10		23	22.3	

3.2 Clinical characteristics of adult patients with ascites admitted in Medical wards at Muhimbili National Hospital

Reported symptoms and duration

Of the 103 study participants, about two fifth (38.3%) had symptoms for duration of less than three months, over a quarter (29.1%) had symptoms for 3-6 months, whereas about one third (32.0%) had symptoms for longer than 6 months. The median duration of symptoms was 3 months.

Majority of the study participants reported history of abdominal distension 101 (98.1%), generalized body weakness 94 (91.3%), lower limb swelling 83 (80.6%), loss of appetite 79 (76.7%), difficulty in breathing 67 (65%), nausea 60 (58.3%), dyspnea on exertion 60 (58.3%), and palpitations 57 (55.8%).

Table 2: Frequencies of reported symptoms among adult patients with ascites admitted in Medical wards at Muhimbili National Hospital (N= 103)

Symptoms	Frequency	Percentage
Abdominal distension	101	98.1
Generalized body weakness	94	91.3
Lower limb swelling	83	80.6
Loss of appetite	79	76.7
Difficulty in breathing	67	65
Nausea	60	58.3
Dyspnea on exertion	60	58.3
Palpitations	57	55.8
Abdominal pain	48	46.6
Reduced urine output	46	44.7
Facial swelling	44	42.7
Cough	41	39
Weight loss	40	38.8
Nocturnal cough	38	36.9
Paroxysmal Nocturnal Dyspnea	37	35.9
Altered sleep pattern	37	35.9
Fever	35	34
Jaundice	35	34
Vomiting	31	30.1
Night sweats	30	29.1
Melena	25	24.3
Chest pain	22	21.4
Vomiting blood	13	12.6
Hematuria	8	7.8
Hemoptysis	7	6.8

3.2.1 General Physical signs

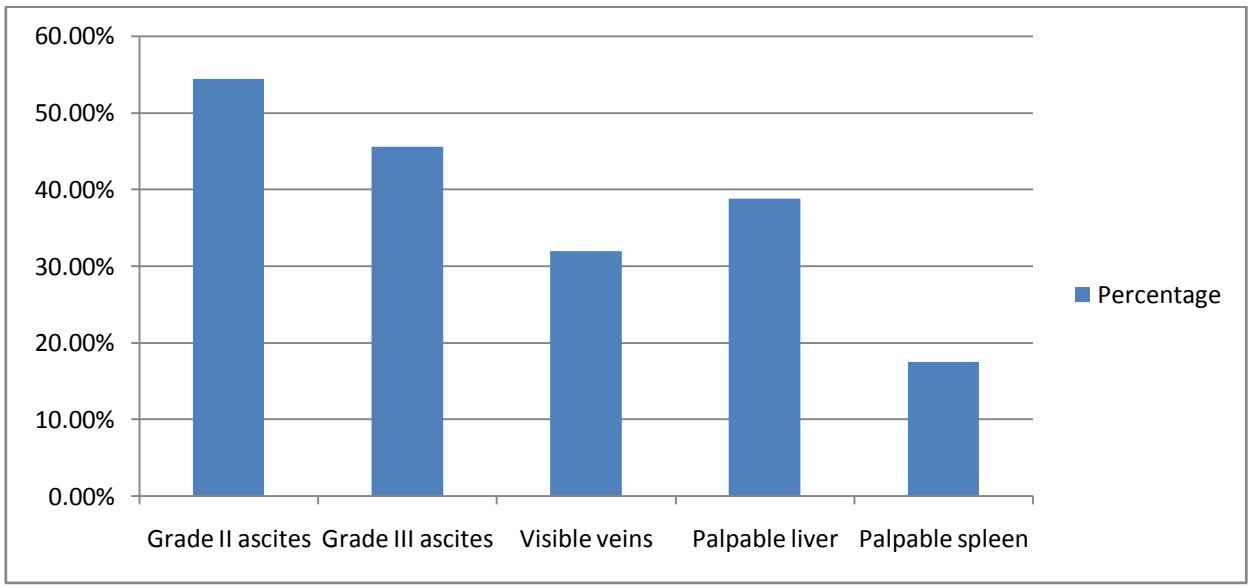
Upon examination of the 103 study participants, majority 76 (73.8%) were pale, 74 (71.8%) had lower limb edema, 64 (62.1%) were wasted, 36 (35.0%) had anasarca, and 31 (30.1%) were jaundiced. But only 10 (9.7%) had finger clubbing, 7 (6.8%) had leuconychia, 6 (5.8%) had duputyrens contractures.

3.2.2 Abdominal signs

Of the 103 study participants, more than half (54.4%) had grade II ascites, while the remainder (45.6%) had grade III ascites, nearly a third (32.0%) had visible veins on inspection, while over a quarter (38.8%) had palpable liver, and over a quarter (17.5%) of them had palpable spleen with size ranging from 3 - 20 cm.

Of the 40 participants who had a palpable liver, the liver span was ranging between 10 to 18cm. More than half (67.5%) of them had a tender liver. The liver surface was smooth (60%), nodular surface (35%), or rough (5%). And the consistency of the liver was either soft (52.5%), firm (30.0%), or hard (17.5%).

Figure 1: Distribution of abdominal signs among adult patients admitted with ascites in Medical wards at Muhimbili National Hospital (N= 103)



3.2.1 Other physical findings

Of the 103 participants, 33 (32.0%) had crackles, 14 (13.6%) had features of consolidation, 12 (11.7%) had pleural effusion, and 2 (1.9%) had rhonchi.

Among the 103 participants, 16 (15.5%) had features of cardiomegally, 16 (15.5%) had features of valvular heart disease, 7 (6.8%) had distant heart sounds, and 2 (1.9%) pericardial rub.

Of the 103 participants, majority 93 (90.3%) had normal CNS examination with Glasgow Coma Scale (GCS) of 15. Nine (8.7%) participants were drowsy, and 2 (1.9%) had tremors on examination. Five (4.9%) participants had GCS of 14, Four (3.9%) had GCS of 10, and one participant had a GCS of 8.

3.3 Laboratory Characteristics of adult patients with ascites admitted in Medical wards at Muhimbili National Hospital

3.3.1 Ascitic Fluid Macroscopic Examination

Of the 103 participants, majority 91 (88.3%) had straw colored ascitic fluid, 7 (6.8%) had hemorrhagic ascitic fluid, 4 (3.9%) had pyogenic ascitic fluid, and only one (1.0%) participant had chylous ascites.

3.3.2 Ascitic Fluid and Serum Biochemistry

103 ascitic fluid samples were analyzed for levels of Albumin, Total protein, Lactate dehydrogenase (LDH), and Glucose. Serum samples were also analyzed for the same parameters.

Ascitic Fluid Total Protein (AF TP) at cut off value of 30g/l, Ascitic Fluid Serum Total Protein ratio (AF/S TP) at cut off value of 0.5, and Serum Ascites Albumin Gradient (SAAG) at cut off value of 11g/l; were used to classify the ascitic fluid into either exudate or transudate (by AF TP, and AF/S TP) or high or low gradient (by SAAG).

A total of forty five (43.7%) ascitic fluid samples were classified as either Exudative or Low Gradient. Without regard to the overlap among the different methods used to classify ascites, thirty four (33%), and thirty two (31%) of the ascitic fluid samples were classified as exudates by AF TP and AF/S TP ratio respectively, while SAAG classified 27 (26.2%) ascitic fluid samples as low gradient.

3.3.3 Ascitic Fluid Microbiology

Ascitic fluid samples from 103 participants, was subjected to microbiology analysis. Among them, only three samples had positive bacterial culture growth. Of these, 2 sample revealed *Klebsiella spp,* and one sample revealed *Escherichia coli*.

Of 45 ascitic fluid samples which were classified as eitherexudative or low gradient and subsequently sent for Mycobacterial culture with Lowenstein Jensen Media,only one sample was positive for *M. tuberculae* after 8 weeks on Lowenstein-Jensen media.

3.3.4 Ascitic Fluid Cytology

Of the 103 ascitic fluid cytology sample done in this study, majority 62 (60.2%) of them revealed features of chronic inflammation, 36 (34.9%) had acellular smear, 3 (2.9%) revealed acute inflammation, and only two (1.9%) of them revealed malignant cells.

Figure 2: Results of Ascitic Fluid Cytology among adult patients with ascites admitted in Medical wards at Muhimbili National Hospital (N=103)

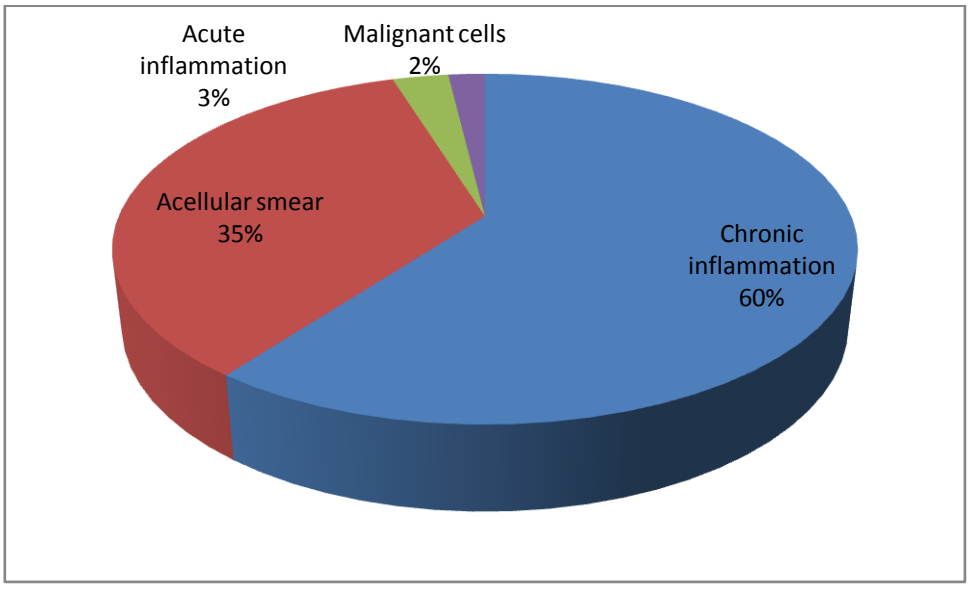


Table 3: Relationship of Ascitic fluid cytology to serum and ascitic fluid total protein, albumin, and lactate dehydrogenase (LDH) among adult patients with ascites admitted in Medical wards at Muhimbili National Hospital (N=103)

	Acellular Smear		Acute Inflammation		Chronic Inflammation		Malignant Cells		Total	
	(N=36)		(N=3)		(N=62)		(N=2)		(N=103)	
	n	%	n	%	n	%	n	%	n	%
AF TP										
Transudate	27	75.0	3	100	38	61.3	1	50.0	69	67.0
Exudate	9	25.0	0	0.0	24	38.7	1	50.0	34	33.0
AF/S TP Ratio										
Transudate	27	75.0	2	66.7	42	67.7	0	0.0	71	68.9
Exudate	9	25.0	1	33.3	20	32.3	2	100	32	31.1
AF LDH										
Transudate	26	72.2	1	33.3	51	82.3	1	50.0	79	76.7
Exudate	10	27.8	2	66.7	11	17.7	1	50.0	24	23.3
AF/S LDH Ratio										
Transudate	28	77.8	1	33.3	49	79.0	1	50.0	79	76.7
Exudate	8	22.2	2	66.7	13	21.0	1	50.0	24	23.3
SAAG										
Low Gradient	10	27.8	1	33.3	15	24.2	1	50.0	27	26.2
High Gradient	26	72.2	2	66.7	47	75.8	1	50.0	76	73.8

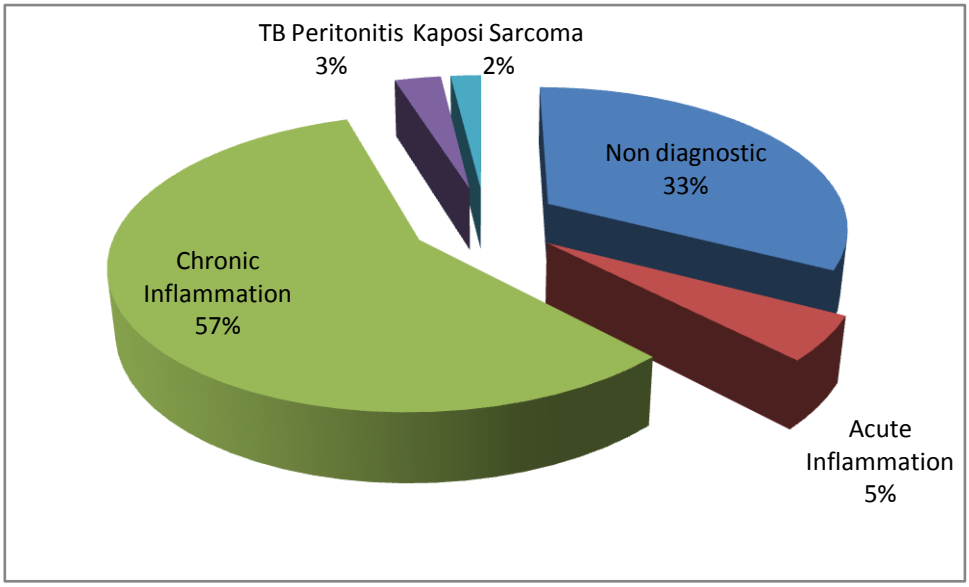
Of the 62 participants with chronic inflammation on fluid cytology, most of them had either transudates or high gradient ascites. Sixty one percent (61.3%), 67.7%, 83.7%, and 79.0% were found to have exudative ascites by AF TP, AF/S TP ratio, AF LDH, and AF/S LDH ratio respectively; and 75.8% had high gradient ascites by SAAG. Similar findings werealso observed among those with acute inflammation, and acellular smears. However, those with malignant ascites had an almost equal distribution of both exudate/low gradient and transudate/high gradient ascites.

3.3.5 Peritoneal Biopsy

Of the 103 peritoneal biopsies done in this study, 33 (32.0%) were non diagnostic (revealing normal peritoneum or muscular tissue), but over half 58 (56.3%) of them showed chronic inflammation, 5 (4.9%) showed acute inflammation, 3 (2.9%) showed Tuberculous Peritonitis, and 2 (1.9%) for each showed Kaposi sarcoma, and adenocarcinoma.

Generally, of all the 103 peritoneal biopsies only 7 (6.8%)of them were diagnostic of either TB Peritonitis or malignancy. The rest of the histology were either not diagnostic, or they showed either acute or chronic inflammation.

Figure 3: Results of Peritoneal Biopsy among adult patients with ascites admitted in Medical wards at MNH (N=103)



The commonest complications after peritoneal biopsy were pain 92 (89.3%), and mild swelling 47 (45.6%) at the incision site. One 67 years old male patient with hemorrhagic ascites developed subcutaneous infiltration of the ascitic fluid, which subsided spontaneously after five days. And two male patients complained of scrotal edema after the procedure, which later on subsided spontaneously. This was thought to be due to scrotal edema that was present prior to the procedure but became prominent after the ascitic fluid was drained.

Table 4: Relationship of peritoneal histology with serum and ascitic fluid total protein, albumin, and lactate dehydrogenase (LDH) among adult patients with ascites admitted in Medical wards at Muhimbili National Hospital (N=103)

	Non Diagnostic		Acute Inflam		Chronic Inflam		TBP		Kaposi Sarcoma		Adeno carcinoma		Total	
	(N=33)		(N=5)		(N=58)		(N=3)		(N=2)		(N=2)		(N=103)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
AF TP														
Transudate	23	69.7	5	100	11	19.0	0	0.0	0	0.0	0	0.0	69	67.0
Exudate	10	30.3	0	0.0	47	81.0	3	100	2	100	2	100	34	33.0
AF/S TP														
Transudate	24	72.8	5	100	42	72.4	0	0.0	0	0.0	0	0.0	71	68.9
Exudate	9	27.2	0	0.0	16	27.6	3	100	2	100	2	100	32	31.1
AF LDH														
Transudate	25	75.6	3	60.0	47	81.0	2	66.7	2	100	0	0.0	79	76.7
Exudate	8	24.2	2	40.0	11	19.0	1	33.3	0	0.0	2	100	24	23.3
AF/SLDH														
Transudate	29	87.9	3	60.0	45	77.6	0	0.0	2	100	0	0.0	79	76.7
Exudate	4	12.1	2	40.0	13	22.4	3	100	0	0.0	2	100	24	23.3
SAAG														
Low Gradient	5	15.2	1	20.0	15	25.9	3	100	2	100	1	50.0	27	26.2
High Gradient	28	84.8	4	80.0	43	74.1	0	0.0	0	0.0	1	50.0	76	73.8

Of the 58 participants with chronic inflammation on peritoneal biopsy, only about a third had exudative or low gradient ascites, but the majority had transudative or high grade ascites as measured by AF/S TP (72.4%), AF LDH (81.0%), AF/S LDH (77.6%), and SAAG (74.1%). Similar findings were observed among those with acute inflammation. However, all participants with TB Peritonitis, Kaposi sarcoma, and adenocarcinoma had exudative or low gradient ascites.

3.4 Distribution of causes of ascites among patients admitted in Medical wards at Muhimbili National Hospital

Of the 103 participants, several causes of ascites were identified. Most of the diagnoses were unknown prior to their admission, except for a few who were being re-admitted. However, the same protocol of investigations was followed for all patients.

The commonest cause of ascites was Liver cirrhosis 35 (34.0%), followed by Malignant Ascites 25 (24.3%), Heart Failure 18 (18.4%), Chronic Kidney Disease 13 (12.6%), and TB Peritonitis 9 (8.7%). Less common causes were Nephrotic Syndrome 2 (1.9%), and Chronic Pancreatitis 1 (1.0%).

Of these 103 participants, 17 (16.5%) were positive for HIV, and11 (10.7%)had mixed causes of as cites.

Figure4: Distribution of causes of as cites among patients admitted in Medical wards at Muhimbili National Hospital (N= 103)

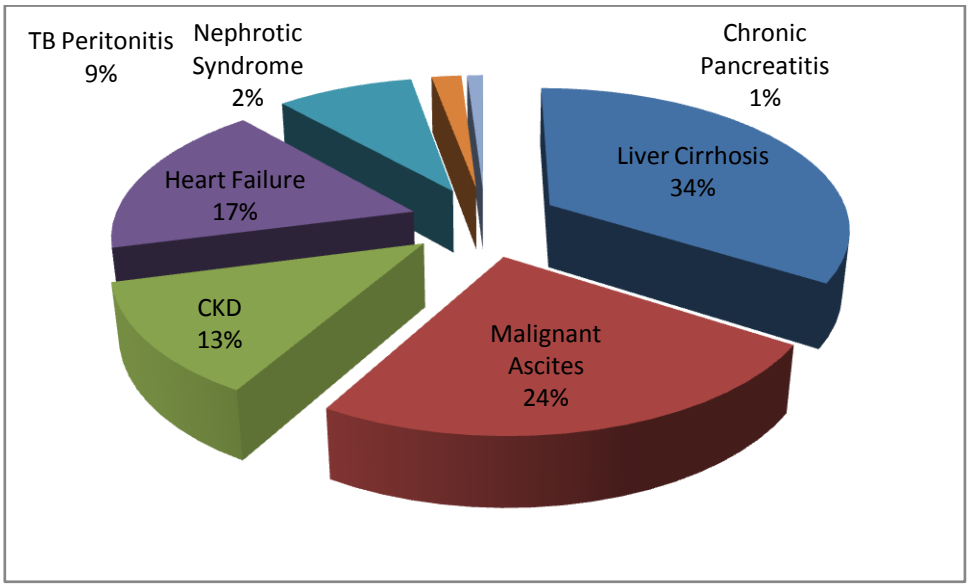


Table 5: Ascitic Fluid (AF) and Serum Total Protein (TP), Albumin and Lactate dehydrogenase (LDH) in adult patients with ascites admitted in Medical wards at Muhimbili National Hospital (N=103)

	Portal Hypertensive Causes [LC, HCC, CKD, HF, NS]		**Non-Portal Hypertensive Causes [TBP/MA/CP]**		**Total**	
	(N= 83)		**(N=20)**		**(N= 103)**	
AF TP						
	n	%	N	%	N	%
Transudate <30g/l	66	79.5	3	15.0	69	67.0
Exudate ≥30g/l	17	20.5	17	85.0	34	33.0
AF/S TP Ratio						
Transudate < 0.5	68	81.9	3	15.0	71	68.9
Exudate ≥ 0.5	15	18.1	17	85.0	32	30.1
AF LDH						
Transudate < 180 U/l	66	79.5	13	65.0	79	76.7
Exudate ≥ 180 U/l	17	20.5	7	35.0	24	23.3
AF/S LDH Ratio						
Transudate < 0.6	70	84.3	9	45.0	79	76.7
Exudate ≥ 0.6	13	15.7	11	55.0	24	23.3
SAAG						
High Gradient ≥ 1.1g/l	73	88.0	3	15.0	76	73.8
Low Gradient <1.1g/l	10	12.0	17	85.0	27	26.2

Over two thirds of the participants with portal hypertensive causes of ascites had transudative or high gradient ascites. However, majority of those with non-portal hypertensive causes had exudative or low gradient ascites by AF TP, AF/S TP ratio, AF/S LDH ratio and SAAG with the exception of AF LDH.

3.4.1 Liver Cirrhosis

Thirty five participants with Liver cirrhosis were diagnosed on the basis of suggestive history, examination findings, and consistent abdominal ultrasound features.

Of the thirty five participants with Liver Cirrhosis, over a half 19 (54.3%) of them were males, and most 23 (65.7%) were aged 18-39 years, followed by 8 (22.8%) aged 40-59 years, and only four (11.4%) were aged 60 years and above.

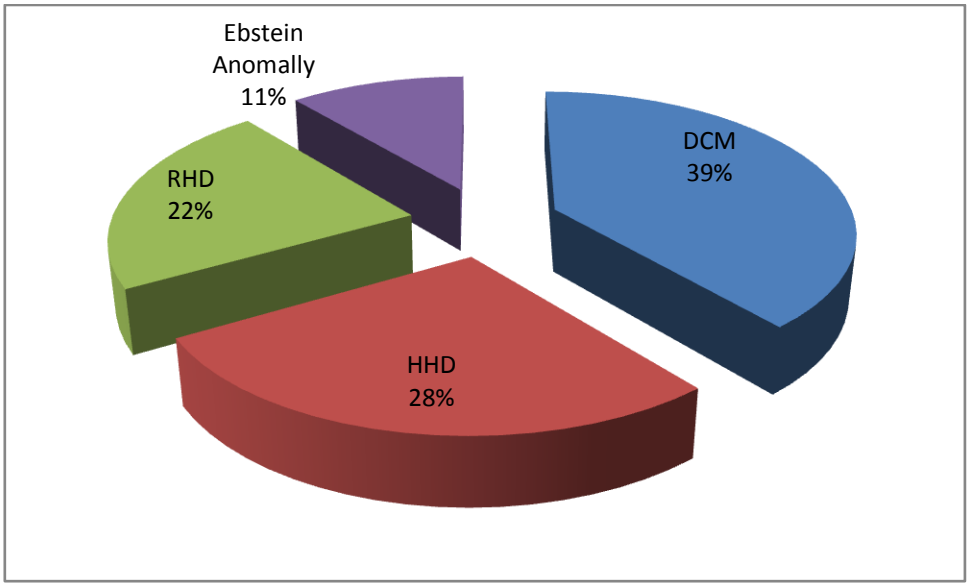
Over a third 34.3% (12/35) of the participants with liver cirrhosis were positive for Hepatitis B Surface Antigen. And three participants with liver cirrhosis had features of CKD, and one had Heart failure.

3.4.2 Heart Failure

Of the 18 participants with heart failure, all presented with features of heart failure as suggested by the Framingham Criteria (see Appendix VII). However, echocardiography was done to all patients, which revealed Dilated Cardiomyopathy in 7 participants, 5 Hypertensive Heart Disease, 4 Rheumatic Heart Disease, and 2 Ebstein Anomaly.

More than three quarter 14 (77.8%) of these patients with heart failure were females, and over a half 10 (55.6%) of them were aged 18-39 years, 2 (11.1%) aged 40-59 years, and six participants (33.3%) were aged 60 years and above.

Figure 5: Distribution of Echocardiographic findings among adult patients with HF with ascites admitted in Medical wards at Muhimbili National Hospital (N=18)



3.4.3 Tuberculous Peritonitis

Of the 9 patients with TB Peritonitis,5 had concurrent features suggestive of PTB (two of them with positive sputum for AFB), one had concurrent pleural tuberculosis, and three were diagnosed by peritoneal biopsy (one of them with positive culture for *M.tuberculae*).Two patients were also diagnosed with heart failure, and chronic kidney disease each.

Five (55.5%) of these patients were females, and 4 (44.4%) were aged 18-39 years, 4 (44.4%) aged 40-59 years, and one patient (11.1%) aged 60 years or above.

3.4.4 Chronic Kidney Disease (CKD)

Thirteen participants were diagnosed with CKD. All of them had ultrasound features of CKD, and GFR below 60 ml/min/1.73m^3.

3.4.5 Nephrotic Syndrome (NS)

Two participants had Nephrotic syndrome, and both of them were females. The first was aged 20 years and the second was 28 years old.

3.4.6 Malignant Ascites (MA)

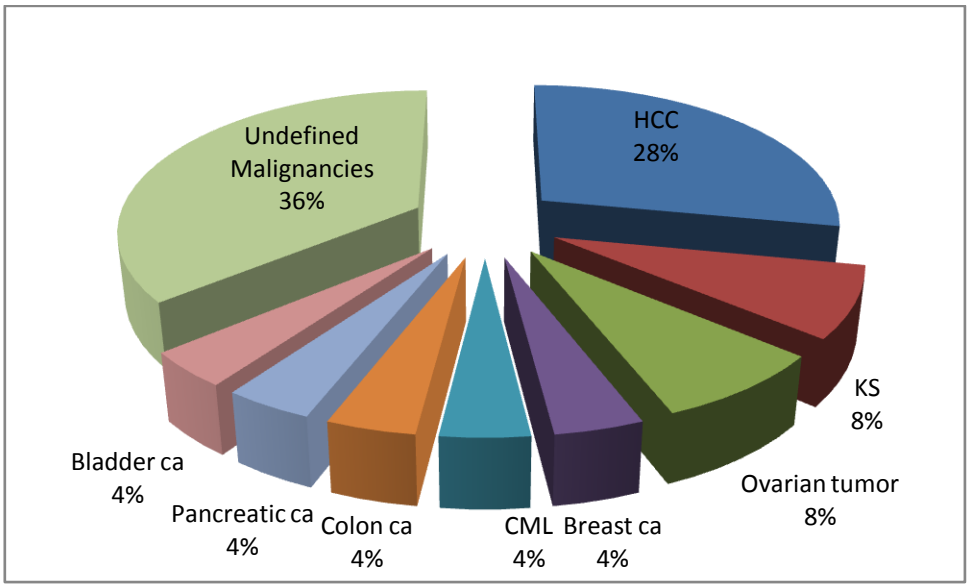
Malignant ascites was diagnosed on the basis of suggestive history, physical findings of ascites, with or without features of abdominal or any other mass elsewhere, plus cytological, histological, or imaging evidence of malignancy.

Twenty five participants were diagnosed to have Malignant Ascites. Among them 15 (60%) were males, and 13 (52%) were aged 18-39 years, 6 (24%) were aged 60 years or above.

Of the twenty five participants with Malignant Ascites, seven (28%) had Hepatocellular carcinoma, two (8%) had ovarian tumors, two (8%) Kaposi sarcoma, one (4%) participant each had breast carcinoma, chronic myeloid leukemia, cancer of the colon, pancreatic cancer, and urinary bladder cancer respectively.

The ascitic fluid cytology was diagnostic of malignant ascites in only two (8%) of these patients. It showed features of adenocarcinoma in a patient with ovarian tumor; while it revealed non-specific malignant cells in the second patient with urinary bladder cancer.

Figure 6: Distribution of the causes of Malignant Ascites among adult patients admitted in Medical wards at Muhimbili National Hospital (N=25)



However, the primary tumor site could not be identified in 9(36%) participants with malignant ascites. All of them had features of metastatic hepatic mass on ultrasound, with chronic inflammation on peritoneal histology and ascitic fluid cytology, and normal α-feto protein. No other mass was identified on abdominal ultrasound or chest x-ray.

3.4.6.1 Hepatocellular Carcinoma (HCC)

Of the 7 patients with Hepatocellular carcinoma, all had ultrasound features of HCC, high α- fetal protein levels (> 350 ng/ml), and two participants had fine needle aspiration cytology (FNAC) of the liver diagnostic of HCC.

3.4.6.2 Kaposi Sarcoma (KS)

Both of the participants with Kaposi Sarcoma were HIV infected, and they had high serum ascites albumin gradient. But both skin and peritoneal biopsy were diagnostic of KS.

3.4.6.3 Chronic Myeloid Leukemia

A 32 years old lady with Chronic Myeloid Leukemia and Pulmonary TB presented with constitutional symptoms, productive cough, and massive ascites for two months prior. On examination she had bilateral coarse crepitations in the chest, and massive splenomegally. Chest x-ray was suggestive of pulmonary tuberculosis, sputum was positive for AFB. She had an exudative and low gradient ascites, and both ascitic fluid cytology and peritoneal biopsy revealed chronic inflammation, but bone marrow biopsy showed features of chronic myeloid Leukemia.

3.4.6.4 Breast cancer

A 26 years old lady was diagnosed with Metastatic Breast cancer. She presented with six months history of right breast swelling, of which an earlier histology revealed adenocarcinoma of the breast tissue. She also had a recent onset ascites, right pleural effusion, and anemia. Her ascitic peritoneal biopsy showed features of adenocarcinoma.

3.4.6.5 Ovarian Tumors

Two patients were diagnosed with ovarian tumors. The first was a 56 years old lady with ovarian cancer. She presented with history of abdominal distension, and weight loss for one year. Ascitic fluid cytology revealed adenocarcinoma, and abdominal ultrasound showed a right ovarian mass.

The second was a 46 years old lady who was diagnosed with endometrial cyst. She presented with history of abdominal distension for four months. Abdominal paracentesis revealed hemorrhagic ascitic fluid. Her ascitic fluid cytology and peritoneal biopsy showed chronic inflammation. Laparotomy and excision biopsy was done, which revealed features of endometrial cyst.

3.4.6.6 Colon Cancer

One 67 years old male patient was diagnosed with colon cancer. He presented with history of abdominal swelling, weight loss, and melena. Ascitic fluid cytology showed chronic inflammation, peritoneal biopsy revealed adenocarcinoma, and abdominal CT Scan revealed a mass with infiltrations in the descending colon and rectum.

3.4.6.7 Pancreatic Cancer

A 65 years old man was diagnosed with Cancer of the head of the pancrease. He presented with history of yellowish discolorations of the eyes, generalized itching, and weight loss. On examination, he was cachexic, deeply jaundiced, with generalized scratch marks. Abdominal examination revealed only features of ascites. Both ascitic fluid cytology and peritoneal biopsy showed chronic inflammation. But abdominal CT scan revealed a mass at the head of the pancrease. He died before laparotomy was done.

3.4.6.8 Urinary Bladder Cancer

A 57 years old man was diagnosed with both urinary bladder cancer and Pulmonary TB. He presented with history of hematuria, productive cough, evening fevers, and weight loss. On examination he was wasted, with some pallor, moderate ascites, and features of consolidation and right pleural effusion. Ascitic fluid cytology showed non-specific malignant cells, and peritoneal biopsy showed chronic inflammation. Chest x-ray was

suggestive of pulmonary TB, and sputum for AFB was positive. Abdominal ultrasound revealed urinary bladder mass. Cystoscopy was done and tissue biopsy was taken, which revealed a transitional cell carcinoma.

3.4.7 Chronic Pancreatitis

Only one male participant aged 60 years was diagnosed with chronic pancreatitis. He had a prior history of smoking, and heavy alcohol intake for more than 30 years, and presented with history of recent onset vomiting, abdominal pain and distension. On examination, he was wasted with tense ascites. Serum α Amylase (882U/l); and serum Lipase (590U/l) were both highly elevated, with characteristic findings on abdominal CT scan.

3.4.8 HIV Infection

Of the 103 participants, 17 (16.5%) were infected with HIV. Among them 2 had Kaposi Sarcoma, 1 had Hepatocellular Carcinoma, 3 had TB Peritonitis, 4 had other malignancies, 4 had Liver cirrhosis, 2 had Heart Failure, and 1 had CKD.

3.4.9 Mixed Ascites

Of the 11 (10.7%) with mixed causes of ascites, 4 patients had features of both Liver cirrhosis and CKD, 3 patients had CKD and Heart failure, and 4 patients with TB Peritonitis; of whom one each had Bladder cancer, CML, CKD, Heart failure.

3.4.10 Spontaneous Bacterial Peritonitis (SBP)

Of the 103 participants, only 6(5.8%) had features suggestive of SBP. Three participants had positive bacterial culture; two with *E.coli*, and one with *Klebsiella spp*. And another three participants had ascitic fluid cytology showing acute pyogenic inflammation. However, since ascitic fluid differential cell counts were not done in this study, it was difficult to diagnose these cases.

CHAPTER FOUR

4.0 DISCUSSION

This study has shown that liver cirrhosis is the leading cause of ascites among adults admitted in medical wards in our setting, followed by malignant ascites, and heart failure. There was an equal sex distribution, and participants had a mean age of 40.9 ± 1.5 years. The most common symptoms were abdominal distension, generalized body weakness, and lower limb swelling. In addition to ascites most participants were wasted, had conjuctival pallor, and lower limb edema. About a third (32.0%) of the peritoneal biopsies were not diagnostic, while over half (56.3%) of them showed chronic inflammation, 5 (4.9%) revealed acute inflammation, and only 6.8% of them were diagnostic of either TB peritonitis, or malignancy.

4.1 Socio-demographic characteristics of adult patients with ascites

The study population comprised of 103 adult patients with ascites, of which there was an almost equal distribution of males and females. There are conflicting reports on the sex distribution among patients with ascites. While Bandar, A reported male predominance at 72% in Saudi Arabia[74]; others reported a female predominance ranging from 60-75% [8, 14, 15]. These differences in sex distribution probably reflect differences in the prevalence of the various causes of ascites in these populations. While Bandar AA, had 69% of the participants with liver cirrhosis[74];Anjun A, et al[14], and Mahmood K, et al[15]had majority of their patients with either tuberculosis or malignancy. However, due to limitations inherent in consecutive sampling, a possibility of a selection bias in this study can't be excluded.

In this study, over a half (57.3%)of the participants were aged 18-39 years, with mean age of 40.9 ± 1.51 years. These finding was much lower compared to a studies in Asia, and Europe[74, 112, 113]. Malabu, et al did not report on the mean age of his patients in Nigeria[8]. However, these finding is similar to those reported in Ivory Coast and Gambia[92,111]. This observation suggests the fact that the onset of ascites is probably earlier in Africa, compared to the rest of the world. But it may also reflect to differences in the distribution of the various causes of ascites in the different populations. While liver cirrhosis is a

disease of the middle aged in Asia[91], in our study a significant proportion of participants had liver cirrhosis, heart failure, and malignant ascites (especially Hepatocellular carcinoma), of which majority presented before 40 years of age.

Three quarters (74.8%) of the study participants had primary education and below, and a significant proportion (37%) of them were not employed. Among those who were involved in gainful employment, most of them were either peasants (22.3%), or petty traders (23.3%). This is consistent with other previous observations in Africa which have associated ascites with low socio-economic status[2].

4.2 Clinical Characteristics of adult patients with ascites

The mean duration of symptoms was 3 months, which is similar to duration reported by Luck et al[66] in Pakistan, indicating that most patients with ascites delay seeking health care both in Asia and Africa.

The frequency of symptoms of abdominal distension, abdominal pain, weight loss, and fever were similar to findings by other studies in Asia[14, 15, 66]. This similarity may be due to the chronic nature of most causes of ascites in these populations.

Fever which was reported by 34% of the respondents in this study was less common compared to 44 to 73% reported previously[15, 66]. However, this difference may be due to the fact that both Mahmood et al[15], and Luck et al[66]studied only patients with exudative ascites.

Almost three quarters (73.8%) of the study participants had conjuctival pallor, similar to 66.7% reported by Luck et al in India[66]. This may suggest a high frequency of anemia among these patients, which may be due to many causes including poor appetite, hypersplenism, or chronic illness.

However, jaundice (30.1%), splenomegally (17.5%), and hepatomegally (38.8%) were more common in this study population compared to just 1%, 1%, and 24.4% respectively as reported by Luck NH[66]. The high proportion of splenomegally may be due to the

corresponding high proportion of portal hypertensive causes (such as liver cirrhosis and heart failure); while hepatomegally may be due to many causes including heart failure, Hepatocellular carcinoma, lymphoma, or systemic infections. The high proportion of jaundice in this population may be contributed by participants with liver cirrhosis, and Hepatocellular carcinoma some of whom had features of Decompasated liver disease.

4.3 Laboratory Characteristics of adult patients with ascites

4.3.1Ascitic Fluid cytology

Majority (60.2%) of the ascitic fluid cytology showed chronic inflammation, similar to 86.6% reported by Mahmood K, et al[15]. This may be due to the fact that most patients with transudative ascites, such as those with heart failure or liver cirrhosis also had their ascitic fluid cytology showing chronic inflammation. Similar observations were also reported in Uganda among patients with EMF[109].

Only 8%of the participants with malignant ascites had positive ascitic fluid cytology for malignant cells. These findings are similar to those reported by Mahmood K, et al[15] who reported malignant cells in only 6.7% of patients with malignant ascites[15]. This may be due to the low sensitivity of this test[85].

However, this finding could be partly explained by the fact that nearly a third (28%) of the participants with malignant ascites in this study had Hepatocellular carcinoma, which normally has a negative ascitic fluid cytology. The mechanism of ascites in patients with Hepatocellular carcinoma is not peritoneal metastases but rather portal hypertension[26].

4.3.2 Peritoneal Biopsy

Majority (56.3%) of the peritoneal biopsies showed chronic inflammation, which was comparable to 40% to 46% reported by Mahmood K, et al[15]and Anjun, et al[14]. And only 7 (6.8%) of theperitoneal biopsy specimens were suggestive of a diagnosis (such as malignancy or TB Peritonitis). These findings are lower compared to 13.3% and53.3% of biopsies among patients with ascites by Anjun A, et al[14], and Mahmood K, et al[15] respectively.

This observation may be due to the fact that over half (56.3%) of participants in this study had transudative or high gradient ascites, while both Anjun, et al[14], and Mahmood, et al[15], involved only patients with exudative ascites, and low gradient ascites respectively.
This observation may suggest that peritoneal biopsy may be more useful in well selected patients, especially those with exudative or low gradient ascites.

Similarly, only a third (33.3%)of the peritoneal biopsy specimens among patients with TB Peritonitis was diagnostic, while the majority of the biopsies showed chronic non-specific inflammation. This finding is similar to 39.9% reported by Anjun et al[14]. This observation may suggest that the diagnosis of this condition depends largely on other clinical, imaging, and laboratory parameters.

The frequency of complications following percutaneous peritoneal biopsy were pain (89.3%), and mild swelling (45.6%), similar to those reported by Mahmood, K, et al[15]. This shows that the procedure is generally safe.

4.4. Causes of ascites

This study showed that liver cirrhosis was the most common cause of ascites, affecting 34% of the participants, followed by malignant ascites (24.3%), heart failure (17.5%), chronic kidney disease (12.6%), and TB peritonitis (8.7%). While nephrotic syndrome 1.9% and chronic pancreatitis 1% were the least causes of ascites in this population. These findings are similar to other studies in Africa and Asia, which also reported that liver cirrhosis was the leading cause of ascites, affecting 44-65% of the study participants[8, 74].

Of patients with liver cirrhosis, a third (34.3%) tested positive for Hepatits B surface Antigen, which is less compared to a previous study in Africa which reported that 59% of the patients with liver cirrhosis had HBsAg positive[92]. Since the current prevalence of Hepatitis B Virus infection among adults in Tanzania is estimated to be 6-8% [98]; this observation highlights the importance of other etiologies to liver cirrhosis in our population.

Our findings differ from to those of Malabu et al in Nigeria[8], who reported a lower proportion of heart disease (6%), and a higher proportion of nephrotic syndrome (5%).A higher proportion of heart failure(17.5%), and renal failure (12.6%), with lower proportion of nephrotic syndrome (1.9%)in this study population may be due to differences in the prevalence of these conditions in these populations; since generally heart failure, and renal failure contribute up to 7%, and 3% of all medical admissions in Sub-Saharan Africa[69, 93].

About a third (30.8%) of the participants with CKD had other causes of ascites. This is similar to previous reports by Luck et al reported chronic kidney disease as a co-morbidity to other causes of ascites[66]. Indicating that CKD, is also an important cause of mixed ascites. Similarly, a majority (61.5%) of these patients were males. This finding is similar to previous studies which had reported ascites in up to 26% of patients with chronic renal failure, majority of them being males[87, 88].

Majority (88.8%)of the 18 patients with heart failure had either rheumatic heart disease, hypertensive heart disease, or dilated Cardiomyopathy; and over three quarter of them (77.8%) were females. This is consistent with previous findings that these heart conditions account for up to 65% of patients with heart failure in Africa[69, 70]. The burden of these conditions in out setting is largely unknown, but these findings may call for further studies in this area.

The proportion of TB peritonitis (8.7%) in this population was similar to10.6% reported by Bandar, et al[74]in Saudi Arabia, but less common compared to a proportion of 20-23% reported in Nigeria and India[8,15]. And the highest proportions were reported at 43-66% among patients with exudative ascites in Asia[14, 66]. The lower proportion of TB Peritonitis in this study may be due the fact that we included all patients with ascites while others had included only patients with exudative ascites. Nonetheless, these observations may also be due to differences in the prevalence of tuberculosis in these populations. Since the prevalence of Tuberculosis 2011 in Pakistan, and India was reported to 350, and 249per 100,000 population respectively; compared to only 177, and 171 per 100,000 population in Nigeria, and Tanzania respectively[94].

HIV epidemic has been associated with increased prevalence of TB Peritonitis, and has been reported to account for up to 20-50% of all cases of ascites [10, 11]. However, in this study population only 33.3% (3/9) of the participants with TB peritonitis were infected with HIV. This may explain the low proportion of TB peritonitis in this study population.

In this study, Malignant Ascites (MA) was reported among of 24.3% the participants, similar to previous studies in Nigeria[8], and Zaire[9] who reported a proportion ranging from 17-22%. However, the distribution of the types of malignancies differs much from previous studies. In this study, the most common tumors were Hepatocellular carcinoma, ovarian tumor, Kaposi sarcoma, and other malignancies were less prevalent; while in Nigeria the commonest being ovarian carcinoma, gastric carcinoma, and breast carcinoma[8].

This difference may be due to the fact the study in Nigeria included predominantly women, and excluded patients with Hepatocellular carcinoma, while this study had an equal sexual distribution, and we included patients with HCC. But it may also be accounted to lack of adequate diagnostic facilities in our study to identify all primary malignancies, and the fact that only patients admitted in medical wards were included in this study. This may have contributed to a selection bias.

Hepatocellular carcinoma was the most common malignancy in our study population, accounting for 14.6% of all study participants, similar to 13.3% reported in Zaire[9]. Other studies investigating the causes of ascites did not report about HCC, or they excluded them[8, 74].

Studies done in Asia reported metastatic colon cancer as the most common malignancy in patients with ascites[14, 15], but only one such patient was found in this study; probably due to lack of adequate diagnostic facilities. This calls for further studies in this area to further define patients with malignant ascites.

Kaposi sarcoma has also been associated with ascites, especially among AIDS patients[95]. In this study two (1.9%) participants had peritoneal Kaposi Sarcoma, and both of them

were HIV infected. It is interesting to note here that both of these two patients had a diagnostic peritoneal histology. There are a few reports in literature reporting on peritoneal biopsies in these patients, but most of them were done by either laparoscope, laparatomy[95,96].

Interestingly, 10.7% of the patients in this study had mixed causes of ascites. This was similar to previous studies, which reported mixed ascites in up to 15% of the patients[4]. However, contrary to the developed world where most of these patients usually have liver cirrhosis plus another cause; in our study only four of these patients had liver cirrhosis. This may be due to differences in the proportion of the causes of ascites in these populations.

A low proportion (7.7%) of the study participants was found to have Spontaneous Bacterial Peritonitis (SBP), compared to previous reports where up to 25% of patients with ascites had SBP[80]. This may be due to limitations of obtaining ascitic fluid cell count in our study. However, only three participants were found to have either *E.coli* or *Klebsiella spp*, similar to previous observations[81].

CHAPTER FIVE

5.0 CONCLUSION AND RECOMMENDATIONS

5.1 CONCLUSION

From the findings of this study we can draw the following conclusions

1. Ascites among adult patients affect both sexes with variable distribution between studies. And it is more common in the younger age group here in Africa compared to the rest of the world.

2. The clinical presentation of adult patients with ascites in this study population issimilar to those of previous studies, with a mean duration of symptoms of three months.

3. Peritoneal biopsy is probably more useful among patients with exudative or low gradient ascites.

4. The most common causes of ascites in this setting (liver cirrhosis, malignant ascites, heart failure, chronic kidney disease, and TB Peritonitis) are similar to findings from previous studies in Africa, and Asia.

5.2 RECOMMENDATIONS

In view of our observations in this study we recommend that

1. Peritoneal biopsy should be utilized in the work up of all patients with exudative ascites, and those who are difficult to find a diagnosis.
2. Another study is needed to describe the characteristics of patients with malignant ascites in our settings.

5.3 STUDY LIMITATIONS

This study had several limitations:

1. Since ascites was clinically determined, only patients with moderate to severe (Grade II and III) ascites were included. Therefore patients with clinically undetectable mild (Grade I) ascites was missed
2. The inclusion of only patients with ascites admitted in medical wards in this study could have contributed to a selection bias, especially among patients with malignant ascites.
3. Due to budgetary constraints, we were not able to adequately investigate patients with malignant ascites, especially where CT- Scan or Gastrointestinal Endoscopy were indicated.
4. The diagnosis of liver biopsy was made based on Plain abdominal ultrasound which has limited sensitivity[97], instead of the liver biopsy, which has a sensitivity of up to 100% [99]depending on the biopsy site.
5. Spontaneous Bacterial Peritonitis (SBP) was not properly diagnosed, due to lack of facilities to perform differential ascitic fluid cell count

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APPENDICES

Appendix I: Questionnaire

TITLE: PATTERN OF ASCITES AMONG ADULT PATIENTS ADMITTED IN MEDICAL WARDS AT MUHIMBILI NATIONAL HOSPITAL, DAR ES SALAAM

PART I: DEMOGRAPHIC CHARACTERISTICS

Date of interview _____

Serial Number _____

File Number _____

Tel Number _____

Name _____

1. Sex	Male	0
	Female	1
2. Age _____years		
	Below 25 yrs	0
	26 – 30 yrs	1
	31 – 35 yrs	2
	36 – 40 yrs	3
	41 – 45 yrs	4
	46 – 50 yrs	5
	51 – 55 yrs	6
	56 – 60 yrs	7
	Above 60 yrs	8
3. District _____		
4. Ward _____		
5. Marital status		
	Single	0
	Cohabiting	1
	Married	2
	Divorced	3
	Widowed	4

6. Highest formal education achieved

None	0
Primary school	1
Secondary school	2
Post Secondary	3

7. What is your occupation _____

Government employee	0
Private sector employee	1
Petty trade	2
Housewife	3
Not employed	4
Other (mention) _____	

PART II: HISTORY

	Yes	**No**	**Duration/When**
8. Abdominal distension	1	2	_____
9. Abdominal pain	1	2	_____
10. Loss of appetite	1	2	_____
11. Nausea	1	2	_____
12. Vomiting	1	2	_____
13. Vomiting blood	1	2	_____
14. Fever	1	2	_____
15. Yellow coloration of eyes	1	2	_____
16. Altered sleep pattern	1	2	_____
17. Weight loss	1	2	_____
18. Night sweats	1	2	_____
19. Cough	1	2	_____
20. Hemoptysis	1	2	_____
21. Chest pain	1	2	_____
22. Difficulty in breathing	1	2	_____
23. Lower limb swelling	1	2	_____
24. Facial swelling	1	2	_____

25. Body weakness	1	2	_____
26. Palpitations	1	2	_____
27. Dyspnea on exertion	1	2	_____
28. Paroxysmal nocturnal dyspnea	1	2	_____
29. Nocturnal cough	1	2	_____
30. Reduced urine output	1	2	_____
31. Hematuria	1	2	_____
32. Melena	1	2	_____
33. History of Blood transfusion	1	2	_____
34. History of Schistosomiasis	1	2	_____

PART III: PHYSICAL SIGNS

35. Temperature ____^{o}C
36. Weight _____kg
37. Height _____cm
38. BP _____/_____mmHg
39. PR _____b/m
40. RR _____b/m

General	**Yes**	**No**
41. Pallor	1	2
42. Jaundice	1	2
43. Oral lesions	1	2
44. Wasted/Cachexic	1	2
45. Lower limb edema	1	2
46. Sacral edema (Anasarca)	1	2
47. Finger clubbing	1	2
48. Leukonychia	1	2
49. Palmar Erythema	1	2
50. Dupuytrens contracture	1	2
51. Spider naevi	1	2
52. Scratch marks	1	2

Abdominal Exam

53. Grade of Ascites _____
54. Distended veins on inspection 1 2
55. If yes, draining?
    a. Cephalic 1 2
    b. Caudally 1 2
56. Spleen palpable 1 2
    a. Size (BLCM) _____cm
    b. Venous hum 1 2 3
57. Liver palpable 1 2
    a. Span _____ cm
    b. Tenderness 1 2 3
    c. Consistency
        a) Soft 1 2 3
        b) Firm 1 2 3
        c) Hard 1 2 3
        d) NA 1 2 3
    d. Surface
        a) Smooth 1 2 3
        b) Rough 1 2 3
        c) Nodular 1 2 3
        d) NA 1 2 3
    e. Bruit heard 1 2 3
58. Any palpable mass 1 2
59. If yes, describe
    a. Location _____
    b. Size _____ cm
    c. Consistency _____

Respiratory Examination

60. Crackles 1 2 _____
61. Rhonchi 1 2 _____

62. Consolidation 1 2 _____
63. Pleural effusion 1 2 _____
64. Other _____

CVS Exam

65. Distant heart sounds 1 2
66. Valvular heart disease 1 2 _____
67. Cardiomegally 1 2
68. Pleural rub 1 2
69. Pericardial effusion 1 2
70. Other _____

CNS Exam

71. Flapping tremors 1 2
72. Drowsy 1 2
73. Glassgow Coma Scale (E____, M ____, V ____); Total _____
74. Others _____

PART IV: CLINICAL DIAGNOSIS

75. Clinical diagnosis(es) on the day of interview

1) _____
2) _____
3) _____
4) _____
5) _____

PART V: CHECKLIST OF INVESTIGATIONS DONE

1) Ascitic Fluid- Biochemistry, Cytology, C/S
2) Serum LDH, TP, Albumin
3) Serum Electrolytes, LFT, RFT
4) FBP+ ESR
5) HIV Test
6) Abdominal USS
7) CXR
8) Peritoneal Biopsy
9) Other tests, specify _____

Appendix II: Investigation Form

PART I: Laboratory Tests

Test	**Results**	**Normal Range**	**Interpretation**
WBC		4.0-11.0 K/UL	
Neutrophils		2.0-6.9	
Lymphocytes		0.6-3.4	
Monocytes		0.0-0.9	
Eisonophils		0.0-0.7	
Basophils		0.0-0.2	
Hemoglobin		12.6-18.1 g/dl	
MCV		80.0-97.0 fl	
MCH		27-31.2 pg	
Platelets		142-424 K/L	
ESR		10- 20 mm/ 1st hr	
Serum LDH (>180U/l)		125-243U/l	
Serum Total Protein (TP)		60- 80 g/l	
Serum Albumin		35- 50 g/l	
Ascitic Fluid Macroscopic Appearance			
Ascitic Fluid- LDH			
Ascitic Fluid – TP			
Ascitic Fluid – Albumin			
AF/S TP Ratio (0.5)			
AF/S LDH Ratio (>0.6)			
SAAG (>1.1g/l)			
Serum AST			
Serum ALT			

Serum AlkP			
Bilirubin- Total			
Bilirubin- Direct			
Na			
K			
Ca			
Phosphate			
Serum Creatinine			
Serum Urea			
Serum Uric acid			
HIV test			
OTHER TESTS			
Sputum for AFB*2			
ά feto protein			
Serum Ά Amylase			
Urine dipstick Protein			
24 hr Urine Protein			

PART II: Other Investigations

1. Ascitic Fluid Cytology

   _____

   _____

2. Ascitic Fluid Culture

   Growth_____

   Sensitivity

   _____

3. Peritoneal Biopsy

   _____

4. Abdominal USS

   Liver_____

   Spleen_____

   Pancrease_____

   Kidneys_____

   _____

   Para-aortic Lymphnodes _____

   Other findings _____

   Conclusion _____

5. CXR

   Mediastinum_____L

   ung fields_____

   Cardiac shadow _____

   Cardiophrenic angles _____

   Costophrenic angles _____

   Conclusion _____

6. Other Investigations done, specify

   _____

   _____

PART III: FINAL DIAGNOSIS

1. _____

2. _____

3. _____

4. _____

5. _____

Appendix III: Information Sheet

Greetings Sir/Madam!

My name is Dr. Masolwa Ng'wanasayi, working here at Muhimbili National Hospital. I am conducting a study on patients with ascites who are admitted in this ward.

Purpose of the Study

The aim of this study is to describe the clinical and demographic characteristics of patients with ascites, and finding out the various causes of ascites in this hospital.

What does Participation Involves?

It involves taking a brief history and physical examination of the patient, which will be followed by several investigations; some of which may be unique to some patients. These will include

- Hematological and Biochemical analyses
- Ascitic Fluid analysis
- Peritoneal Biopsy
- HIV testing
- Abdominal Ultrasound
- Chest X ray
- Other relevant investigations

Confidentiality

All information obtained from you during the conduct of this study will remain confidential, and will only be shared to you and other personnel involved in your care.

Risks

There are several inconveniences that you may experience. The blood tests and peritoneal aspiration may cause some pain. Peritoneal biopsy will be done under local anaesthesia, to try and minimize pain as much as possible. But there will be some discomfort as the anaesthetic is being injected, and during the procedure.

There is also a possibility that ascitic fluid may drain for prolonged time after the procedure, or blood may bleed internally. If you notice anything abnormal please notify the nurse in the ward immediately.

Benefits

All the investigations done will be filled in your records and will be used in your care.

Rights to Participate and Withdraw

You are free to decide whether or not to participate in this study, and you may decide to withdraw at any time after you have consented.

Who to Contact

If you have any questions about this study,

Please contact me, Dr Masolwa Ng'wanasayi, Department of Internal Medicine, Muhimbili university of Health and Allied Sciences (MUHAS), P.O.Box 65001, Dar-es-Salaam. Mobile: 0713 586149.

If you have any questions about your rights as a participant in this study,

Please contact Prof. Aboud, The Chairman of the Research and Publications Committee, MUHAS, P.O.Box 65001, Dar-es-Salaam. Tel: 022 2152489.

Appendix IV: Consent Form

I declare that I have read (or read for) and understood all the information above, and I hereby willingly and without coercion agree to participate in this study.

Signature of the Patient _____

Name of the Patient_____

Note: A guardian/caretaker can sign on behalf if the patient is too weak, or not fully conscious and oriented

Signature of the Guardian/Caretaker_____

Name of the Guardian/Caretaker_____

Signature of Witness_____

Name of the Witness_____

Appendix V: Information sheet (Swahili version)

FOMU YA MAELEZO

Salaam!

Jina langu ni Dr. Masolwa Ng'wanasayi, ninafanya kazi hapa katika hospitali ya Taifa Muhimbili. Ninafanya utafiti mwiongoni mwa wagonjwa wenye tatizo la maji kujikusanya tumboni, ambao wanalazwa katika wodi hii.

Lengo la Utafiti

Ni kujua sifa za wagonjwa, na sababu za sababu za maji kujikusanya tumboni miongoni mwa wagonjwa wanao lazwa katika hospitali hii.

Ushiriki wako unajumuisha nini?

Ushiriki wako unajumuisha kutoa historia ya ugonjwa wako, kufanyiwa uchunguzi wa mwili, na vipimo kadhaa. Vipimo hivyo ni pamoja na

- Vipimo vya damu
- Maji ya tumboni
- Biopsy ya utando tumboni
- Virusi vya ukimwi
- Ultrasound ya tumbo
- X-ray yakifua, na
- Vipimo vingine vitakavyo hitajika

Usiri

Taarifa zote utakazotoa na zitakazopatika na wakati wa utafiti huu zitakuwa siri, na zitatolewa tu kwa wafanyakazi wengine wa afya wanaohusika na matibabu yako.

Hatari zinazoweza kutokea

Yako mambo kadhaa ya hatari au yenye usumbufu yanayoweza kutokea wakati wa vipimo. Vipimo vya damu na maji tumboni, vinaweza kukusababishia maumivu. Kipimo cha biopsy ya utando wa tumboni kitafanyika baada kuchoma ganzi ili kupunguza maumivu. Lakini unaweza kupata usumbufu wakati dawa ya ganzi inachomwa, na wakatiwa kipimo.

Kuna uwezekano pia wa damu au maji kuchuruzika kwa muda baadaya kipimo, au damu kuvilia tumboni.

Ukiona au kuhisi jambo lolote ambalo si la kawaida, tafadhali muarifu nesi aliyeko wodini.

Faida

Vipimo vyote vitakavyofanyika vitawekwa katika rekodi zako, na vitatumika katika matibabu yako.

Haki ya kushiriki na kujitoa

Unauhuru wa kuamua kukubali au kukataa kushiriki utafiti huu. Pia unaweza kujitoa wakati wowote.

Nani wa kuwasiliana naye

Ukiwa na maswali yeyote kuhusu utafiti huu tafadhali wasiliana nami

Dr. Masolwa Ng'wanasayi, Idara ya Tiba, Chuo Kikuu cha Tiba na Sayansi za Afya Muhimbili, S.L.P 65001, Dar-es-Salaam, Simu ya Mkononi: 0713 586 149.

Ukiwa na swali lolote kuhusu haki zako kama mshiriki wa utafiti huu tafadhali wasiliana na Professor Aboud, Mwenyekiti wa Kamatiya Utafiti na Uchapishaji, Chuo Kikuu cha Tiba na Sayansi za Afya Muhimbili, S.L.P 65001, Dar-es-Salaam. Simu ya ofisini: 022 2152489.

Appendix VI: Consent Form (Swahili vesrion)

FOMU YA IDHINI

Nathibitisha kwamba nimesoma (au kusomewa) na kuelewa maelezo yote hapo juu. Na kwa hiyari yangu, bila kushurutishwa ninakubali kushiriki katika utafiti huu.

Sahihi ya mgonjwa _____

Jina la mgonjwa _____

NB: Mbadala anaweza kusaini badala ya mgonjwa iki wamgonjwa hawezi, au hana ufahamu timamu.

Sahihi ya Mbadala _____

Jina la Mbadala _____

Sahihi ya Shahidi _____

Jina la Shahidi _____

Appendix VII: Framingham Criteria for Congestive Heart Failure

Major Criteria

History

- Paroxysmal nocturnal dyspnea
- Orthopnea
- Weight loss in response to treatment
- Neck vein distension

Physical Examination

- Rales
- S_3 gallop
- Hepatojugular reflux

Chest x ray

- Cardiomegally
- Pulmonary edema

Minor Criteria

History

- Dyspnea on exertion
- Nocturnal cough

Physical examination

- Hepatomeggaly
- Bilateral ankle edema
- Tachycardia

Chest x ray

- Pleural effusion

Pulmonary function tests

- Vital Capacity decreased by one third from maximum