GHANA COLLEGE OF PHYSICIANS AND SURGEONS

FACULTY OF INTERNAL MEDICINE

(SUBSPECIALTY - GASTROENTEROLOGY)

EVALUATION OF UPPER GASTROINTESTINAL ENDOSCOPIC FINDINGS IN PATIENTS WITH LIVER CIRRHOSIS AT THE KOMFO ANOKYE TEACHING HOSPITAL, GHANA

A Dissertation submitted to the Faculty of Internal Medicine, in partial fulfilment of the requirements for the conferment of Fellowship of the Ghana College of Physicians (FGCP)

BY

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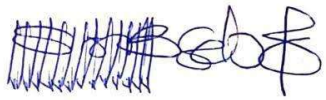
DECLARATION

I, **Bright Oppong**, hereby declare that the study conducted and discussed in this book was conducted at the Komfo Anokye Teaching Hospital, Kumasi, Ghana. This work is original unless otherwise acknowledged. This work has not been presented to any other college for a Fellowship, nor has it been submitted elsewhere for publication.



Dr Bright Oppong
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CERTIFICATION

We certify that this work was carried out by Dr Bright Oppong at the Komfo Anokye Teaching Hospital under our supervision

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DEDICATION

This book is dedicated to the Almighty God, my wife and my three wonderful children –Nana Osei Tutu, Paapa Annor Baffour and Opanin Yaw Danso, and to all the patients who participated in the study.

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My deepest gratitude goes to my wife, Frances Boakye Oppong and children whose constant support and encouragement have brought me this far.

ABSTRACT

Introduction: Liver cirrhosis remains an important cause of hospitalization, morbidity, and mortality in sub-Saharan Africa. A common complication of liver cirrhosis is acute upper gastrointestinal bleeding. The objective of this study was to assess the prevalence of upper gastrointestinal endoscopic findings and to correlate the presence of these findings with the severity of liver cirrhosis in patients at the Medicine Directorate, Komfo Anokye Teaching Hospital (KATH).

Methods: This was a descriptive cross-sectional study of patients accessing care at the KATH. Consecutive sampling was used to recruit patients with cirrhosis of the liver, diagnosed by transabdominal ultrasound scan. A structured questionnaire was administered to assess socio-demographic characteristics and clinical information. Liver chemistry, full blood count, HBsAg, anti-HCV antibodies and INR tests were done for all the patients. An upper gastrointestinal tract endoscopy was performed for all patients and the severity of the cirrhosis was assessed using the Child-Turcotte-Pugh score.

Data was collected with the REDcap tool and exported to STATA statistical software for analysis. Descriptive analysis was performed by using frequencies, percentages and means. Chi-square and Fisher exact tests were used to determine the association between severity of cirrhosis and other predictor variables. Logistic regression and partial proportional odds assumption model were used to determine the odds ratio and possible factors that influenced the severity of cirrhosis.

Results: The study included 145 participants. The mean age (standard deviation) of participants was 46.5 ± 12.0. the ratio of males to females was 3:1. Seventy percent had oesophageal varices and 46.2% and 47.6% had portal hypertensive gastropathy and gastritis respectively. Other lesions were gastric ulcer (23.5%) and duodenal ulcer (10.3%). Seventy five percent had hepatitis B infection. Majority of the participants (76.5%) had class C disease and Helicobacter. Pylori (H. pylori) was detected in 87.6%. The presence of oesophageal varices and lax Lower Oesophageal Sphincter (LES) correlated positively with severity of the liver cirrhosis. Oesophageal varices was strongly associated with patients who had finger clubbing (p-value, <0.001), leukonychia (p-value, <0.001), silky hair(p-value, <0.001),, ascites(p-value, <0.036),, palmar erythema(p-value, <0.001),, and spider naevi(p-value, <0.003),

Conclusion: Hepatitis B infection is the leading cause of liver cirrhosis at KATH. The most prevalent endoscopic finding was oesophageal varices (mostly medium and large varices) but a significant number of participants had non-variceal lesions. H. pylori infection is common in this population. Screening endoscopy is recommended in cirrhosis to detect lesions which can predispose to upper GIT bleeding.

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LIST OF ABBREVIATIONS

AAA	Aromatic Amino Acids
AASLD	American Association for study of liver diseases
ALD	Alcoholic Liver disease
AOR	Adjusted Odds Ratio
AOUR	Area Under Re-operative curve
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
APC	Argon Plasma Coagulation
APRI	Aspartate Platelet Ratio Index
AR	Attrition rate
ASGE	American Society for Gastrointestinal Endoscopy
AST	Aspartate Aminotransferase
BCAA	Branched-chain Amino Acids
CAGE	Cut, Annoyed, Guilty, Eye opener
CHRPE	Committee on Human Research Publication and Ethics
CI	Confidence Interval
CT	Computed Tomography
DALYs	Disability Adjusted-life Years
DNA	Deoxyribonucleic Ac
ECM	Extracellular Matrix
EDTA	Ethylenediaminetetraacetic acid
EENT	Ear Eye Nose and Throat
eNOS	Endothelial Nitric oxide synthase
FIB-4	Fibrosis-4 score
GAVE	Gastric antral vascular ectasia
GI	Gastrointestinal
GIT	Gastrointestinal Tract
GGT	Gamma Glutamyl Transferase
GOO	Gastric Outlet Obstruction
GOV-1	Gastroesophageal varice-1

GOV-2	Gastroesophageal varice-2
HBC	Hepatitis B and C co-infection
HBD	Hepatitis B and D co-infection
HBsAg	Hepatitis B surface Antigen
HBV	Hepatitis B Virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C Virus
HE	Hepatic Encephalopathy
HIV	Human Immunodeficiency Virus
HPS	Hepatopulmonary Syndrome
HRS	Hepatorenal Syndrome
HPV	Human Papilloma Virus
HVPG	Hepatic Vein pressure gradient
ICU	Intensive care Unit
IGV-1	Isolated Gastric Varice-1
IGV-2	Isolated Gastric Varice-2
IL	Interleukin
INR	International Normalized Ratio
IRB	Institutional Review Board
JHS	Junior High School
KATH	Komfo Anokye Teaching Hospital
KBTH	Korle Bu teaching hospital
KNUST	Kwame Nkrumah University of Science and Technology
LDH	Lactate dehydrogenase
LES	Lower oesophageal sphincter
LESP	Lower Esophageal Sphincter pressure
LOLA	L-Ornithine L- aspartate
LSEC	Liver Sinusoidal endothelial Cells
MAA	Macro Aggregated Albumin
MELD	Model for End-stage Liver Disease
MDR	Multiple Drug Resistance

MHE	Minimal Hepatic Encephalopathy
MRI	Magnetic Resonance Imaging
NAFL	Non-Alcoholic Fatty Liver
NAFLD	Non-Alcoholic Fatty Liver Disease
NASH	Non-Alcoholic Steatohepatitis
Nd:YAG	Neodymium -doped Yttrium Aluminium Garnet
NO	Nitric Oxide
OHE	Overt Hepatic Encephalopathy
NSAID	Non-Steroidal Anti-inflammatory Drug
OGD	Oesophagogastroduodenocopy
OR	Odds Ratio
OTSC	Over The Scope Clip
PBC	Primary Biliary Cholangitis
PHD	Portal hypertensive Duodenopathy
PHG	Portal Hypertensive Gastropathy
PMNL	Polymorphonuclear Leukocytes
PPOA	Partial Proportional Odds Assumption
PPOM	Partial Proportional Odds Model
PSC	Primary Sclerosing cholangitis
PUD	Peptic Ulcer Disease
REDCap	Research Electronic Data Capture
SBP	Spontaneous Bacterial Peritonitis
SD	Standard Deviation
SIRS	Systemic Inflammatory Response syndrome
SSA	Sub-Sahara Africa
SWE	Short Wave Elastography
TIPSS	Trans-jugular Intrahepatic Porto systemic Shunt
UGIB	Upper Gastrointestinal Bleeding
UGIT	Upper Gastrointestinal Tract
US	Ultrasonography
USA	United States of America

VBL	Variceal Band Ligation
WHO	World Health Organization
2-D SWE	2-Dimensional Short wave elastography

DEFINITION OF TERMS

Duodenitis: the presence of erythema, oedema and friability of the duodenal mucosal surface with or without mucosal haemorrhage or erosions.

Erosion: Superficial mucosal breaks.

Gastritis: the presence of erythema, oedema, and friability of the gastric mucosal surface with or without mucosal haemorrhages or erosions.

GAVE (Gastric Antral Vascular Ectasia): dilatation of small blood vessels in the gastric antrum

GOV – 1: extension of oesophageal varices along the lesser curvature

GOV – 2: extension of oesophageal varices along the greater curvature

IGV – 1: varices found in the gastric fundus that do not extend into the oesophagus or cardia

IGV – 2: ectopic varices that occur in other parts of the stomach

Oesophagitis: the presence of erythema, oedema and friability of the oesophageal mucosal surface.

Portal hypertensive gastropathy: friability of the gastric mucosa with ectatic vessels.

Portal hypertensive duodenopathy: friability of the duodenal mucosa with ectatic vessels.

Ulcer: an ulcer crater, which typically has a fibrin-covered base.

Varices: prominent submucosal veins that balloon into the lumen and are graded on a scale from I to IV as follows:

Small: varices that measures less than 5mm in diameter.

Medium: varices that measures between 5mm-10mm in diameter.

Large: varices that measures greater than 10mm in diameter.

CHAPTER ONE

INTRODUCTION

Background

Liver cirrhosis is a clinicopathological condition characterized by hepatic fibrosis and the conversion of normal liver architecture into abnormal nodules. It has a high rate of complications and is associated with significant morbidity and mortality. Liver cirrhosis is the 11th most common cause of death worldwide.[1] Although there is a paucity of data on the prevalence and epidemiology, liver cirrhosis continues to be a major public health concern in most sub-Saharan African countries.[2] The main complications from liver cirrhosis are upper GI bleeding, portal hypertension, coagulopathy, ascites, hepatocellular carcinoma and hepatic encephalopathy.[3]

Globally, cirrhosis currently causes 1.16 million deaths, and liver cancer 788,000 deaths, making them the 11th and 16th most common causes of death, respectively, each year Combined, they account for 3.5% of all deaths worldwide. This marks an increase from 2000, when liver-related mortality accounted for 3% of all deaths, with cirrhosis and liver cancer ranking as the 13th and 20th leading causes of death, respectively.[1]

Liver cirrhosis-related deaths doubled in sub-Saharan Africa between 1980 and 2010, and the Central African Republic, Gabon, Malawi, Uganda, and Cote d'Ivoire were among the highest 10% of countries for these deaths in 2010.1 Most cases of cirrhosis were attributed to hepatitis B virus (HBV), alcohol misuse, and hepatitis C virus (HCV), but around 30% were unrelated to these causes.[4] The understudied non-alcoholic fatty liver disease probably has a role in these latter cases, considering the increase in obesity in sub-Saharan Africa, and traditional herbal medicine could also contribute, because its use is associated with a substantial increase in liver fibrosis.[5,6]

In predicting the outcome of patient with Liver cirrhosis, the Model for End-stage Liver Disease (MELD) and Child-Turcot-Pugh scores have been widely accepted and used. Their clinical significance and prognostic value have been widely studied and accepted worldwide. These prognostic models aid in identifying high-risk patients.[7]

The prevention of the first bleeding episode from oesophageal varices and the management of acute upper GI bleeding has improved markedly in developed countries. Sub-Saharan Africa, however, lag due to inadequate data regarding the prevalence of oesophageal varices and other upper GI lesions in patients with liver cirrhosis.

Ideally, all patients with a confirmed diagnosis of liver cirrhosis, platelet count <150,000 per microliter of blood and Liver stiffness measure of >20kiloPascals should be screened for oesophageal varices.[8] Once varices develop, they tend to increase in size and eventually rupture and bleed. This study was therefore carried out to determine endoscopically, the prevalence of upper GI findings in patients with liver cirrhosis and to correlate the presence of these upper GI endoscopic findings (lesions) with the severity of liver disease at the Komfo Anokye Teaching Hospital.

1.2 Statement of the Problem

Liver cirrhosis remains an important cause of hospitalization, morbidity, and mortality in SSA.[4] Liver cirrhosis has a high rate of complications, with a common one being acute upper GI bleeding , the cause of which can be variceal or non-variceal. The more common of the two is variceal bleeding which can be from oesophageal, gastroesophageal, or isolated gastric varices.[9]

Non-variceal bleeding can be caused by peptic ulcer disease, oesophagitis, angiodysplasias, and gastric and duodenal erosions.[10,]

In Ghana and other developing countries, there is a paucity of data on the prevalence of endoscopically diagnosed upper GI lesions in patients with liver cirrhosis. Also, endoscopic facilities are not readily available, making it difficult in performing endoscopy in patients with liver cirrhosis presenting with upper GI bleeding. In most instances, based on the clinical findings, treatment is initiated before endoscopy can be done to determine the source of the bleeding.

The Child-Turcot-Pugh and Model for End-stage Liver Disease (MELD) scores have been widely accepted for their use in predicting outcomes and their clinical significance in identifying patients at high risk of rebleeding.[7] A study evaluating the prevalence of upper GI endoscopic lesions in patients with liver cirrhosis, establishing the likely predictors of these lesions and correlating these lesions with the severity of the liver disease will be invaluable, aiding clinicians in decision-making and further management

1.3 Rationale for the study

Although current literature recommends high-risk patients with liver cirrhosis have OGD to rule out varices, this vital endoscopic tool is not readily available in most centres in Ghana and most countries in the West African sub-region. Determining patients' characteristics that predict the presence of these upper GI tract lesions using the Child-Pugh score will enable their categorization into likely pathophysiological causes. This will enable the identification of patients with a likely pathologic lesion and thus require a particular intervention before endoscopy is done. For patients with characteristics, the likely pathologic lesion could be determined, and endoscopy can be performed on an outpatient basis, reducing cost and strain on health facilities. These will hopefully improve the care of liver cirrhosis patients, reducing morbidity and mortality. The results of the study may be usefully applied in other medical centers in Ghana and the West African sub-region.

1.4 Research questions

1. What is the prevalence of upper gastrointestinal lesions in patients with liver cirrhosis?
2. What is the correlation between upper gastrointestinal lesions and the severity of liver disease?
3. What are the patients' characteristics that predict the presence of these upper gastrointestinal endoscopic lesions?

1.5 Objectives of the study

1.5.1 General Objectives

To determine the prevalence and determinants of upper gastrointestinal endoscopic lesions in patients with liver cirrhosis at the Komfo Anokye Teaching Hospital

1.5.2 Specific Objectives

1. To determine endoscopically, the prevalence of upper gastrointestinal lesions in patients with liver cirrhosis at the Komfo Anokye Teaching Hospital.
2. To correlate the upper gastrointestinal lesions with the severity of the liver disease.
3. To determine patients' characteristics that predict the presence of these upper gastrointestinal endoscopic findings (lesions)

1.6 Hypotheses

Null hypothesis (H_o): There is no significant relationship between upper gastrointestinal endoscopic lesions and the severity of liver cirrhosis.

The alternate hypothesis (H_a): There is a significant relationship between upper gastrointestinal endoscopic lesions in patients with severe liver disease.

1.7 Scope of the study

The study's scope involved its conceptual, geographical and time scope.

1.7.1Contextual scope

The study's scope stretches to determine endoscopically the prevalence of upper gastrointestinal lesions and its correlation with liver cirrhosis as well as determine the predictors of upper gastrointestinal lesions. Additionally, the study's context is limited to factors that influence the development of severe liver disease in patients with cirrhosis.

1.7.2 Geographical scope

Geographically, the study was limited to the Ashanti region. The Ashanti region serves as the most cosmopolitan of the entire regions in Ghana with varying categories of people with distinct cultural identities staying in the region. Komfo Anokye Teaching Hospital in the region serves as the main referral centre for the middle and northern parts of Ghana.

1.7.3 Time scope

The study was conducted between September 2019 and March 2020

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

2.1.1 Introduction

Liver cirrhosis is a severe liver disease characterized by loss of liver cells, impaired liver function and irreversible scarring of the liver (fibrosis). Fibrosis describes the encapsulation or replacement of injured tissue by a collagenous scar. Liver fibrosis results from the perpetuation of the normal wound-healing response, resulting in an abnormal continuation of fibrogenesis (connective tissue production and deposition). Fibrosis progresses at variable rates depending on the cause of liver disease, environmental factors, and host factors. This leads to portal hypertension and end-stage liver disease.[11]

Recent advances in the understanding of the natural history and pathophysiology of cirrhosis, and treatment of its complications, have resulted in improved management, quality of life and life expectancy of cirrhotic patients. At present, liver transplantation remains the only curative option for a selected group of patients, but pharmacological therapies that can halt progression to decompensated cirrhosis or even reverse cirrhosis are currently being developed.

2.1.2 Epidemiology of liver cirrhosis

Globally, the prevalence of liver cirrhosis ranges from 4.5% to 9.5%.[12] According to the Global Burden of Disease estimate from 1990 to 2017, liver cirrhosis caused 1.3 million deaths contributing to 2.4% of all deaths in 2017 and 31 million Disability Adjusted Life Years (DALYs) are directly related to liver cirrhosis.[13–15] Despite improvement in knowledge and management, the prevalence of cirrhosis has steadily increased across the globe. It is estimated that about 0.1% of the European population suffers from liver cirrhosis with a greater proportion of cases concentrated in the central and eastern parts of Europe.[16]

Although there is a paucity of data on the prevalence and epidemiology, liver cirrhosis continues to be a major public health concern in most sub-Saharan African countries.[2] A systematic review and meta-analysis by Surial et. al revealed a higher prevalence of cirrhosis in the African population due to HBV infection. The prevalence of cirrhosis ranged from 4% in primary health

care settings to 13% in tertiary health facilities.[17] Egypt contributes to a significant proportion of liver cirrhosis in the African region with the highest age-standardized prevalence.[18]
In Ghana, liver cirrhosis is the commonest liver disease associated with significant mortality. Liver cirrhosis is and an important cause of medical admission to the Department of Medicine, Komfo Anokye Teaching Hospital (KATH).[19]

2.2 Causes of liver Cirrhosis

Patients with chronic liver disease (CLD) and liver cirrhosis have been identified with numerous underlining conditions. The increase in non-alcoholic fatty liver disease (NAFLD) contribute to the significant increase in the prevalence of liver cirrhosis worldwide.[20] NAFLD can be further classified into non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH). NAFLD is one of the common causes of cirrhosis, and the second commonest indication for liver transplants in the USA.[21] Setiawan et al in their multiethnic cohort study on the prevalence of cirrhosis by underlying cause in the United States found that 52% of all causes of liver cirrhosis were due to NAFLD.[22] A similar prevalence was observed in a comparative observational study of patients with CLD at a secondary hospital in Italy where cirrhosis was present in 50% of participants with NAFLD.[23] A relatively lower prevalence of 16.6% of NAFLD was observed in a retrospective review of patients diagnosed with liver cirrhosis in New Zealand.[24]

In Ghana, there is limited information on NAFLD in the general population. An unpublished study done by Ansumana Bockarie recorded the prevalence of NAFLD diagnosed by ultrasonography scan among patients attending the medical clinic at the Cape Coast Teaching hospital between January and October 2016 as 24.8%.[25] In a more recent study by Amponsah et al, a prospective study on 96 surgical patients aged 18 and older, without a history of alcohol abuse or liver disease, who presented at the Eastern Regional Hospital in Ghana for elective general and gynaecological procedures between September and December 2018, the prevalence of NAFLD was found to be 56%, more than twice that of the adult American population of 25%.[26]
Liver cirrhosis is a common complication of alcoholic liver disease (ALD). The prevalence of alcoholic fatty liver disease in patients with cirrhosis has been widely documented. In a population-based survey in the USA, the prevalence of alcoholic cirrhosis was found to be 21% and ranked as the second commonest cause of cirrhosis of the liver.[22] A cross-sectional multicenter retrospective study conducted in Mexico reported that 31.2% of all liver cirrhosis cases in eight

hospitals studied were caused by ALD.[27] This phenomenon however is not unique to the American population.

A Norwegian study aimed at exploring the incidence rates and causes of cirrhosis in the population reported a 53% prevalence among patients with cirrhosis[28]. A 2010 Global Burden of Disease study demonstrated that cirrhosis mortality in sub-Saharan Africa doubled between 1980 and 2010, and aetiologies included alcohol (18%).[29] Data on the aetiologies of liver cirrhosis in Ghana is scarce, therefore the incidence is likely to be underestimated. Few studies have been carried out on liver diseases burden in Ghana. One such study reported chronic HBV infection and excess alcohol consumption as the main causes of liver cirrhosis in the country.[30]

Hepatitis C virus (HCV) infection is one of the most common causes of liver disease worldwide. An estimated 170 million persons representing 3% of the world's population are infected with HCV. Many HCV infections are asymptomatic with approximately 45% - 85% of people unaware they are infected.[31,32] The correlation between HCV infection and liver cirrhosis is well studied. Two multi-centre studies on the aetiology of liver cirrhosis in Mexico revealed a prevalence of 36.2% and 36.6% respectively. These two studies involved patients with Liver cirrhosis admitted to various health facilities with a previous diagnosis of chronic HCV infection[27,33] Another Brazilian study reported a 14.5% prevalence of HCV infection among patients diagnosed with cirrhosis.[34] In 2008, a nationwide survey in the United States of patients with liver cirrhosis including all patients in tertiary health facilities and hospitals that offer treatment for cirrhosis found that 60.9% had previously been diagnosed with HCV infection.[31] HCV- associated cirrhosis seems to be a bigger health problem in the Asian and Sub-Saharan African countries.[35,36] In Egypt, HCV prevalence rates reach 13% of the population equating to an estimated 12 million Egyptians of whom around 8 million people are living with chronic hepatitis C with or without cirrhosis or liver cancer. In rural Egypt, the prevalence of HCV is higher, reaching 24% which is 10- to 20-fold higher than in the United States.[37] In west Africa, Kuniholm et al in a study to explore the aetiology of liver cirrhosis found that patients with chronic HCV infection are 3 times more likely to develop liver cirrhosis.[38]

In Ghana, a Sub-Saharan West African Country, HBV is endemic with prevalence rates of 6.7%-12.3% among the population.[19] A study by Blankson et.al recorded an HCV prevalence of 7.1% in patients with Liver cirrhosis in Ghana.[39]

Soni et al in a study on seroprevalence of HBV among patients with Liver cirrhosis in Natal, South Africa, found 16 out of 77 (21%) positive for Hepatitis B surface antigen (HBsAg).[40] Kato et al in Japan found that 255 (64%) of their study participants tested positive for HBsAg and antibody to the hepatitis C virus (anti-HCV),[41] whilst Liakina observed an HBV prevalence of 41.1% among 114 patients with Liver Cirrhosis in Jakarta, Indonesia.[42]

2.3 Pathophysiology of liver cirrhosis

The intrahepatic microvascular unit is made up of several discrete units, including portal venules, hepatic arterioles, sinusoids, central venules, and lymphatics. The cellular elements in these structures include endothelial cells, smooth muscle cells, and in the sinusoid, pericyte-like hepatic stellate cells. It is important to recognize that these cells are intimately associated with one another, where they have paracrine and autocrine effects on each other and themselves. An established example is the paracrine effect of nitric oxide (NO), released by sinusoidal endothelial cells on smooth muscle cells and stellate cells.[43]

The majority of hepatic endothelial cells reside within the hepatic sinusoids; these cells, are known as liver sinusoidal endothelial cells (LSECs). The LSEC phenotype is uniquely different, not only from endothelial cells in other portions of the liver but also from endothelial cells in other organs.[44] Fenestrae are organized in typical sieve plates.[43] A key signature of most forms of liver injury/disease is the loss of many of these unique phenotypes.

During liver injury, the LSEC phenotype changes dramatically.[44] One of the most remarkable phenotypic changes is “capillarization”, characterized by loss of fenestrae and abnormal deposition of a basement membrane matrix on the luminal surface of LSEC.[44] In addition to these anatomical changes, several biochemical changes also occur in the LSEC phenotype. For example, it is now well established that endothelial Nitric oxide synthase(eNOS) activity is diminished in LSEC after liver injury, consistent with an endotheliopathy in liver disease.[45,46] This has several important effects on portal hypertension, including a reduction in intrahepatic NO, which appears to be a critical component of the intense vasoconstrictive nature of the injured liver.[47]

Cirrhosis is an advanced stage of liver fibrosis that is accompanied by distortion of the hepatic vasculature. The resultant vascular distortion leads to shunting of the portal and arterial blood supply directly into the hepatic outflow (central veins), compromising exchange between hepatic

sinusoids and the adjacent liver parenchyma—i.e., hepatocytes. The hepatic sinusoids are lined by fenestrated endothelia that rest on a sheet of permeable connective tissue in the space of Disse, which also contains hepatic stellate cells and some mononuclear cells. The other side of the space of Disse is lined by hepatocytes that execute most of the known liver functions. In cirrhosis, the space of Disse is filled with scar tissue and endothelial fenestrations are lost, a process is known as sinusoidal capillarisation.[48]

Histologically, cirrhosis is characterized by vascularized fibrotic septa that link portal tracts with each other and with central veins, resulting in hepatocyte islands surrounded by fibrotic septa that are devoid of a central vein. The major clinical consequences of cirrhosis are impaired hepatocyte (liver) function, increased intrahepatic resistance (portal hypertension), and the development of hepatocellular carcinoma. The general circulatory abnormalities in cirrhosis (splanchnic vasodilation, vasoconstriction and hypoperfusion of kidneys, water, and salt retention, increased cardiac output) are intimately linked to the hepatic vascular alterations and resulting portal hypertension. Cirrhosis and its associated vascular distortion are traditionally regarded as irreversible but recent data suggest that cirrhosis regression or even reversal is possible.[49,50]

The underlying causes of liver cirrhosis are mostly alcohol abuse, chronic hepatitis B virus (HBV), hepatitis C (HCV) infection and other non-alcoholic liver diseases.[51] Depending on the stage at diagnosis and clinical presentation, liver cirrhosis may be classified as compensated or decompensated. Compensated cirrhosis is mostly asymptomatic and rarely diagnosed at this stage. Decompensated liver cirrhosis however is characterized by severe liver injury and presents with symptoms including extreme fatigue, jaundice, oedema, ascites, and hepatic encephalopathy.

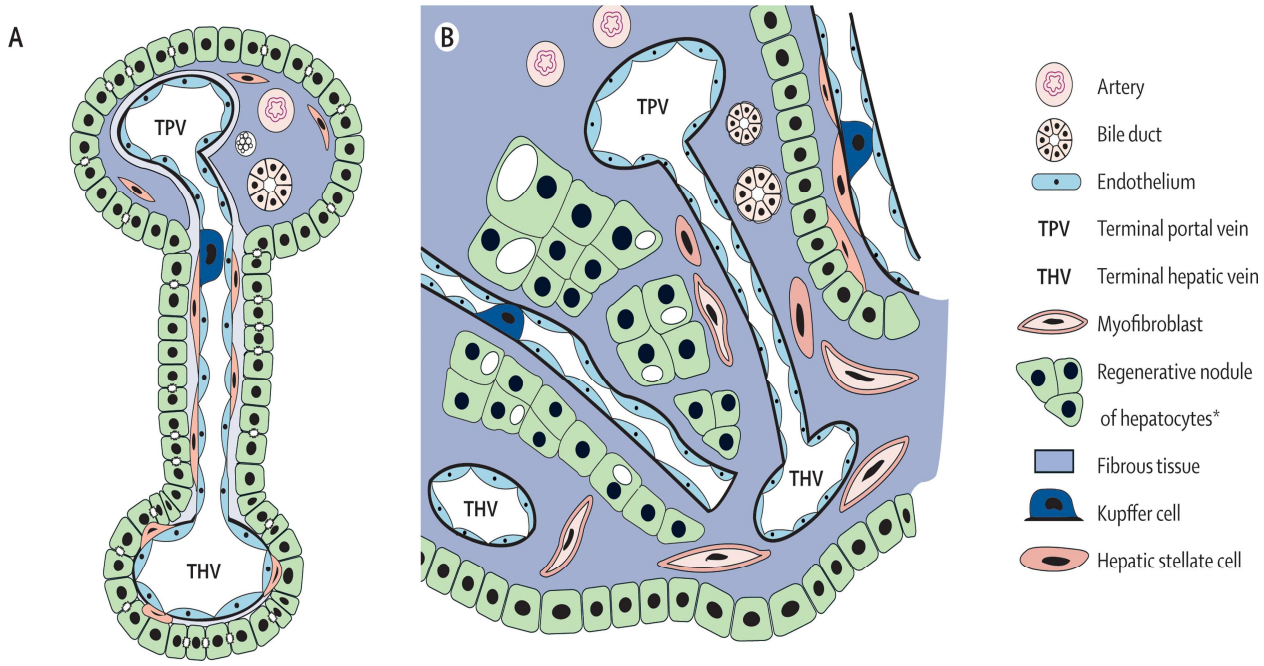

Figure 1: Schuppan, D/2008 / *Vascular and architectural alterations in cirrhosis* /The Lancet /March 2008, Vol. 371 Issue 9615, P838-851[accessed 30 May 2022]

Figure 1: Vascular and architectural alterations in cirrhosis Mesenteric blood flows via the portal vein and hepatic artery that extend branches into terminal portal tracts. (A) Healthy liver: terminal portal tract blood runs through hepatic sinusoids where fenestrated sinusoidal endothelia that rest on loose connective tissue (space of Disse) allow for extensive metabolic exchange with the lobular hepatocytes; sinusoidal blood is collected by terminal hepatic venules that disembogue into one of the three hepatic veins and finally the caval vein. (B) Cirrhotic liver: activated myofibroblasts that derive from perisinusoidal hepatic stellate cells and portal, or central-vein fibroblasts proliferate and produce excess extracellular matrix (ECM). This event leads to fibrous portal-tract expansion, central-vein fibrosis and capillarization of the sinusoids, characterised by loss of endothelial fenestrations, congestion of the space of Disse with ECM, and separation or encasement of perisinusoidal hepatocyte islands from sinusoidal blood flow by collagenous septa. Blood is directly shunted from terminal portal veins and arteries to central veins, with consequent (intrahepatic) portal hypertension and compromised liver synthetic function

2.4.4 Clinical features of cirrhosis

Jaundice
Jaundice is a yellowish discolouration of skin, cornea, and mucous membranes. This results from compromised hepatocyte excretory function and occurs when the total serum bilirubin is >34.2μmol/L (> 2mg/dL).[52,53,54]

Ascites
Ascites, the accumulation of proteinaceous fluid in the abdominal cavity, is clinically detected when ≥1.5 L and results from portal hypertension.[52,54,]

Spider naevi (angiomata)
Spider naevi (angiomata):, a central arteriole with tiny radiating vessels, mainly on the trunk and face resulting from elevated estradiol, due to decreased estradiol degradation.[,55]

Nodular liver
Nodular liver with an irregular hard surface on palpation resulting from fibrosis, irregular regeneration.[53]

Splenomegaly
Splenomegaly resulting from portal hypertension, and splenic congestion.[53]

Caput Medusae
Caput medusae are prominent veins radiating from the umbilicus due to portal hypertension and reopening of the umbilical vein that shunts blood from the portal vein.

Palmar Erythema
Palmar Erythema spares the central portion of the palm due to elevated estradiol from decreased estradiol degradation by liver.[53]

Leukonychia
Leukonychia, horizontal white band and or proximal white nail plate.[55]

Finger clubbing
Finger clubbing is a painful proliferative osteoarthropathy of long none from hypoxemia due to right to left shunting and Porto-pulmonary hypertension. [55]

Dupuytren's contracture

Dupuytren's contracture results from fibrosis and contraction of the palmar fascia from enhanced oxidation stress, elevated hypoxanthine (alcohol exposure or diabetes)[56]

Gynaecomastia

Gynaecomastia, results from the benign proliferation of the glandular male breast tissue due to the enhanced conversion of androstenedione to estrone and estradiol decreases estradiol degradation in the liver. [57]

Hypogonadism

Hypogonadism, mainly in alcoholic liver cirrhosis and haemochromatosis from the direct effect of iron or alcohol.[53,]

Flapping tremors (asterixis)

Flapping tremors (asterixis) are asynchronous flapping motions of dorsiflexed hands from diminishing motor neurons.[53]

Silky hair

Silky hair results from low albumin level.[55]

2.5 Investigations of Liver cirrhosis

Cirrhosis is frequently indolent, asymptomatic, and unsuspected until complications of liver disease present. A sizeable proportion of these patients never come to clinical attention, and previously undiagnosed cirrhosis is still frequently found at autopsy.[58] The diagnosis of asymptomatic cirrhosis is usually made when incidental screening tests such as liver transaminases or radiologic findings suggest liver disease and patients undergo further evaluation and liver biopsy.

The laboratory findings in cirrhosis include Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT), which are often normal or moderately elevated. Alkaline phosphatase (ALP) is usually elevated < 3-fold, except for Primary Biliary Cholangitis (PBC) and Primary Biliary Sclerosis (PSC) due to cholestasis. Gamma-glutamyl Transferase (GGT), more specific for the liver than ALP, is high in active alcoholics due to cholestasis. Bilirubin elevated than GGT and

ALP, an important predictor of mortality, may result from cholestasis and decreased hepatocyte and renal excretory function. Albumin decreased in cirrhosis because of decreased hepatic production, and sequestration into ascites and interstitium (exacerbated in systemic inflammation). International Normalised Ratio (INR) is decreased in advanced liver cirrhosis due to reduced hepatic production of factor V/VII while thrombin production is maintained. Anaemia could be macrocytic, normochromic, or microcytic depending on the cause of cirrhosis, whether folate deficiency, hypersplenism, direct toxicity, or GIT blood loss.

Thrombocytopenia and leukopenia from hypersplenism, dysfibrinogenemia, and reduced hepatic thrombopoietin production

2.5.1 APRI Score

APRI stands for AST-Platelet Ratio Index. It is calculated in the following way: APRI = [AST level /(ULN)/Platelet counts (10^9 /L)] × 100 and is one of the simplest marker panels that can diagnose significant fibrosis and cirrhosis with acceptable accuracy.[59] It has been extensively evaluated in HCV.

The World Health Organization (WHO) guidelines on the assessment of the degree of liver fibrosis and cirrhosis in hepatitis C patients suggested that "In resource-limited settings, the aspartate aminotransferase/ platelet ratio index (APRI) or Fibrosis-4 (FIB-4) tests be used for the assessment of hepatic fibrosis rather than other noninvasive tests that require more resources such as elastography or Fibrotest". (of note, this was a conditional recommendation, based on the low quality of evidence).[60]

2.5.2 Liver Biopsy

A biopsy is considered the gold standard for diagnosis of cirrhosis, and sequential histological grading of inflammation and staging of fibrosis can assess the risk of progression. However, a biopsy is prone to considerable sampling variability in all liver diseases.[61-62]

2.5.3 Imaging

Ultrasonography, computerized tomography (CT) and magnetic resonance imaging (MRI) are not sensitive to detect cirrhosis, and the final diagnosis still relies on histology, however, their specificity is high when an obvious cause is present and imaging reveals an inhomogeneous

hepatic texture or surface, rarefied hepatic central vein, an enlarged caudate lobe, splenomegaly or collateral veins,[63] Ultrasonography is the first imaging modality for suspected Hepatocellular carcinoma HCC, but its sensitivity and specificity to detect (HCC) is below that of CT or MRI,[64] Conventional CT and MRI are not useful to define the severity of cirrhosis,[65] while helical triphasic CT scan and MRI with contrast are the modalities of choice when HCC or vascular lesions are suspected.[66] In a comparative study, MRI was superior to helical triphasic CT for detection of small HCC of 1-2cm size.[67] MRI has also been shown to be effective in determining hepatic iron and fat content in hemochromatosis and liver steatosis, respectively.[68,69]

2.5.4 Other Non-invasive techniques

Shear wave elastography (SWE)

Shear wave elastography (SWE) use acoustic radiation force to induce microscopic tissue movements, producing shear wave in the tissue. In SWE methods, deformation force and tissue deformation are known, and for that reason, quantitative estimation of tissue stiffness expressed as young's modulus (kilopascal) or shear wave velocity (m/s), can be obtained. Two-dimensional SWE are the only method that can provide real-time measurements of liver stiffness[70]

A very recent study was conducted by Zheng et al[71] that included 198 patients with chronic liver disease from different aetiologies (HCV, HBV, autoimmune hepatitis, PBC, drug-induced liver disease) using liver biopsy as a reference standard for most of them. They evaluated the individual and combined performances of 2D SWE and conventional US in assessing liver fibrosis and cirrhosis to determine when 2D SWE should be added to the routine US. Two-dimensional SWE was significantly superior to the conventional US in detecting liver fibrosis, but for diagnosis of decompensated cirrhosis, there was no significant difference between 2D SWE and conventional US.[71]

2.5.5 Fibrotest

"Fibrosure in the US" patented by Biopredictive, Paris, France is probably the most validated of the established panels. It is a proprietary combination of five serum biochemical markers (alpha2-macroglobulin, apolipoprotein A1, haptoglobin, γ-glutamyl transpeptidase, and bilirubin) that are altered with liver fibrosis.[72] Its score is correlated with the degree of liver damage. A meta-analysis of eight studies, involving 1842 patients, showed a median AUROC of 0.84 for the diagnosis of advanced fibrosis,[73] confirming previous studies that indicated the validity of the test for the

diagnosis of advanced fibrosis and cirrhosis but not of mild or intermediate fibrosis.[74] Scores may be influenced by acute inflammation, which leads to increases in serum α 2-macroglobulin and haptoglobin levels.[75] Reduction in the Fibrotest score was also observed after treatment of patients,[76,77] although in a recent study the change was not as significant with Fibrotest as with other tests.[78]

2.6 Management of liver cirrhosis and its complications

Cirrhosis can remain compensated for years before the development of decompensating events such as jaundice, ascites, encephalopathy and/or variceal haemorrhage. The median survival of patients with compensated cirrhosis is much longer than in patients with evidence of decompensation and is about 9 years.[79] The main goals of management of compensated cirrhosis are (1) treatment of underlying aetiology; (2) early recognition and treatment of complications; and (3) preventing superimposed insults. Specific therapy directed against underlying aetiology has been shown to improve survival, long-term outcomes and regression of fibrosis.[80- 81]

Evidence favouring regression of cirrhosis has now been documented in the entire spectrum of chronic liver diseases including viral hepatitis, autoimmune hepatitis, primary biliary cholangitis, biliary obstruction, NASH and hemochromatosis.[82-83] There has been a significant improvement in cure rates for chronic liver disease especially viral hepatitis through the use of more effective antiviral therapy for hepatitis B virus (HBV) and Hepatitis C Virus (HCV).[84,85] More importantly regression of fibrosis associated with anti-viral therapy is associated with improved liver function.[86] Patients with established cirrhosis should be monitored for complications and when possible steps should be taken to prevent their occurrence. The two complications in particular warranting screening are esophageal varices and hepatocellular carcinoma (HCC). If not already immune all patients with cirrhosis should be immunized against Hepatitis A and Hepatitis B.[87-88] Other vaccines such as influenza, pneumonia, tetanus, diphtheria, zoster, meningococcal and human papillomavirus (HPV) vaccination are also recommended.[87] All efforts should be made to avoid agents that are associated with a liver injury such as alcohol, non-steroidal anti-inflammatory drugs (NSAIDs) and prescribed drugs with hepatotoxic potential e.g., phenytoin.[89-90,]

The major complications of cirrhosis include gastrointestinal tract bleeding, ascites, hepatic encephalopathy (HE), hepatopulmonary hypertension, hepatocellular carcinoma, hepatorenal syndrome, spontaneous bacterial peritonitis, and coagulation disorders. These can occur secondary

to portal hypertension, abnormal synthetic function, or a combination of both. Portal hypertension can lead to the formation of venous collaterals, biochemical (increased production of vasoconstrictors, vascular endothelial growth factor, nitric oxide, and other splanchnic vasodilators) and functional abnormalities (plasma volume expansion and increased cardiac output), and thus contribute to the pathogenesis of many of the complications of cirrhosis. Measurement of the hepatic venous pressure gradient (HVPG) can help quantify portal hypertension. Portal hypertension is present when HVPG is > 5mmHg but is clinically significant when > 10mmHg.[91]

2.6.1 Upper Gastrointestinal Tract (GIT) bleeding

The main causes of bleeding in patients with liver cirrhosis are varices (oesophageal, gastroesophageal or isolated gastric varices), gastritis, erosions, portal hypertensive gastropathy, GAVE, peptic ulcers and oesophageal candidiasis.[92]

While the prevalence of upper GI findings is extensively studied elsewhere, there is a dearth of data about this subject matter in Ghana. A study conducted at the Korle Bu Teaching hospital, the main tertiary referral center in Accra showed acute upper GI haemorrhage form gastro-oesophageal varices as the as the predominant cause of death with a sharp rise from 46% to 76% between 2010 and 2013.[93] Massive acute upper GI bleeding has a poor outcome with 38% of fatalities occurring within the first 24 hours.[93]

2.6.2 Varices

Varices are portosystemic collaterals — i.e., vascular channels that link the portal venous and the systemic venous circulation. They form because of portal hypertension (a progressive complication of cirrhosis), preferentially in the submucosa of the lower oesophagus. They result from distended veins that arise from blood shunted away from a structurally damaged liver and occur in up to 50% of cirrhotic patients. Variceal haemorrhage occurs in up to one-third of patients with cirrhosis, and each episode has substantial mortality. As such, it is recommended that an upper gastrointestinal tract endoscopy is performed at the time of diagnosis of liver cirrhosis, to screen for varices and to institute prophylactic therapy if needed.

Varices could involve only the oesophagus and termed oesophageal, or involve the oesophagus and stomach, referred to as Gastroesophageal (GOV) or limited to only the stomach, thus Isolated gastric varice (IGV).

Oesophageal varices are classified as small (< 5mm) or large (> 5 mm), and the use of prophylactic treatments is in part based on their sizes.

Gastroesophageal varices are classified as either GOV 1 when it extends from the oesophagus via the lesser curve of the stomach and GOV2 when it extends via the fundus along the greater curvature (Figure 2.1).

Isolated gastric varice could be limited to only the fundus (IGV1) or limited to the antrum or the duodenum (IGV2). Gastric varices can occur in the presence of esophageal varices or isolated (Figure 2.1). In addition to size and the degree of underlying liver dysfunction, gastric variceal bleeding is also influenced by location, with those located in the fundus possessing a higher risk of haemorrhage.[94] In patients with gastric varices, a mosaic-like pattern of the gastric mucosa is more associated with patients with liver cirrhosis, also associated are petechiae, red spots and gastric erosions according to a study by Taranto et al.[95]. Duodenal varices are rare in patients with liver cirrhosis, occurring in 0.4% of the patients.[96] However, a prevalence of 45% had been reported by Cho et al in patients with hepatic portal hypertension undergoing angiography[97]

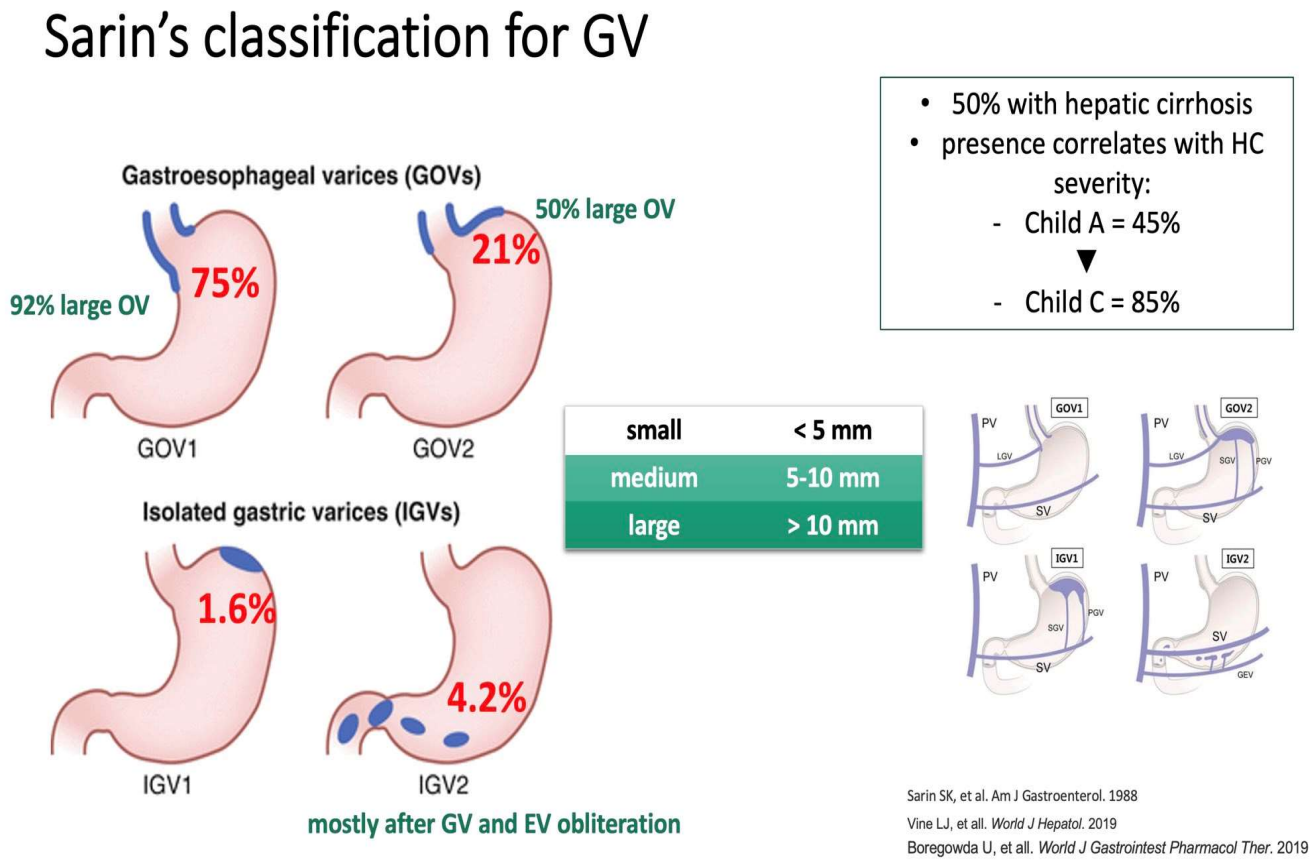

Figure 2. 1: Sarin's Classification Gastroesophageal Varices

The development of portal hypertension and the formation of portosystemic shunts is a major event in the natural history of liver disease. Measurement of the portal pressure gradient is invasive and not widely available for clinical use; instead, the hepatic venous pressure gradient (HVPG) is commonly used in clinical practice and it is of prognostic value: HVPG ≥ 10 mmHg strongly predicts the development of oesophageal varices.[98] Similarly, the most significant risk factor associated with failure to control bleeding or early rebleeding of oesophageal varices is HVPG > 20 mmHg. This is also associated with increased mortality.[99]

It is recommended that all patients with a confirmed diagnosis of liver cirrhosis, platelet count <150,000 per microliter of blood and Liver stiffness measure of >20kiloPascals should be screened for oesophageal varices.[8] Thereafter, guidelines for the interval of endoscopic screening vary. Currently, the American Association for the Study of Liver (AASLD) recommends that, if no varices are present at index endoscopy, this should be repeated at 2-3 years in compensated cirrhosis and annually in decompensated cirrhosis.[98] The British Society of Gastroenterology

recommends annual screening if grade 1 varices are present at initial screening and an interval of 3 years if there is no evidence of varices at index endoscopy.[100]

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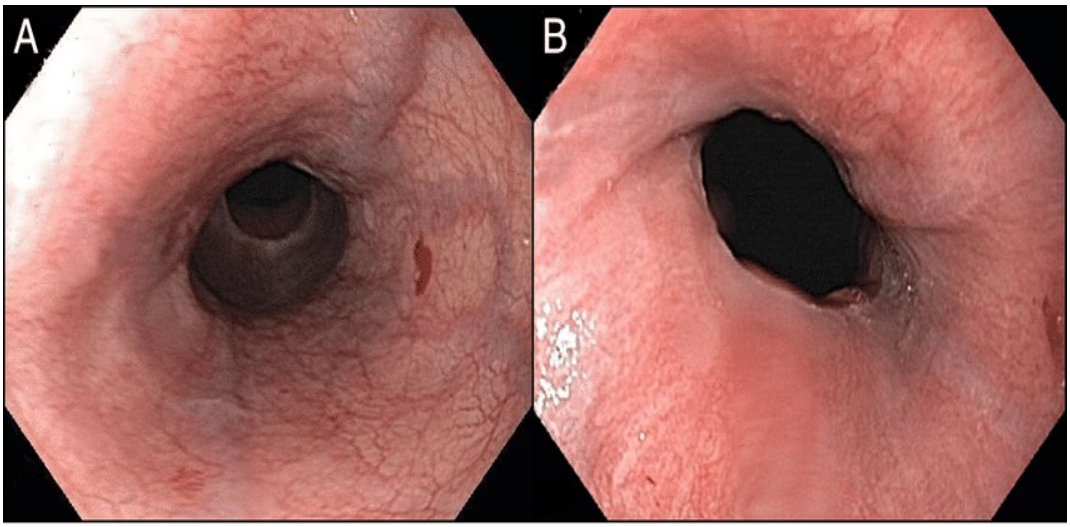

Figure 2. 2: Endoscopy showing Small oesophageal varices

Available from www.researchgate.net/figure/endoscopy-showing-small-oesophgeal varices-with -red-wale-stigmata_fig_312962356 endoscopy-campus.com) [Accessed 30th April 2022]

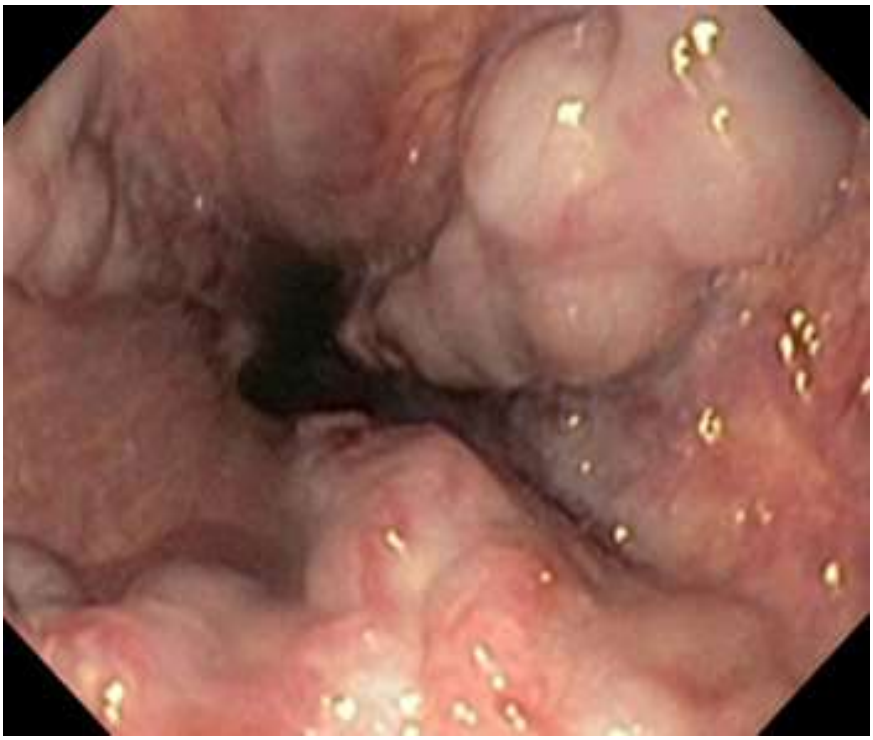

Figure 2. 3: Endoscopy showing Large oesophageal varices

Available from www.researchgate.net/figure/endoscopy-showing-large-oesophgeal varices_fig_212962356 endoscopy-campus.com) [Accessed 30th April 2022]

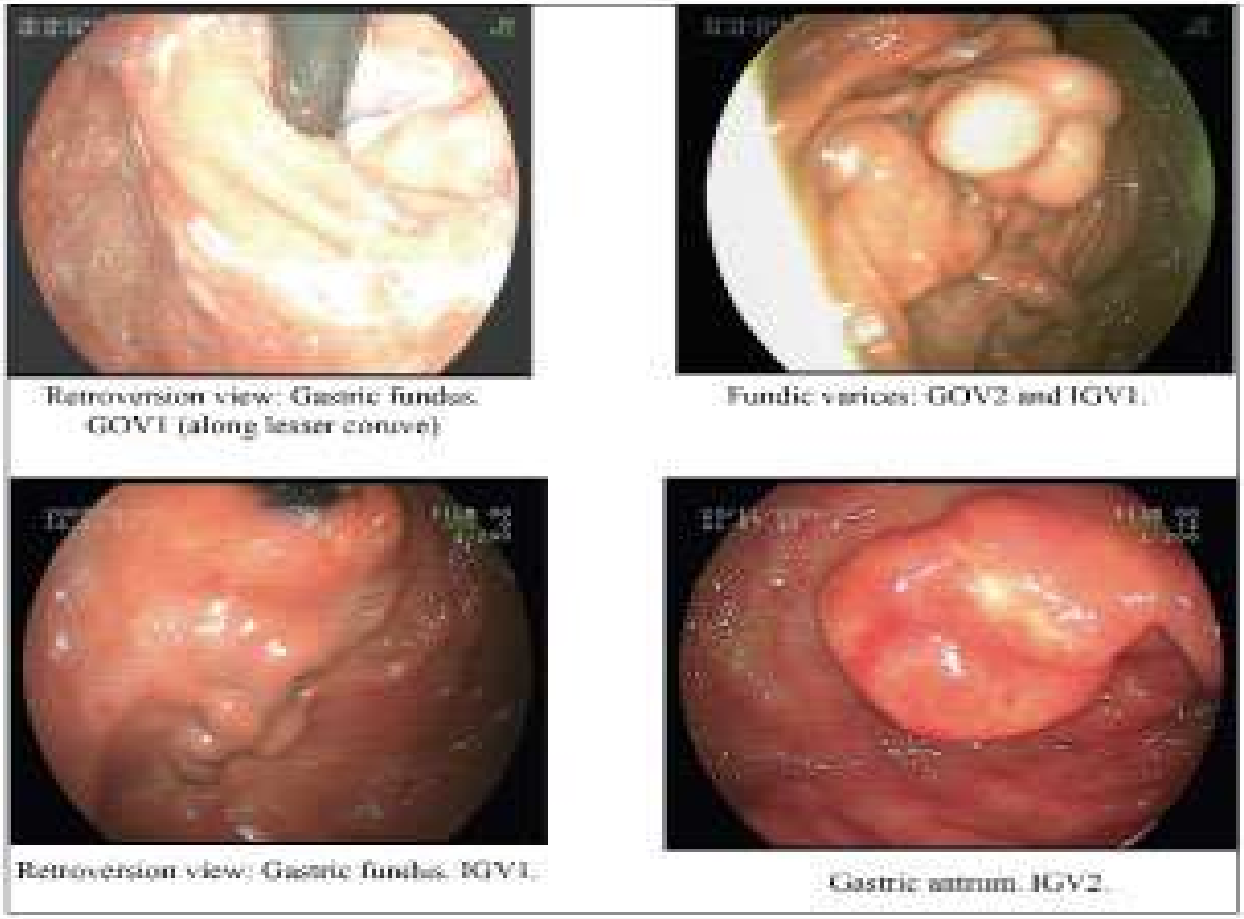

Figure 2.4 Sarin, S.K; Kumar A/1989 / Gastric varices/American Journal of Gastroenterology (Spring Nature). Oct 1989, Vol. 84 Issue 10, P1244-1249.6p)
[accessed 30 May 2022]

Oesophagogastric varices may eventually rupture and bleed and are one of the most common complications and causes of death in patients with liver cirrhosis.[101] Rupture and bleeding from oesophagal varices are major complications of portal hypertension and are associated with a high mortality rate. Variceal bleeding accounts for 10–30% of all cases of upper GI bleeding. Oesophageal varices are also the most important causes of hospitalization in patients with liver cirrhosis.[102] It is for this reason that most guidelines recommend screening for oesophagogastric varices once a diagnosis of liver cirrhosis is made.[103]

A study in Tanzania by Gunda et al found a prevalence of 39.5% of oesophageal varices amongst patients with liver cirrhosis[103]A study by Akere et al found a prevalence of oesophageal varices of 96.4% amongst patients with liver cirrhosis at endoscopy.[104]

Another study in Nepal found a prevalence of 57.3% and 71% for oesophageal varices, and portal hypertensive gastropathy respectively in their patients with liver cirrhosis.[9]

Akere et al found the prevalence of oesophageal varices as 96.4% which was substantially higher than the 53.6% prevalence reported by Ajayi et al.[104] Although both studies were of comparable sample size and conducted in the same geographic zone–Ibadan and Ekiti–in Nigeria, the marked difference in the prevalence of oesophageal varices could be explained by the inclusion of cases with only G11-GIII varices in the Ekiti study, whereas the Akere et al included GII-GIII in addition to G1 varices which constituted the highest prevalence (37%). The reported prevalence of oesophageal varices by Akere et al is higher than the 75% reported by Achinge et al.[105] in Jos Plateau State, Nigeria. While the sample size of the Achinge study was greater than that of Akere et al, the difference observed in the prevalence could be due to the enrolment of only newly diagnosed patients with liver cirrhosis in the study. This prevalence (96.1%) reported by Akere et al is also higher than that reported in other parts of the world. Sacchetti et al in Italy reported the prevalence of oesophageal varices as 61% in a retrospective study with a much greater sample size.[106] The stringent criteria that ensured the exclusion of patients with active GI bleeding at admission, those who had previously undergone one form of treatment for oesophageal varices, and those on primary prophylaxis for variceal bleeding could explain the lower prevalence reported in the study. Also, a lower prevalence of 65% was reported by Saleh Mohammed et al. in a retrospective review of endoscopy data in India[107].

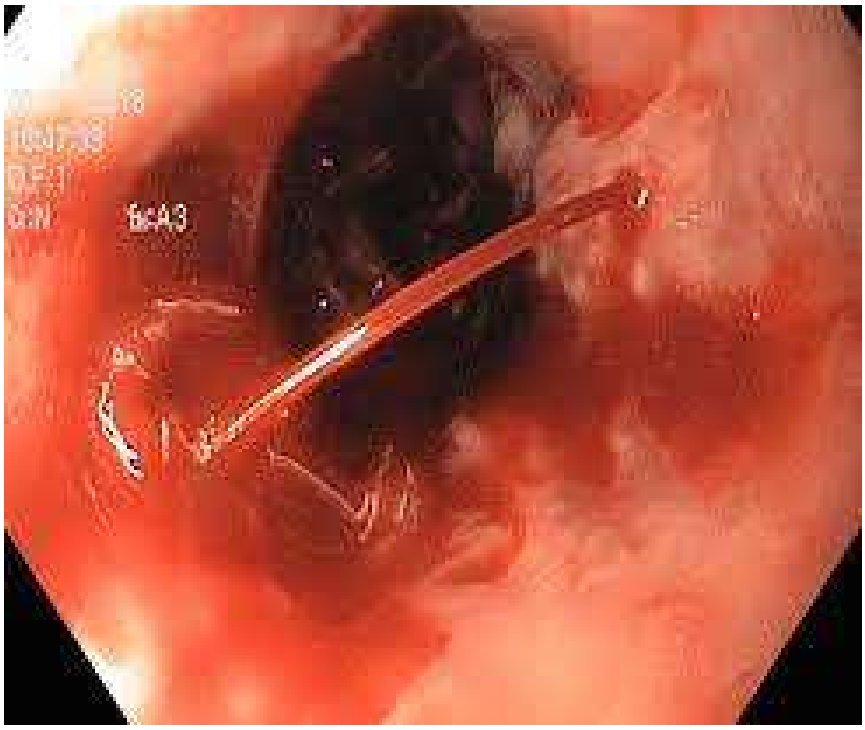

Figure 2.5 Bleeding oesophageal varices/Scientific Figure on ResearchGate. / Available from: https://www.researchgate.net/figure/Bleeding-esophageal-varices_fig4_330522828 [accessed 30 May 2022]

2.6.2.1 Management

Patients with small varices should have surveillance endoscopy repeated within 1 year. Patients with large varices are offered treatment, endoscopy should be performed every 2 to 3 years in compensated cirrhosis and annually in decompensated cirrhosis.[98]

For patients with end-stage liver cirrhosis, liver transplantation is the gold standard, however, whilst on the waiting list, the disease progress in its natural history.[108] With liver cirrhosis, most patients may eventually develop portal hypertension as portal pressure increases with the development of oesophagogastric varices.[101]

The management of oesophageal varices may be divided into pre-primary, primary and secondary prophylaxis, and control of active bleeding. At present, there is no evidence to support treatment to prevent the development of varices in patients with liver disease (preprimary prophylaxis).[109] For primary prophylaxis of oesophageal varices, there is no evidence that variceal band ligation (VBL) is superior to β-blockade.[110]

Due to issues with access to endoscopy and patient preference, non-selective β-blockade, typically with propranolol, is often first-line when treatment is indicated.[110] Carvedilol is a potent non-selective β-blocker, with weak vasodilating properties. A reduction in the HVPG in the range of 10%-43% has been reported with a 12.5 mg/day dose. Carvedilol has therefore been adopted as the β-blocker of choice for primary prophylaxis of variceal bleeding in some centres.[111,112,113]

Primary prophylaxis with VBL is recommended if there are contraindications to β-blockers or concerns about patient compliance.[98] Secondary prophylaxis is indicated for patients who have had an episode of variceal haemorrhage. β-blocker monotherapy is not used as secondary prophylaxis, and patients should either be entered into a variceal banding program or receive a combination of a β-blocker and nitrate.[113] AASLD recommends a combination of β blockade and VBL.[98] However, there is no strong evidence to suggest that this strategy is associated with reduction of mortality.[114] VBL should be repeated every 2 weeks until obliteration of varices is achieved. Following this, a surveillance endoscopy at 1-3 months to confirm eradication is required, and this should be repeated every 6-12 months.[98] VBL is a safe technique: although asymptomatic banding ulcers are common after VBL, the rate of bleeding from these and requiring hospitalization does not exceed 5%.[115] The combination of terlipressin and VBL is the preferred treatment for acute variceal bleeding in many centers and using terlipressin before endoscopy is not unreasonable if there is a delay in the endoscopy. Endoscopic hemostasis is usually achieved in the majority of cases.[98] Trans-jugular intrahepatic portal-systemic shunt (TIPSS) may be considered if VBL has been unsuccessful or there is an early re-bleed (defined at Baveno V as a repeat bleed within 5 d of the index bleed). The use of sclerosing agents (variceal sclerotherapy) is no longer recommended as first-line treatment, because of increased mortality rates for secondary prophylaxis because VBL treatment is safer and more effective.[116] Recently, endoscopic placement of a specifically designed self-expanding covered metal stent has proved effective in the treatment of oesophagal varices in patients in whom initial endoscopic methods have failed to achieve hemostasis.[117] This method appears to be a safe and effective means of controlling ongoing bleeding. The stent is usually removed one week after the acute bleed. Currently, this technique is limited by its relative complexity of stent insertion in acute bleeding, but stenting with covered biodegradable stents when available, which do not require removal, and may play an important role in the management of acute oesophagal variceal bleeding.[118]

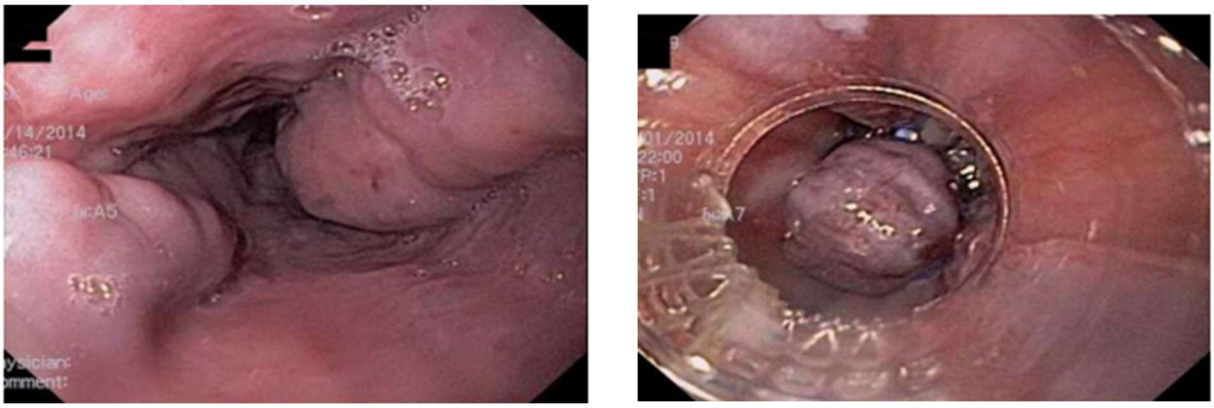

Figure 2.6 oesophageal variceal band ligation / Available from: http://www.learnpicu.com/gi/gi-bleed/varices2.png [accessed 30 May 2022]

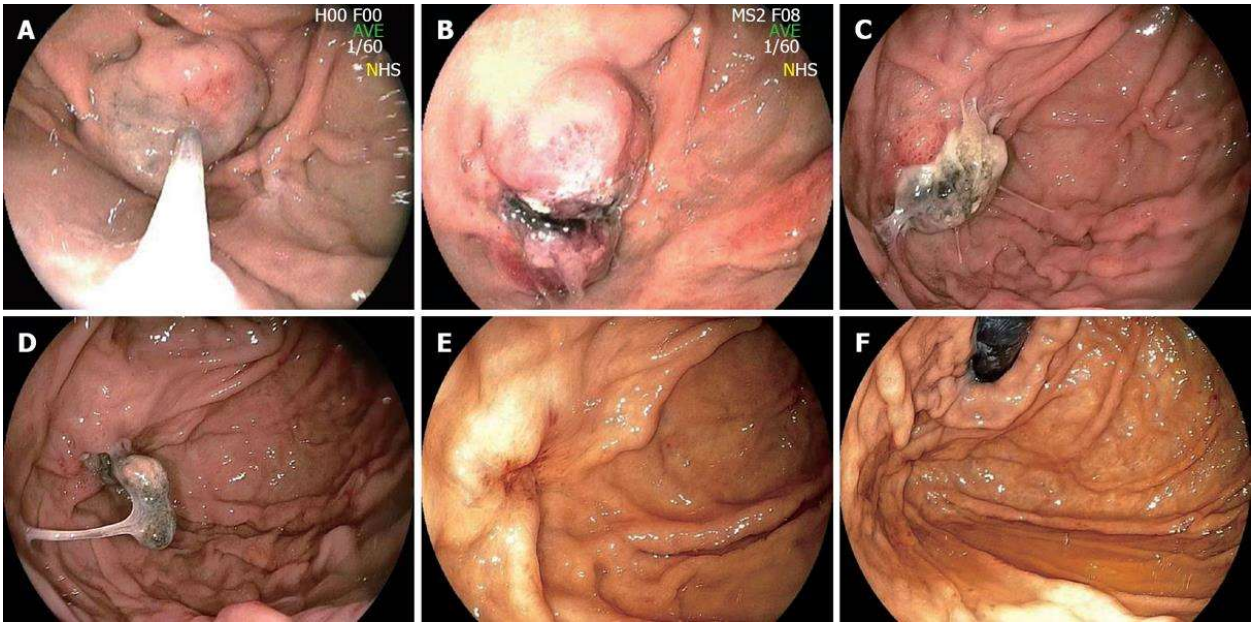

Figure 2.7 Shi B, Wu W, Zhu H/ 2008 / successful endoscopic sclerotherapy for bleeding gastric varices with combined cyanoacrylate and aethoxysklerol. / World J Gastroenterol 2008; 14(22): 3598-3601[accessed 30 May 2022]

2.6.3 Non-variceal

2.6.3.1 Peptic Ulcer Disease

The presence of peptic ulcers in patients with liver cirrhosis may be associated with some ulcerogenic factors that are specific to patients with liver cirrhosis. Among the proposed factors is hypergastrinemia, decreased gastric prostaglandin E2 levels, and the observed portosystemic shunting in liver cirrhosis, which may prevent ulcerogenic factors from being cleared by the liver.[119–121] The data on the prevalence of non-variceal upper GI tract pathology in patients with liver cirrhosis are inconsistent. Several studies have reported a higher prevalence of PUD in patients with liver cirrhosis than in the general population[122,123], whereas others have shown lower or comparable prevalence.[124–126]

The presence of portal hypertension and portal hypertensive gastropathy (PHG) may predispose the gastric mucosa and duodenal mucosa to damage by the ulcerogenic factors, as well as impair the ability of these to repair the damage, this may explain the high prevalence of peptic ulcer observed.[127]

Peptic ulcer is an important finding because gastroduodenal ulcers may be a source of upper GI bleeding (UGIB) in some patients with liver cirrhosis. It is therefore paramount not to attribute every case of UGIB in patients with liver cirrhosis to varices alone. Significant prevalence of PUD have been reported in several studies.[106,128–130]

In a study by Gado et al, peptic ulcer was the commonest cause of bleeding in patients with liver cirrhosis who had acute non-variceal UGIB accounting for 60% of cases. Also, peptic ulcer was diagnosed in 17% of patients with acute variceal UGIB.[131]

Several studies evaluating the prevalence of GI lesions are fraught with some methodological issues which may have compromised the findings. These are the inclusion of patients with GI symptoms and signs, dyspepsia and GI hemorrhage[125] as well as those taking non-steroidal anti-inflammatory drugs or actively drinking alcohol[130]

Upper GI endoscopy has largely replaced upper GI barium x-ray series for the evaluation of upper GI tract disease or symptoms because it allows direct visualization, tissue acquisition, and therapeutic interventions. This guideline is an update of a previous American society of Gastrointestinal endoscopy (ASGE) document[132] and defines the role of upper GI endoscopy in the diagnosis and management of patients with known or suspected PUD.

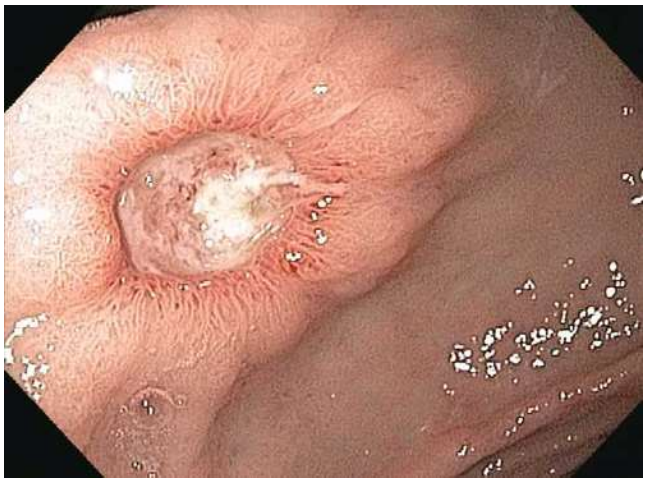

Figure 2. 8: Dr Alexander Mantas / Gastric ulcer/Available from https://i2.wp.com/mantasmd.com/wp-content/uploads/ [accessed 30 May 2022]

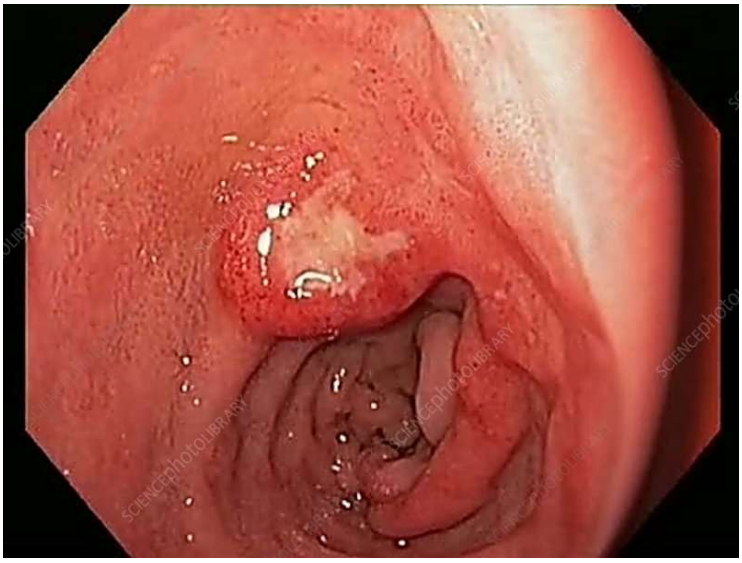

Figure 2. 9: Duodenal Ulcer/Available from: https://www.gastrointestinalatlas.com/videos/Ulcer [accessed 30 May2022]

There are four major complications of PU bleeding, perforation penetration, and obstruction. Despite improvements in medical management and the lower overall incidence of PUD, there are conflicting data about the incidence of potentially life-threatening ulcer complications.[133] Complications can occur in patients with peptic ulcers of any aetiology. Giant ulcers and pyloric channel ulcers may be associated with a higher rate of complications. In recent decades the incidence of PUD has increased, especially in the elderly.[134,135]

Haemorrhage is the most frequent PUD complication, and its incidence is increasing in comparison to perforation and stenosis. Peptic ulcers caused by Helicobacter pylori or nonsteroidal anti-inflammatory drugs (NSAIDs) can be very serious if they cause haemorrhage or perforate the stomach or duodenum. Up to 15% of people with ulcers experience some degree of bleeding, which can be life-threatening. Ulcers caused by NSAIDs are more likely to bleed than those caused by H. pylori. Populations at greatest risk are the elderly and those with other serious conditions, such as liver cirrhosis.[133] Gastrointestinal bleeding happens when the ulcer in the stomach lining erodes a blood vessel.

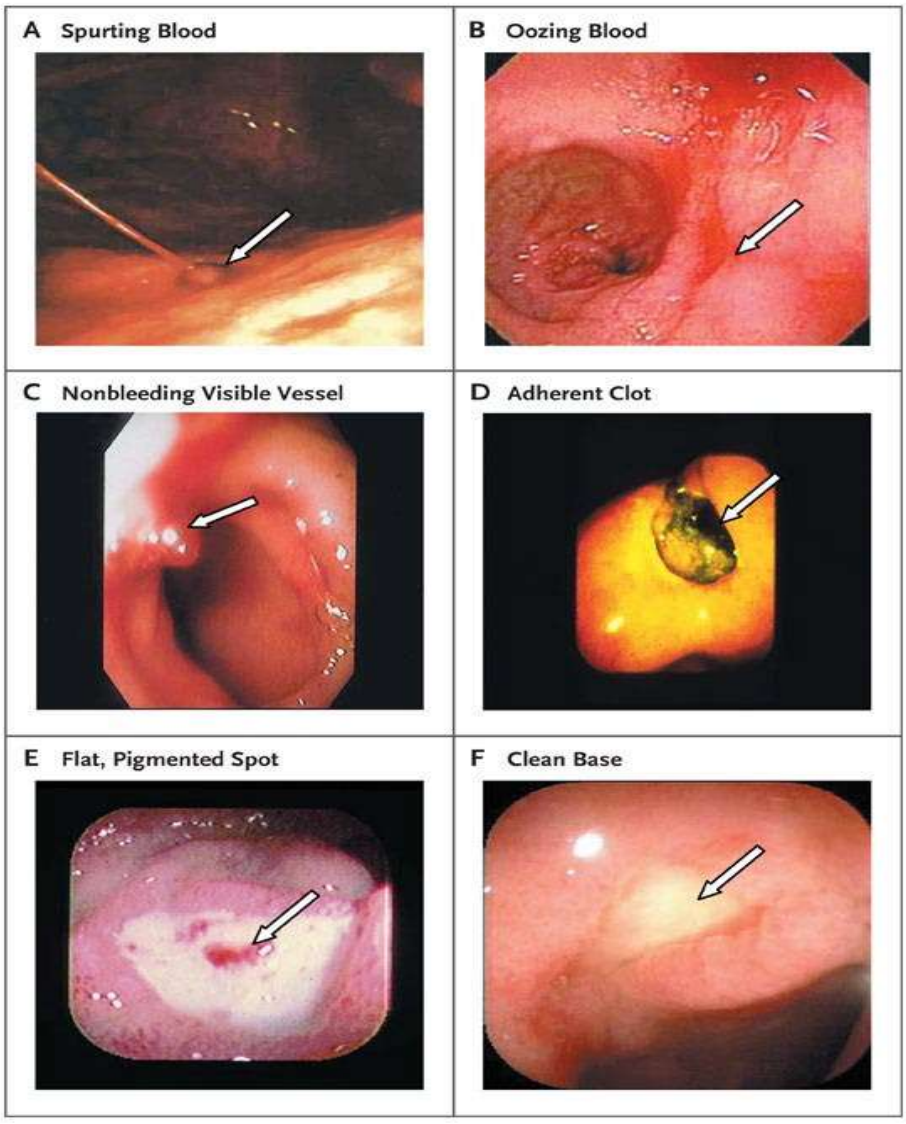

Figure 2.10: Gralnek M. I. /2008 / Duodenal ulcer / New England Journal of medicine /August 2008, Vol. 359 P 928-937/accessed 30 May 2022/

Historically, gastric outlet obstruction (GOO) has been considered a disease process synonymous with chronic peptic ulcer disease. With the advent of proton pump inhibitors, the complications from PUD have drastically decreased.[136] Most patients with GOO present with vomiting as their cardinal symptom tend to develop dehydration and dyselectrolytemia if untreated. Malnutrition and weight loss are frequent when the condition approaches chronicity. The initial experience with endoscopic balloon dilatation in cases with GOO from PUD came after the first report by Benjamin in 1982. Such studies suggest that endoscopic balloon dilatation in GOO related to PUD does not achieve long-term remission and most patients require surgery, but recently published analyses confirmed that benign pyloric stenosis can be readily treated with endoscopic balloon dilatation and should be the first-line therapy with a favourable long-term outcome.[137,138]

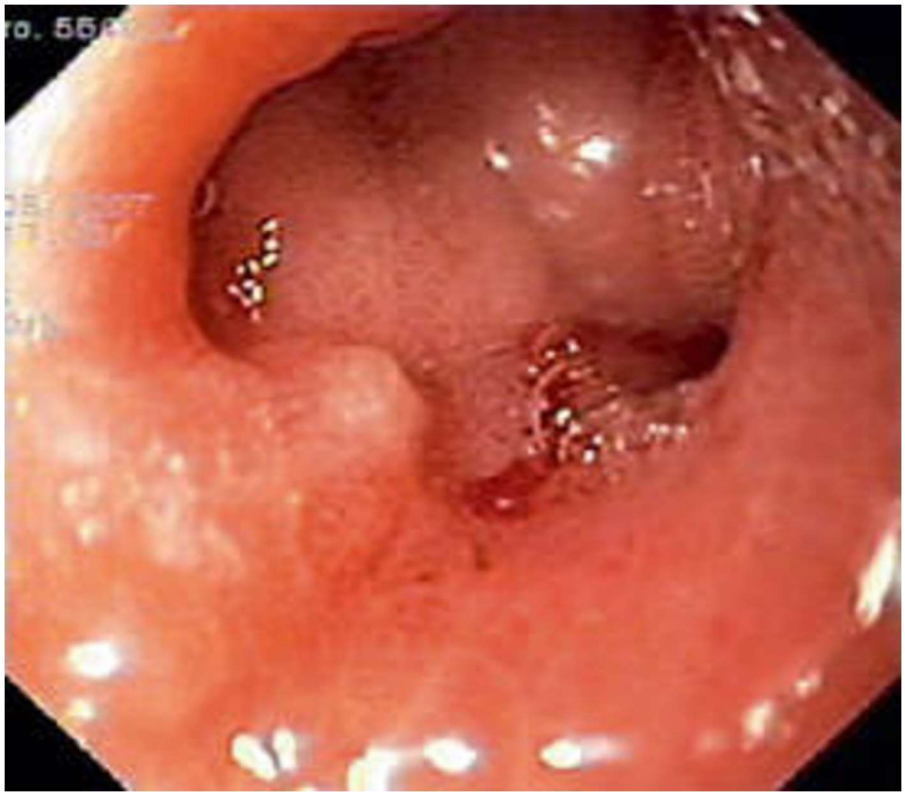

Figure 2.11 Cristina Carretero / pyloric dilatation of gastric outlet obstruction/Scientific Figure on ResearchGate. Available from http://www.researchgate.net/figure/Endoscopic view of pyloric stenosis_fig4_239782653[accessed 5 Oct, 2022]

2.6.3.2 Portal hypertensive Gastropathy

Portal hypertensive gastropathy (PHG) and Portal Hypertensive Duodenopathy (PHD) , with its typical "snakeskin" appearance, is present in approximately 80% of patients with cirrhosis.[139] PHG accounts for 8% of non-variceal bleeds in patients with liver disease, although this condition more commonly presents with anaemia.[140] Patients with cirrhosis and severe PHG-related bleeding may respond to β-blockade. Prophylaxis against bleeding in asymptomatic PHG is not recommended; however, in the setting of chronic anaemia, nonselective beta-blockers should be initiated[141] TIPSS should be reserved for those patients with pharmacological treatment failure.[142] Portal hypertensive duodenopathy is present in around half of the patients with cirrhosis, and it is more common in patients with severe PHG.[143] Bleeding from PHG has traditionally been thought not to be amenable to endoscopic therapy, but recent investigations demonstrated a reduction in transfusion requirements and less clinically significant upper GI bleeding in patients treated with argon plasma coagulation (APC).[144]

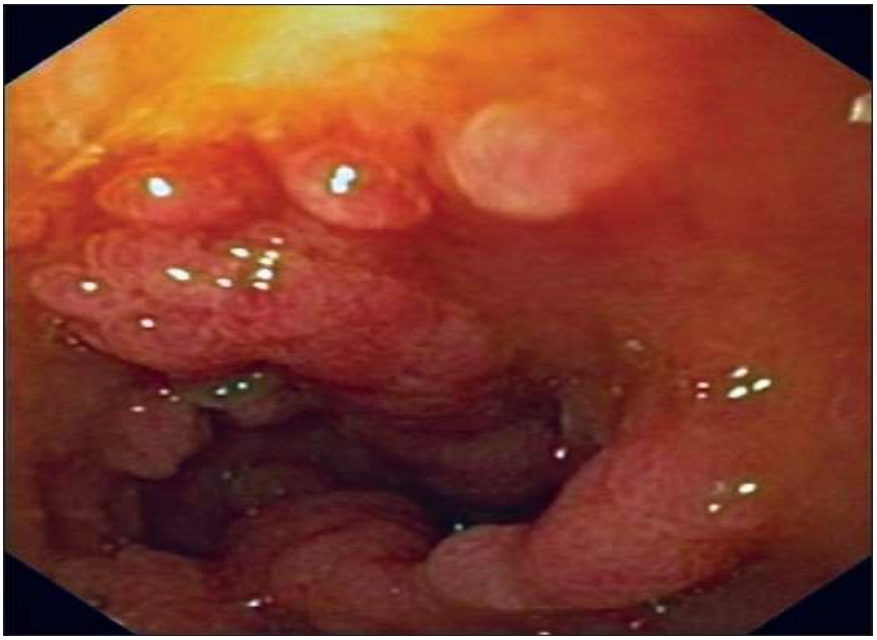

Figure 2.12: Pillai et al/2002/ Portal hypertensive Duodenopathy,/Indian Journal Pathol. Microbiology,0ct. 2022) [Accessed 30 May 2022]

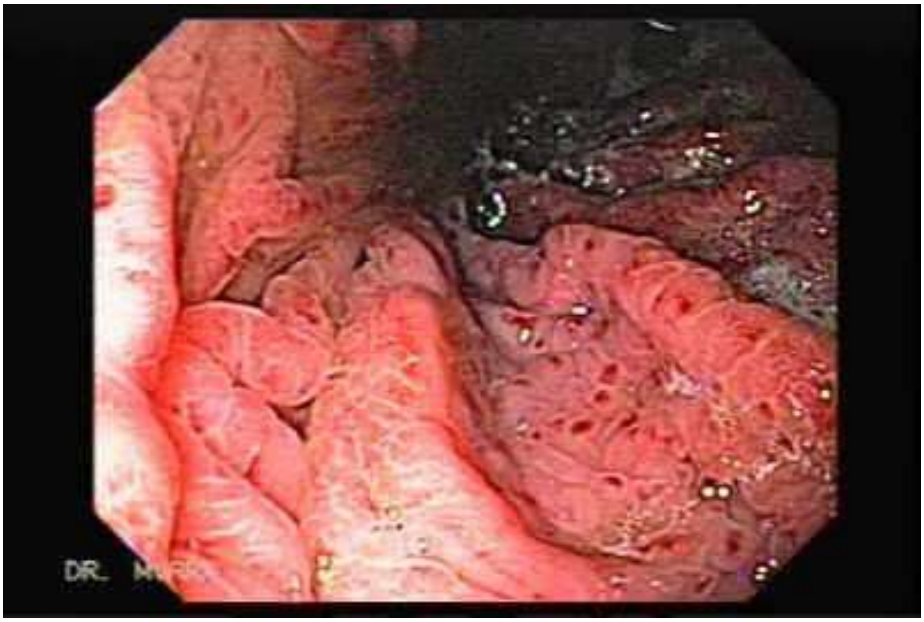

Figure 2.13: Portal hypertensive Gastropathy/Available from Gastrointestinalatlas.com, San Salvador, El Salvador) [Accessed 30 May 2022]

2.6.3.3 Gastric Antral Vascular Ectasia (GAVE)

The pathogenesis of GAVE remains poorly understood. GAVE is related to portal hypertension in about 30% of patients and accounts for 4% of non-variceal upper GI bleeds.[145] Unlike PHG, GAVE does not respond well to a reduction in portal pressure.[146]

Endoscopically, GAVE can have the appearance of ‘‘watermelon stomach,’’ with erythematous stripes projecting radially from the pylorus or as diffuse red spots representing dilated antral blood vessels (Fig2.9).[147] GAVE, similar to PHG, most commonly presents as chronic anaemia, but unlike PHG, its management is primarily endoscopic.[144]

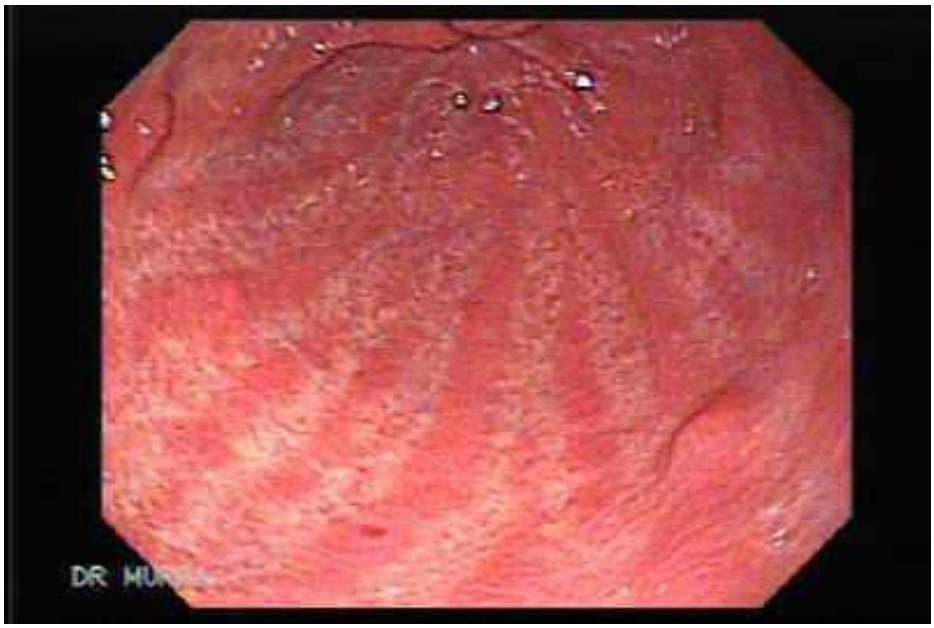

Figure 2.14: Gastric antral vascular ectasia / Available from Gastrointestinalatlas.com, San Salvador, El salvador) [Accessed 30 May 2022)

Management

The Nd:YAG laser has been widely used in the treatment of GAVE and is the most commonly reported endoscopic modality in cirrhotic and non-cirrhotic patients, with a reported overall success rate of almost 90%, although the authors did not distinguish the aetiology of GAVE when reporting the outcomes.[148] APC has also proven to be effective for the treatment of GAVE-related bleeding, with a success rate of > 85%, Success is defined as control of bleeding, stabilization of haemoglobin at > 10g/dL, or haemoglobin increase > 10% from pretreatment level, and reduction of transfusion requirements by > 50% in transfusion-dependent patients. An average of four sessions of APC is usually required. In two published studies, with a total of 37 patients with cirrhosis, success rates in controlling bleeding were very high, and the reported rebleeding rates were between 12% and 20% after 2 years of follow-up.[148,149] Although the success rates of the two aforementioned modalities are comparable, APC treatment is probably the therapy of choice due to the technical ease, safety and low cost.[146] Other endoscopic techniques have been positively reported in small series, such as VBL.[150]

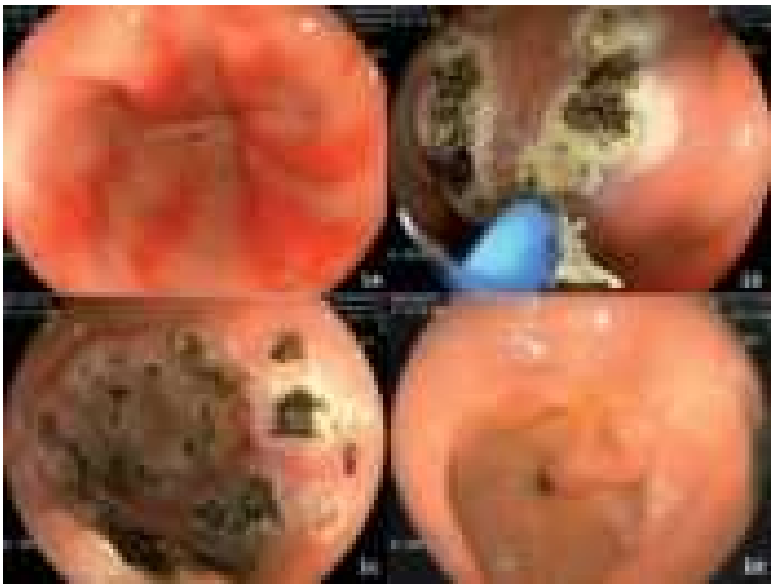

Figure 2.15: Roberto Candia/ 2016/ Argon Plasma Therapy for Gastric antral vascular ectasia / Gastroenterol. latinoam 2016; Vol 27, Nº 1: S 9-S 13) [Accessed 30 May, 2022]

2.6.4 Oesophageal candidiasis

Oesophageal candidiasis remains one of the most common and challenging infections of the oesophagus, especially in patients with low immune function[151] as in the case of patients with liver cirrhosis. In a retrospective study by Ou et al., Liver cirrhosis was found to be an independent risk factor for oesophageal candidiasis and may be asymptomatic in cirrhotic patients.[152]

The mucous membrane of the oesophagus is naturally lined by the protective innate immune mechanical barrier called the nonkeratinized stratified squamous epithelium. Because of this, Candida albicans may be part of the commensal that colonizes the oesophagus in some individuals, accounting for about 20%.[153] However, processes that impair the immune system, as well as those that cause local lesions in the oesophageal upper cortex, can lead to the proliferation and colonization of Candida albicans. Subsequently, candida adheres to the mucous membrane and forms yellow-white patches. Oesophageal plaques could be found on the upper endoscopy and cannot be washed from the mucosa with water irrigation. These plaques can be found diffusely throughout the entire oesophagus or localized in the upper, middle, or distal esophagus.[154]

The clinical manifestations of the patients are often related to the extent of oesophageal mucosal involvement, and the most common symptoms are painful swallowing, difficulty swallowing, and pain behind the sternum. Other symptoms include abdominal pain, heartburn, weight loss,

diarrhoea, nausea, vomiting, and melena.[154] Oesophageal endoscopic examination shows small white spots in the oesophageal mucosa, and X-ray barium examination shows abnormal peristalsis at the upper and lower end of the oesophagus. Only 15% of the patients show oesophagal mucosal damage. Candida esophagitis can be divided into the following: (1) acute infection: extremely weak immunosuppression patients often die of acute fungal infection; (2) subacute infection: subacute infection may result in oesophagal stricture or pseudodiverticulum; (3) chronic infection: usually from childhood, chronic infection is often associated with submucosal fungal infection and immunodeficiency.

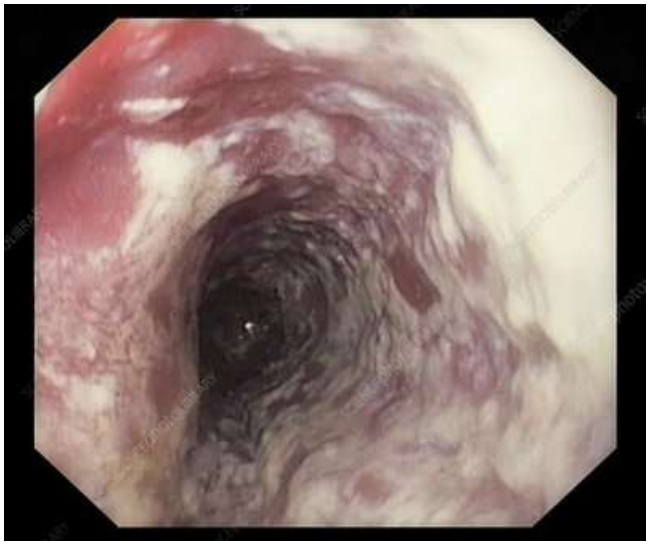

Figure 2.16: Oesophageal candidiasis /Available from Gastrolab/Science Photo Library) [Accessed 30 May 2022.

2.6.5 Gastritis, Duodenitis, Gastric and Duodenal erosions

It has been suggested that patients with cirrhosis have an increased prevalence of chronic gastric ulcers and that they are particularly liable to haemorrhage from acute gastric mucosal erosions.[155] Because chronic gastric ulcers are invariably associated with some degree of chronic gastritis[156] and since gastritis may also be a predisposing factor to erosions, gastric mucosal histology in patients with cirrhosis may have increased susceptibility to these gastric lesions and their associated increased prevalence.[157]

Histopathologic examination of the canine gastric mucosa following sudden production of portal hypertension by portal vein ligation shows that the increased venous pressure under these artificial conditions is reflected in the vessels of the mucosa. When portal hypertension develops naturally

and gradually in cirrhosis of the liver, however, the hypertension is contained within the submucosa and no vascular dilatation develops within the mucosa. Degenerative gastritis with a prominent, erosive element, leading to blood loss, is an important complication of cirrhosis with portal hypertension.[156] Both endoscopic and histopathologic gastritis appears entirely similar to that encountered in patients who have no liver or portal disease. The most significant abnormality is necrobiosis of the cells of the mucosa's neck stratum. In thinking about, the cause, the blame cannot be placed on interstitial haemorrhage from the mucosal capillaries, nor can mucosal plethora with capillary stasis be considered an etiologic factor. The presence of venous dilatation in the submucosa suggests the possibility that secondary mucosal hypoxia, due to stasis without mucosal engorgement, might be sufficient--it is known that the neck stratum is particularly susceptible to the hypoxic influence of ischemia. Although this has by no means been proved, it seems at this time a more acceptable explanation than the only reasonable alternative, the influence of a noxious circulating metabolite.[156]

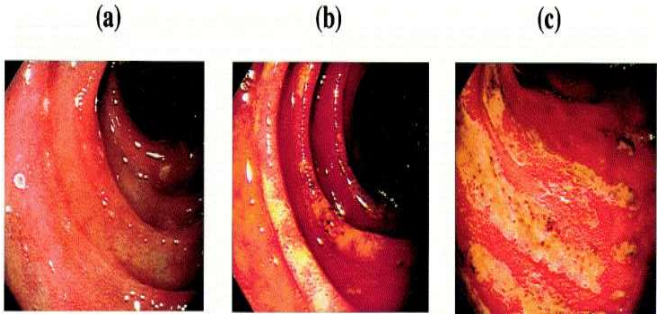

Figure 2.19: a,b,c all show Duodenal erosions (Source : https://www.sciencedirect.com) [Accessed 30 May, 2022)

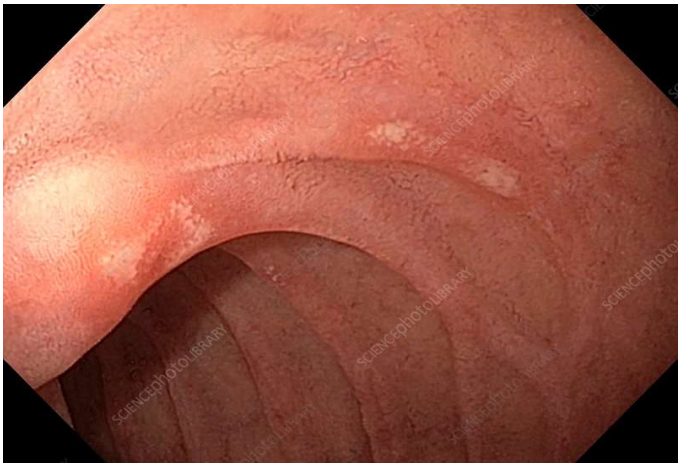

Figure 2.20 shows Duodenitis (Source: https://www.sciencedirect.com) [Accessed 30 May 2022)

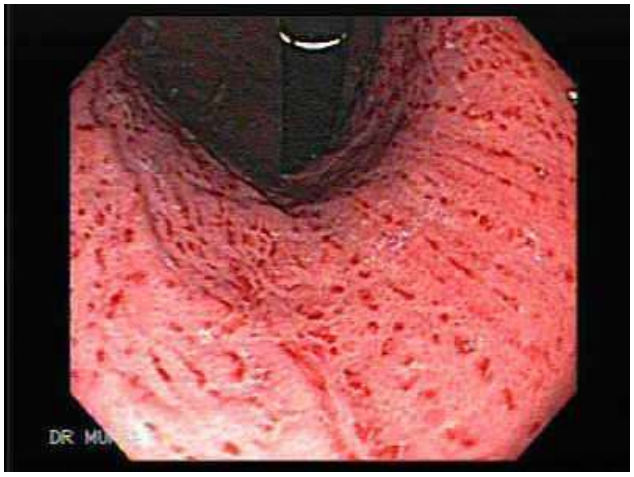

Figure 2.21 shows gastritis *(Source*:2000-2019 Gastrointestinal atlas.com, San Salvador, El Salvador) [Accessed 30 May 2022)

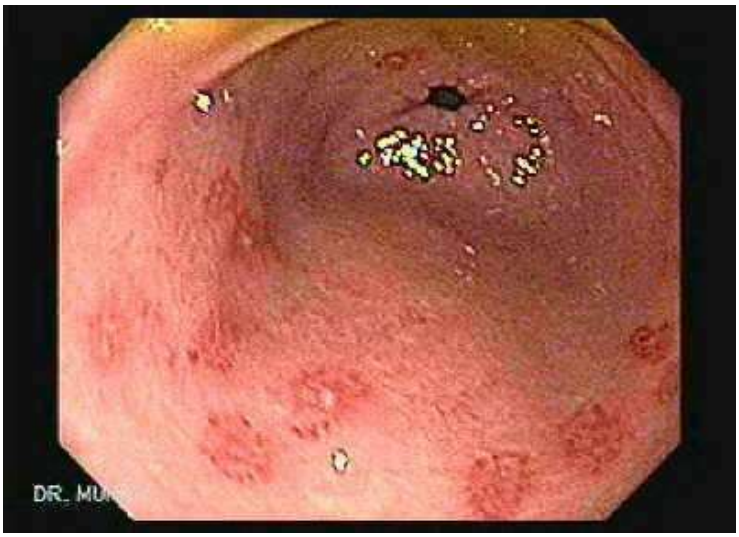

Figure 2.23 shows gastritis erosions *(Source*:2000-2019 Gastrointestinal atlas.com, San Salvador, El Salvador) [Accessed 30 May, 2022)

The prevalence of ulcers of the stomach and or duodenum caused by H. pylori is higher in patients suffering from liver cirrhosis.[158] The most important pathogenic factor of gastroduodenal lesions in end-stage liver disease and cirrhosis is portal hypertension. It could be due to splenic congestion, which interferes with the normal reparative processes of the gastroduodenal mucosa and leads to increased susceptibility to acid and pepsin secretion.[121]

The most common initial findings for chronic gastritis are (1) haematological disorders such as anaemia (iron deficiency) detected on routine check-ups, and (2) positive histological examination of gastric biopsies.[159] For iron-deficiency anaemia (based on blood film showing microscopic and or hypochromic changes as well as iron studies), achlorhydria from chronic gastritis causing impairment of iron absorption in the duodenum and early jejunum is the main cause of the anaemia.[160]

Treatment

Miyaji and colleagues reported that treatment of gastritis and erosion with Proton pump inhibitors, as well as eradication of H. pylori, was effective in patients with diffuse H. pylori infection in the stomach who also had these lesions.[161]Eradication therapy may be beneficial for cirrhotic patients because it diminishes the risk of recurrent gastric lesions and bleeding.

2.6.6 Management of other complications of Liver cirrhosis

Ascites

Ascites is the most common complication of that leads to hospital admission.[162]

The American Association for the Study of Liver Disease (AASLD) recommends that patients with whom ascites are present on imaging modalities, but not clinically detectable, should be imaged again after 3 months or when the ascites become clinically apparent.[163] A diagnostic paracentesis should be performed on all patients with new-onset ascites. Patients often require a combination of pharmacological and non-pharmacological therapies to adequately manage ascites and fluid retention. Controlled salt intake and oral diuretics are the backbones of first-line therapy.[162] Treatment of the underlying aetiology such as cessation of alcohol use can lead to a dramatic improvement of ascites and other reversible components of the disease.[164]

Similarly, treatment of hepatitis B, hepatitis C and autoimmune hepatitis can lead to the resolution of ascites or a heightened response to medical therapy.[165]

Bed rest

In theory, upright posture may further aggravate the plasma renin elevation found in patients with cirrhosis and exacerbate salt retention and impair response to diuretics,[166,167] however, this theory is not supported by controlled clinical trials and is impractical.[162] Thus, bed rest is not advocated as a treatment.[163]

Salt restriction

Treatment often begins with education regarding dietary sodium restriction.[163] Limiting salt intake to 2000 mg/d or 88 mmol/d is often recommended.[163] Fluid and weight loss are related to sodium balance and more stringent dietary restrictions can speed the mobilization of fluid. However, restrictions < 2000 mg/d are not recommended because they are less palatable and create the potential to reduce food intake and worsen the coexisting malnutrition.[168] In addition, a marked reduction in sodium intake does not add efficacy to diuretic treatment and can lead to an increased incidence of diuretic-induced renal failure and hyponatremia.[169] Fluid restriction is not required in the majority of patients with cirrhosis. As previously mentioned, it is the sodium restriction, not the fluid restriction, that is responsible for fluid loss, as loss of sodium leads to a passive loss of fluid.[165]

Pharmacological therapy

If patients adhere to dietary sodium restriction, one of the goals of treatment is to increase the urinary secretion of sodium to greater than 78 mmol/d.[170] About 10%-15% of the patient have spontaneous urinary sodium excretion greater than 78 mmol/day and can be managed with sodium restriction alone.[165] However, when given a choice, most patients would prefer a combination of diuretics and mild sodium restriction to strict sodium restriction alone.[170]

First-line diuretics

The two most commonly used diuretics in patients with cirrhosis are spironolactone and furosemide.[170] Single-agent spironolactone is more efficacious than furosemide.[171] A randomized trial in patients with new-onset ascites and well preserved renal function noted slower diuresis and less need for dose adjustment with spironolactone alone, so the authors recommended this approach could be considered appropriate for outpatients.[172] However, a subsequent study enrolled patients with long-standing ascites, many of whom with significantly impaired renal perfusion favoured the use of combination therapy.[173] In addition, hyperkalemia associated with spironolactone and the drug's long half-life has limited its role as a single agent for patients with minimal fluid retention.[174] The typical initial diuretic regimen consists of daily oral 100 mg of spironolactone and 40 mg of furosemide.[170] Beginning with combination therapy has been supported by the results of randomized trials, which showed that this approach shortens the time to the mobilization of moderate ascites.[172] In addition, most patients with cirrhosis will eventually require combination treatment.[172] If weight loss and natriuresis remain inadequate, the dose can be increased every 3-5 d, maintaining the 100:40 ratio.[170] In general, this ratio helps maintain normokalemia. Post-transplant patients and patients with parenchymal renal disease may tolerate less spironolactone secondary to hyperkalemia.[170,175,176] Hypokalemia is common in patients with alcoholic hepatitis and, in this scenario, furosemide can be temporarily held.[177] The usual maximum daily doses for spironolactone and furosemide are 400 mg and 160 mg, respectively.[170] Dosing at night or more than once daily reduces compliance and results in nocturia.[178]

Second-line diuretics

Triamterene, metolazone and hydrochlorothiazide have been successfully used to treat ascites, however, hydrochlorothiazide can result in extreme hyponatremia when added to a combination of spironolactone and furosemide.[179] Amiloride (10-40 mg/day) is less efficacious and more expensive when compared to spironolactone, but its use can be justified in patients with tender

gynecomastia.[180] Other diuretics, such as eplerenone, torasemide, and bumetanide are expensive and have not been extensively studied in the setting of cirrhosis and ascites. Albumin infusion An unblinded randomized controlled study showed mortality benefits in patients with new-onset ascites who received weekly 25 g infusions of albumin for one year followed by infusions every other week.[181] Another trial noted that a combination of diuretics and albumin results in higher response rates, short hospital stay, lower readmission rates and a lower probability of recurrence.[182] However, further studies are required before this expensive treatment regimen can be advocated by societies like AASLD.

Monitoring of fluid loss

In patients with significant oedema, there is no limit to daily weight loss.[51] After the resolution of oedema, a daily loss of 0.5kg is a reasonable maximum. In addition to fluid mobilization, other factors such as serum sodium levels, serum potassium levels, serum creatinine levels, and the presence of clinical complications like HE should guide therapy.[183]

Paracentesis

Large-volume paracentesis is a safe and effective therapy for patients presenting with tense ascites.[184] However, this procedure should be followed by sodium restriction and diuretics for patients who are diuretic sensitive.

Refractory ascites

Refractory ascites occurs in about 5% of patients with cirrhosis. This condition is defined as ascites that cannot be mobilized despite a sodium-restricted diet and high-dose diuretics and that accumulate after therapeutic paracentesis. Medical treatment options remain limited in patients with refractory ascites. Midodrine 7.5 mg three times a day compared to standard therapy has been shown in a pilot randomized control trial of 40 patients followed for three months to increase urine volume, urine sodium, mean arterial pressures, and survival.[185] The same group in another pilot study compared the combination of midodrine and clonidine to standard therapy and noted an improvement in the above parameters except survival.[185] However, at this time evidence supporting the use of midodrine in this challenging patient population, is weak and bigger studies are needed before routine use of this can be suggested. Other treatment options for this challenging condition include serial therapeutic paracentesis, liver transplantation, and trans jugular

intrahepatic portosystemic shunt (TIPS). Experimental treatment options include weekly albumin infusions of 50 g [181,182] and clonidine, either alone or in combination with spironolacton.[182] midodrine in the treatment of patients with type I HRS. A multicenter randomized trial of terlipressin and albumin vs albumin alone showed an improvement in creatinine, but no survival benefit at 3 months.[186] A recent meta-analysis of vasoconstrictor treatment (terlipressin, octreotide, midodrine and norepinephrine) of type I and type II HRS showed reduced mortality in patients on vasoconstrictors in combination with and without albumin as compared with albumin alone or no intervention.[187] The same study showed a survival advantage with terlipressin and albumin in patients with cirrhosis and its complications. The use of albumin and norepinephrine or vasopressin can be considered in ICU settings.[51] Liver transplantation is an effective treatment: however, the number of transplanted patients is still very low.[187] Hemodialysis is frequently used to correct electrolyte imbalance and azotemia before liver transplantation.[187] If a patient is dialyzed for more than 8 week prior liver transplant, a simultaneous kidney transplant should be considered.[188]

Other medications include methylene blue, allium sativum (garlic), curcumin, somatostatin analogue (e.g., octreotide), nitric oxide synthetase inhibitors, glucocorticoids, beta-blockers, and chemotherapy have been tried with little or no evidence for chronic or acute hepatic disease with advanced hepatic failure and portal hypertension. The trans-jugular intrahepatic shunt (TIPS) has been used to improve gas exchange and shunt fraction in HPS, however, the data is not very encouraging.[189] Intra-arterial coil embolization of discrete pulmonary arteriovenous communications improves right to left shunt and has been used successfully in patients with large fistula amenable to radiographic interventions.[190] Coiled embolization has also been used successfully in a patient with persistent hypoxia six months after liver transplantation.[191]

2.7 Prognosis Of liver Disease

The course of liver cirrhosis depends on both the aetiology and treatment of the underlying cause. Numerous studies have attempted to develop a classification system that can both characterize the degree of liver injury and predict the prognosis of patients with cirrhosis based on clinical and laboratory parameters.

2.7.1 The Child-Turcotte-Pugh score

Due to its low level of complexity and its good predictive value. the Child-Turcotte-Pugh score classification is widely used. One-year survival rates for patients with Child-Turcotte-Pugh score A, B, and C cirrhosis are 100, 80, and 45 per cent, respectively.[192] Child-Turcotte-Pugh score class predicts the development of complications, such as variceal haemorrhage and the response of patients to surgical interventions.[193]

2.7.2 Model for End-Stage Liver Disease *(*MELD)

More recently with the pressure on the allocation of scarce liver donors for transplantation, the Model for End-Stage Liver Disease *(*MELD*)* has been developed to more precisely evaluate short-term Child-Turcotte-Pugh score mortality.[192] MELD best predicts 3-month survival of patients with Liver cirrhosis, irrespective of aetiology. Child-Turcotte-Pugh score and MELD scores can vary greatly when single parameters are modified by medical treatment, such as the substitution of albumin, removal of ascites or diuretic treatment. Here, an increasing MELD score over time is a better predictor of cirrhosis severity and progression.[194]

2.8 Helicobacter. Pylori (H. pylori) infection and liver cirrhosis

Helicobacter pylori (H. pylori) is a microaerophilic gram-negative bacillus, resistant to the activity of gastric juice. The bacteria may take the vegetative form (spiral shape) or sporulation form. H. pylori lives mainly on the surface of epithelial cells of mucous membranes of the pre-pyloric part of the stomach. The cilia present in the bacteria allow it to move into intercellular spaces and adhere to the surface of cells. Infection with these bacteria is one of the most common in the world. In highly developed countries, 50% of the population is infected, whereas in the developing countries the proportion reaches as much as 90%.[195]

H. pylori infection causes local (limited to the gastric mucous membrane) and the general increase of proinflammatory cytokines interleukin (IL)-1, IL-2, IL-4, IL-6, IL-8, IL-10, IL-17, interferon-β, and tumour necrosis factor-α.[196] This phenomenon not only leads to stimulation of local inflammatory reaction but also exacerbates different inflammatory reactions in the organism. H. pylori underlies chronic atrophic gastritis, metaplasia, and dysplasia, leading to the development of gastric cancer. According to the WHO, this bacterium is a class I carcinogenic factor. It may

influence extra gastric organ disturbances, exacerbating cardiovascular diseases, metabolic diseases, and disturbing normal liver function, especially in patients with liver cirrhosis.[197] In the group of patients infected with H. pylori, morphologic studies on the liver of patients infected with hepatitis B virus (HBV), hepatitis C virus (HCV) and patients with chronic non-infectious liver diseases, have demonstrated the presence of H. pylori DNA in the perihepatic tissues. Such an infection is caused by disturbances of immunologic functions in this group of patients.[198] H. pylori infection influences the disturbances of lipid metabolism, manifesting with hypertriglyceridemia and hypercholesterolemia, with concurrent fall in high-density lipoprotein. This is especially important in the metabolism of hepatocytes, steatosis, and liver fibrosis.[199]In the course of liver cirrhosis, pathological lesions often appear in the mucous membranes of the stomach. Portal gastropathy is a chronic inflammatory state that occurs most frequently. Studies on this group of patients point to the high importance of the cytopathological effect of H. pylori on hepatocytes.[198] A study by Pogorzelski et al demonstrated the incidence of H. pylori infections correlated with that of oesophageal varices.[200]

2.9 Correlation between upper gastrointestinal endoscopic findings (lesions) and severity of liver disease

In patients with liver cirrhosis, varices can be found in the stomach or the oesophagus. Oesophageal varices are known to bleed more frequently but less severely than gastric varices. The incidence of variceal bleeding varies from 20% to 30% between studies, and death from uncontrolled bleeding ranges from 6 to 8%.[101] Clinical, as well as endoscopic findings, have been used as prognostic indicators in patients with liver cirrhosis. Using an upper GI endoscopy, oesophageal mucosal findings include erosions, ulceration and candidiasis, and gastric mucosal lesions include erosions and ulcerations.[104] Advanced liver disease and increased severity are positively and independently associated with the development of esophagogastric varices.[103] In another analysis of patients with end-stage liver disease, about a third of all patients had episodes of rebleeding within 6 weeks of the first episode of variceal bleeding.[201] A study by Rabinowitz et al found a significant correlation between the increasing prevalence of oesophageal varices with the increasing severity of disease using the Child-Turcotte-Pugh criteria.[92] However, another study by Vigneri et al found no significant correlation between endoscopic findings, the severity of liver cirrhosis graded by the Child-Turcotte-Pugh score, and the severity of oesophageal varices.[202]

A study by Chaudhary et al also found a significant association between oesophageal varices and the grade of portal hypertensive gastropathy.[9] An Italian study found that all endoscopic parameters in their study were significant predictors of bleeding. Parameters used for the study included location, size, occupancy, blue tone and red colour signs of the lesion.[203] According to a study by Taranto et al, the endoscopic findings of oesophagogastric varices such as mosaic-like patterns and red spots in gastric varices were more associated with severe forms of liver cirrhosis as per the Child-Pugh Score.[95]

2.10 Patients' characteristics predicting the presence of upper gastrointestinal endoscopic findings (lesions)

Oesophagogastric varices remain a common occurrence amongst patients with liver cirrhosis. The occurrence of varices diagnosed endoscopically has been associated with some patient characteristics. A Tanzanian study found that increased age, advanced liver disease, presence of ascites, increased splenic diameter as well as increased portal vein diameter are all independently associated with the development of oesophageal varices.[103] In an analysis of 85 patients, mostly alcoholic and in end-stage liver failure endoscopically diagnosed as having variceal bleeding, a mortality rate of 42% was found at 6 weeks of diagnosis.[201] Factors affecting death from variceal bleeding were the presence of comorbidities and increasing age.[201] Other patient characteristics that predict the presence of upper GI endoscopic findings such as large varices include low platelet count and advanced Child-Turcotte-Pugh class according to a study by Zaman and others.[204] The rough surface of the liver, liver stiffness and splenic thickness have been found as independent predictors of oesophagogastric varices.[205]

CHAPTER THREE

MATERIALS AND METHODS

3.1 Study Design

This was a hospital based descriptive cross-sectional study involving inpatients and out-patients with liver cirrhosis at Komfo Anokye Teaching Hospital. Information on socio-demographic characteristics and clinical history were collected. Data on individual characteristics, including exposure to risk factors, were also collected in addition to information on the outcome.

3.2 Study location

The study was conducted at the Internal Medicine Directorate of Komfo Anokye Teaching Hospital (KATH), in Kumasi, Ghana. The KATH is the second-largest hospital in Ghana. Since its establishment in 1954, the 1,200-bed capacity hospital has served as the main referral center for the middle and northern part of Ghana and is the only tertiary health facility in the Ashanti region. It was the main referral hospital for the Ashanti, Bono, Bono East, Savanna, Western North and Northern regions of Ghana until the upgrade of Tamale regional hospital to a teaching hospital. Komfo Anokye Teaching Hospital has thirteen (13) clinical and two (2) non-clinical directorates Clinical services provided by the hospital include Accident and Emergency care, Anaesthesia and Intensive care, Child Health, Oral Health, Eye, Ear, Nose and Throat (EENT), Family Medicine, General Surgery, Internal Medicine, Laboratory services directorate, Obstetrics and Gynaecology, Oncology, Radiology, and Trauma and Orthopaedics. The hospital provides services in all aspects of specialist care in fulfilment of its mandate to provide advanced clinical care services to people in Ghana

KATH also supports the regional and district hospitals in the northern part of Ghana.[206]

The internal medicine directorate provides specialist clinical care to patients aged 17 years and above within the Kumasi metropolis and receives referrals from district, regional and private health facilities across the country. Services rendered include specialist outpatient and in-patient as well as diagnostic services. Among the specialist clinics run at the Internal Medicine directorate are Hypertension, Asthma, Diabetes, HIV, Chest, Hematology, Neurology, Cardiology, Gastrointestinal, Non-diabetes endocrine, Rheumatology, Nephrology and Dermatology clinics.

The GI unit is a specialized area under the directorate of internal medicine dedicated to providing care for patients with GI and liver diseases as well as diseases of the gall bladder and pancreas. The GI unit currently has two Gastroenterologists, four fellows in training, four rotating house officers who rotate through the unit monthly, seven nurses, one healthcare assistant and one orderly.

The unit has a dedicated endoscopy suite for the provision of diagnostic and therapeutic endoscopy as well as other interventions for GI and liver diseases.

The unit manages on the average, about 25 patients weekly at the Internal Medicine wards as in-patients and about 70 patients on an out-patient basis at the specialist GI and Hepatology out-patients clinic weekly.

Figure 3. 1 THE KOMFO ANOKYE TEACHING HOSPITAL Source (

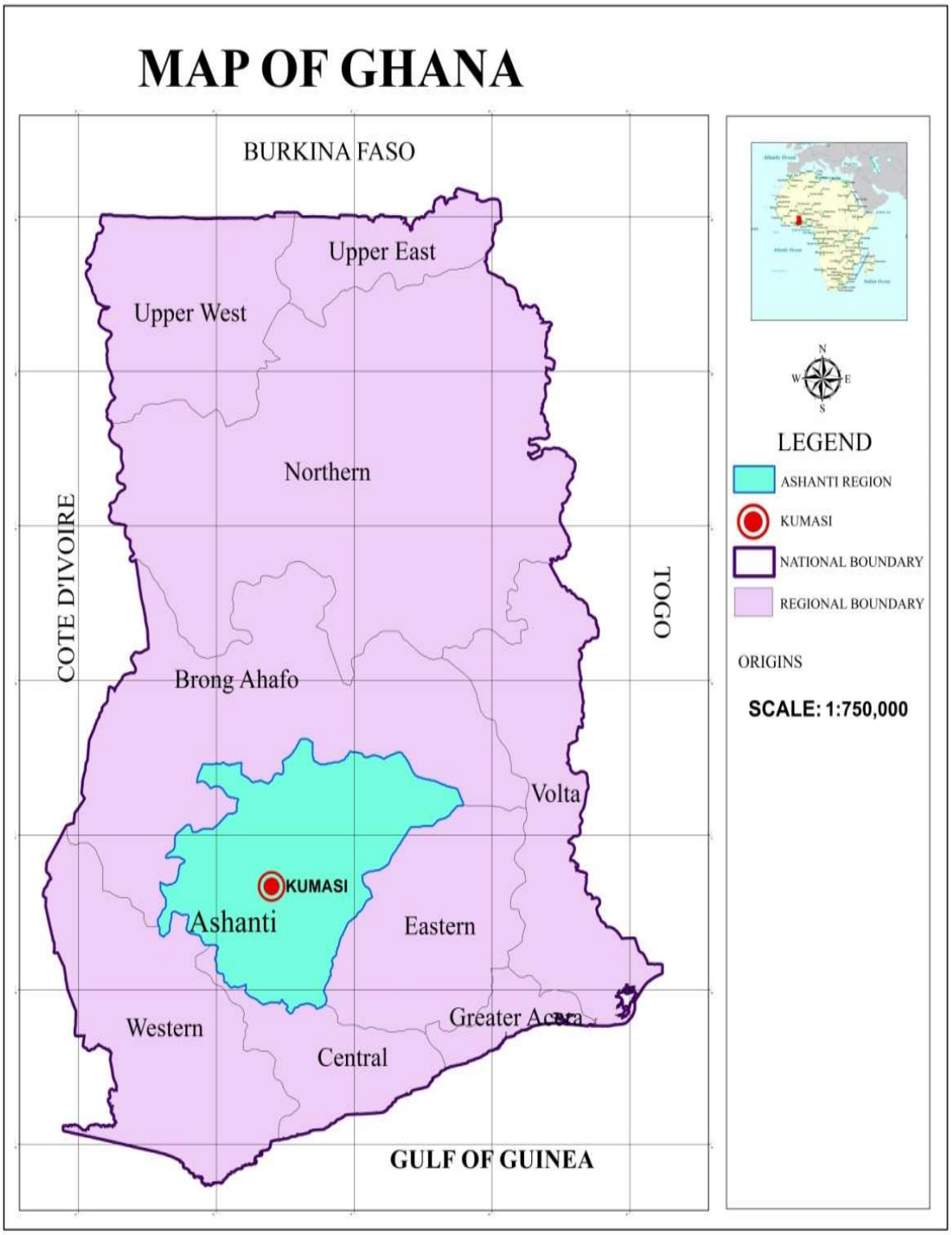

Figure 3. 2:Map of Ghana. Source: Cacciatore et al (2008)

3.3 Study Population and sampling

The study population was drawn from patients in the out-patient Gastroenterology and Hepatology clinic, at the accident and emergency unit, and patients with liver cirrhosis on admission at the directorate of medicine from September 2019 to March 2020, then from April 2021 to make up for a 10% attrition rate.

3.3. 1 Target Population

The target population for this study included persons aged 17 years and above

3.4 Inclusion criteria and exclusion criteria

3.4.1 Inclusion criteria:

Patients with Liver cirrhosis who are 17 years and above who consent to be partake in the study

3.4.2 Exclusion Criteria:

1. Patients below 17 years
2. Patients with non-cirrhotic liver disease, primary and secondary hepatic malignancy, and fulminant hepatic failure
3. All patients with liver cirrhosis who were not haemodynamically stable to undergo oesophagoduodenoscopy.

3.5.1 Calculation of Sample Size:

The sample size was calculated using the formula:

$$n = \left[\frac{z^2pq}{d^2}\right] + AR$$

Where:

n = the desired sample size

z = the standard normal deviate, usually set at 1.96, which corresponds to the 95% confidence level.

p = the proportion in the target population estimated to have liver cirrhosis.

q = The proportion in the target population who do not have liver cirrhosis. i.e., 1-p.

d = Degree of accuracy desired, usually set at 0.05

AR = Attrition Rate

At

Z= 1.96 at 95% confidence interval

P = 9.5% (0.095)

d = 5% (0.05)

AR = 10% (132) = 13.2

n = [(3.8416 x 0.095 x 0.905) / (0.0025)] + 13.2 = 145.11

n = 145

Sample size = 145

3.5.2 Sampling Method

A consecutive sampling technique was used to select 145 eligible subjects for the study. Data was collected over seven months from September 2019 to March 2021. then from April 2021 to make up for a 10% attrition rate.

Patients with liver cirrhosis attending the Gastroenterology clinic and in-patients were enrolled onto the study.

3.6 Study procedure

3.6.1 Training of Research assistant

A research assistant was enrolled and trained to assist in data collection. The research assistant was a Public Health Officer at the Public Health Unit, KATH has a Bachelor of Science (BSc) degree in Public Health (Health Informatics). He has experience in health system research, data management and statistical analysis and had participated in several hospital case-based studies.

He was trained on the various aspects of this study such as data collection, management, informed consent, patient confidentiality, local language etc

3.6.2 Pre-testing

The data collection instrument used to conduct the study was pretested a month earlier before the actual data collection was commenced. Convenient sampling was done to select fifteen (15) respondents at the Family medicine directorate. Although respondents used for the pretesting were not patients diagnosed with liver cirrhosis, the exercise was relevant in testing the questionnaire

for accuracy and validity. The family medicine directorate was selected for the pre-testing because it shares similar characteristics with the directorate of internal medicine. The questionnaire was administered to patients who consented to participate in the study. After respondents have answered the question, the data was entered into the REDCap database and manipulated to check for errors and consistency in the database. Problems identified during the pilot were addressed before the questionnaire was finalized. During the piloting, it was observed that most patients had problems with understanding medical terms. This development informed the decision for the training of the research assistant. A team of gastroenterology specialists, the principal investigator (the candidate) and the research assistant were empaneled for the training.

3.6.3 Informed consent

Patients who met the inclusion criteria for the study were approached and the study procedure was explained to them in a language that they could understand. Patients were made to know in detail that the study involved physical examination, drawing of at least 15mls of whole blood and upper GIT endoscopy. If the subject agreed to be part of the study, the research assistant took them through the consent process for all the procedures. Once the subject has signed/thumb printed the consent form, they were given a study identification number with a unique code and enrolled on the study (Appendix II and III).

3.6.4 Sampling technique

Data collection was done over seven (6) months, from September 2019 to March 2020, and an additional 15 recruited in April 2021. With an estimated sample size of 145 subjects, data was planned to be collected daily for inpatients (i.e., patients with liver cirrhosis admitted to the directorate of medicine wards and the Accident and Emergency unit) at Komfo Anokye Teaching Hospital. Out-patient were enrolled weekly on the day of their visit to the specialist Gastroenterology and Hepatology clinic. Patients were selected consecutively and interviewed between the hours of 8:00 am to 5:00 pm. Data was collected primarily through the administration of the questionnaire. Following enrollment, the study subjects were followed up with clinical examination, laboratory investigations, abdominal ultrasound scans to assess the degree of liver disease and upper GI endoscopy scheduled on the next available endoscopy day. In-patients who

met the inclusion criteria were selected at the medical wards and the emergency departments as and when they presented.

3.7 Data collection and measurement

3.7.1 Data collection

A structured questionnaire was used to collect data from respondents after obtaining consent.
After the questionnaire was administered, a physical (clinical) examination was done, 13 millitres of blood samples was taken for haematology investigation, liver function test and International Normalized Ration (INR). Patients were then sent for an abdominal ultrasound scan by a dedicated senior radiologist and upper GI endoscopy performed at the KATH endoscopy suite by the researcher under the supervision of a consultant to ascertain the presence of any pathological lesions.

Demographics of respondents (age, sex, income status, marital status, level of education, etc.), social histories such as body tattoos, body piercing, alcohol intake and smoking. Drug use (street drugs, steroid use, birth control pills, bodybuilding drugs and oral herbal preparation etc.) and history of liver diseases may influence the development of liver cirrhosis. Participants were examined for signs of liver cirrhosis.
15mls of blood was drawn from any available vein on the forearm, after appropriate cleaning and brief tourniquet application. The blood sample was delivered in required volumes into appropriate sample tubes and stored at an appropriate temperature for the various laboratory analysis including platelet count, International Normalization Ratio (INR), serum albumin, bilirubin, HBsAg and anti-HCV.

3.7.2 Measurements

The main outcome variable: Class A, Class B and Class C cirrhosis were obtained by using the modified Child-Turcotte Pugh. The score was derived from computing examination findings (encephalopathy), ultrasound findings (ascites) and laboratory findings (albumin, bilirubin, and

INR). The Child-Pugh score was used because it has been widely used to assess the severity of liver cirrhosis.

Bilirubin (Total)	<2 mg/dL (<34.2 µmol/L)	+1
	2-3 mg/dL (34.2-51.3 µmol/L)	+2
	>3 mg/dL (>51.3 µmol/L)	+3
Albumin	>3.5 g/dL (>35 g/L)	+1
	2.8-3.5 g/dL (28-35 g/L)	+2
	<2.8 g/dL (<28 g/L)	+3
INR	<1.7	+1
	1.7-2.2	+2
	>2.2	+3
Ascites	Absent	+1
	Slight	+2
	Moderate	+3
Encephalopathy	No Encephalopathy	+1
	Grade 1-2	+2
	Grade 3-4	+3

INR: International Normalized Ratio
CLASS A: 5-6, CLASS B: 7-9 , CLASS C: 10-15

Figure 3. 3:Child-Pugh Score for estimating the severity of Liver cirrhosis

3.7.3 Physical (Clinical) examination

Physical clinical examination was performed looking out for signs of liver cirrhosis such as abdominal swelling/pain, sclera/palmer Jaundice, pedal swelling, Tattoo/ scarification, clubbing, leukonychia, palmar erythema, Dupuytren contracture, asterixis, spider naevi (angioma) ascites, silky hair, and hepatic encephalopathy.

3.7.4 Haematology tests

5 milliliter of whole blood was collected after a thorough physical examination via venesection of a good superficial vein at the endoscopy unit, 5 milliliters into an EDTA tube, stored between 4ºC – 8ºC and subsequently analysed with Sysmex XP-5000 Automated Haematology Analyzer into red blood cells, white blood cell and platelet count. All the haematology samples were analysed at the haematology laboratory of the KATH. The reference range from the haematology laboratory was given as 11.0g/dL to 16.0g/dL for haemoglobin level and 140 k/uL to 400 x10 K/uL for the platelet count.

3.7.5 INR

3 milliliter of blood was collected into a 3.2% sodium citrate tube, stored between 2°C to 8 °C and subsequently analyzed with Meryl automatic blood coagulometer, ClotQuant 2 for the PT and INR. The sample was analyzed at the haematology laboratory of the Komfo Anokye Teaching Hospital.

3.7.6 Liver Chemistry

5 milliliters of whole blood were collected into a plasma separator tube, refrigerated at 2°C to 8 °C and subsequently analyzed for the albumin and bilirubin levels. All the liver chemistry samples were analysed at the Chemical pathology laboratory of the KATH with a Beckman XC700AU Biochemistry analyzer. The range of the serum albumin and bilirubin levels were between 35g/L to 54g/L and 5umol/L to 21umol/L respectively.

3.7.7 Abdominal Ultrasonography Scan

An abdominal ultrasonography scan was performed in the Radiology Unit of the KATH by a dedicated senior radiologist using a Toshiba ECOSEE of Japan a 3.5 MHz curved linear transducer to assess for cirrhosis. Characteristics of the liver such as the size of the liver, consistency, edge and surface regularity, portal, hepatic and splenic vein caliber, spleen size, ascites, hepatic tumours and other masses were assessed and documented.

The diagnosis of liver cirrhosis in each case was established ultrasound scan of the Liver. Splenic vein dilatation was denoted by splenic vein diameter > 10mm, hepatic vein dilatation by a diameter > 6 mm and the portal vein dilatation by a venous diameter > 13mm.

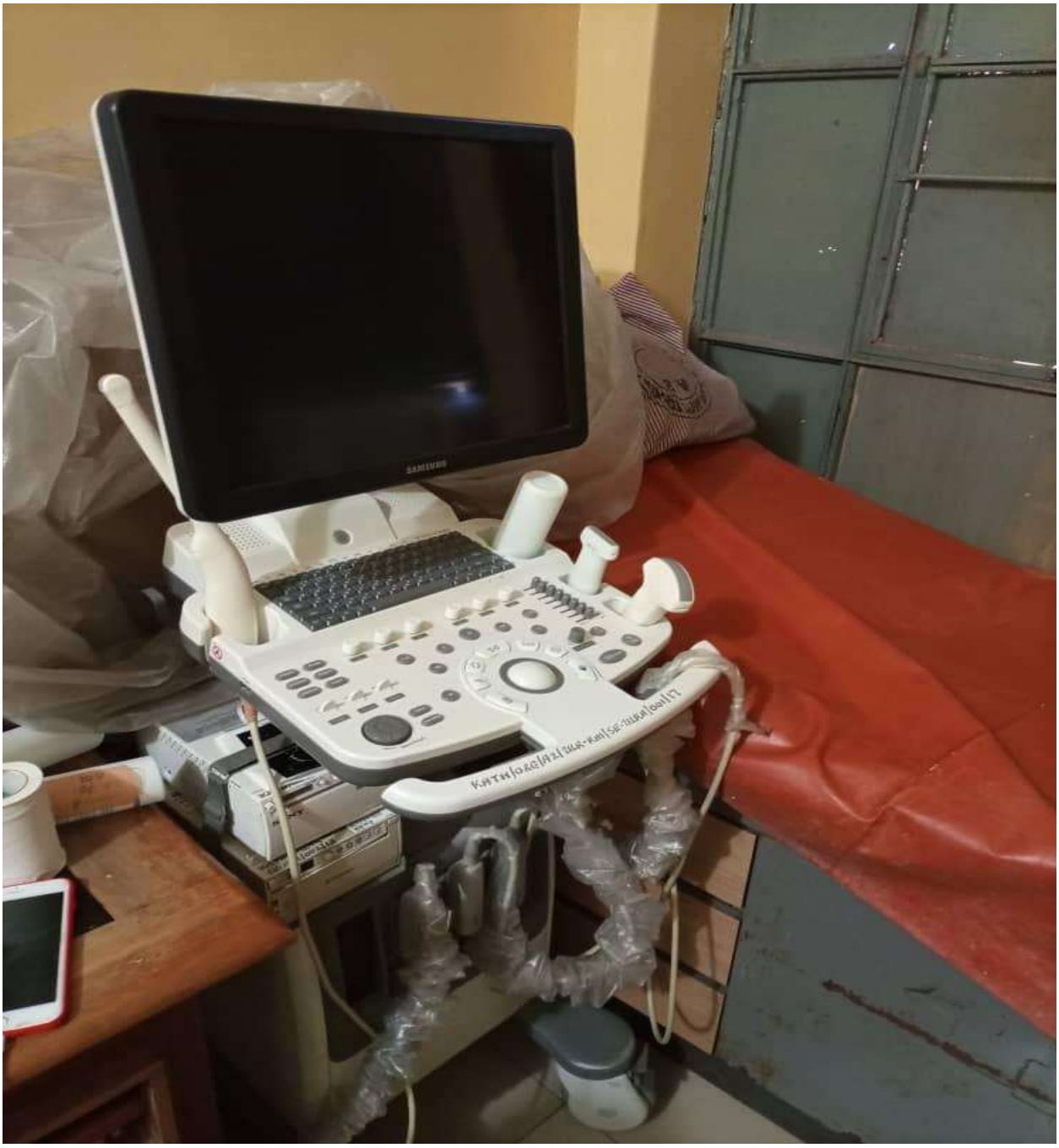

Figure 3. 4:Ultrasound machine and probe

3.7.8 Oesophagogastroduodenoscopy

All upper GI endoscopies were performed in the Gastrointestinal Endoscopy unit KATH by Dr Bright Oppong (principal investigator) under the supervision of a consultant gastroenterologist.

Before the procedure, each patient was counselled on nil per os for at least 6 hours, intravenous access was placed in a vein in the arm for both resuscitation and administration of pre-procedure medications such as, Intravenous Midazolam 2.5mg stat and Hyoscine butylbromide 20mg stat was given by a nurse anaesthetist.

Vital signs including blood pressure, heart rate, and oxygen saturation were monitored before, during and after the procedure.

During the procedure, patients were placed in their left lateral position on an examination bed. An endoscope is carefully passed down the oesophagus into the stomach and the duodenum. Various endoscopic findings were identified using a Karl Storz Videoscope 38094 PKS (Gastro pack 2016 model) commenting on

Lax LES - determined by a space around the endoscope on retroflexion at the fundus

Gastric varices- present or absent and the site.

PHG - present or absent and the grade (mild, moderate, or severe)

Oesophageal Varices - number and grade according to The Japanese Research Society for Portal Hypertension Classification as below:

Small: varices that measures less than 5mm in diameter.

Medium: varices that measures between 5mm-10mm in diameter.

Large: varices that measures greater than 10mm in diameter.

The presence of gastritis, duodenitis, ulcers and/or other lesions was documented

H. pylori testing was done using the H. pylori antigen (CLO test) cassette.

Endoscopic biopsies from the areas with lesions (such as ulcers, polyps or a mass) were taken and sent to the Pathology Department, KATH for histopathology study.

This study was carried out under The Code of Ethics of the World Medical Association (Declaration of Helsinki, revised in 2000) for experiments involving humans.

Figure 3. 5:Endoscopy set up in KATH

Figure 3. 6:Endoscopic procedure being performed at GI unit of KATH, Source KATH

3.8 Data management and Analysis

3.8.1 Data Management

Data were collected with a structured questionnaire and each respondent was exposed to the same questions. After the quantitative data had been collected through the questionnaire, corrections were made. The researcher checked for accuracy, completeness and internal errors in t data collected by the research assistant. The questionnaires were sorted, numbered, and coded into a coding manual before data entry. Data collected were entered into a database designed with Research Electronic Data Capture (REDCap).

3.8.2 Data analysis

The data was exported to STATA (Standard edition) version 16.0 for statistical analysis. Results were enumerated in means and proportions at 95% CI and presented in tables, charts or graphs. Both univariate and bivariate analyses were performed. A multivariate analysis was performed by using multiple logistic and ordinal regression models.

Descriptive analysis was used in summarizing the characteristics of respondents. Chi-square ($\chi 2$) test/Fisher's exact test was performed to test the association between the socio-demographic and other clinical characteristics with the verity of liver cirrhosis. Factors that were significant in bivariate analyses were analyzed using an ordinal regression model to test for the predictors of severe liver disease. The level of significance for association in the bivariate analysis was $P < 0.05$. All significant factors were included in the ordinal regression model using a stepwise ordinal logistic method. The unadjusted (crude) and adjusted odds ratios (OR) and 95% confidence intervals (CIs) were reported. The partial proportional odds model (PPOM) was presumed to bridge the gap between ordered and non-ordered severity modelling frameworks.

3.9 Ethical Consideration

Ethical clearance for this study was obtained from the Committee of Human Research Publication and Ethics (CHRPE), KNUST with written permission from the Research and Development unit, KATH. General Consent forms containing detailed information about the study as well as consent for endoscopy were given and explained to participants. Participants were given ample time to read, understand and voluntarily sign the informed consent to be part of the study. Privacy and confidentiality of the participants were ensured throughout the study.

Participation was voluntary and refusal to participate did not in any way affect the service that was received at the Internal Medicine Directorate. The principles of informed consent and confidentiality were ensured throughout the study.

3.9 Research instruments:

1. Ultrasound Scan: Toshiba SSA 340 ECCOCEE Japan with a 3.5 MHz curved linear transducer, Year of manufacture: 2014
2. Endoscope: Karl Storz gagastroscope3904 PKS & Gastropack 2250, Year of manufacture: 2016
3. Sysmex XP-5000 Automated Haematology Analyzer, Year of manufacture: 2019
4. Meryl automatic blood coagulometer, Clot Quant 2 Year of manufacture: 2020
5. Beckman XC700AU Biochemistry analyzer Year of manufacture: 2019
6. Rapid Urease test kit (Pronto dry) Year of manufacture:

CHAPTER FOUR

RESULTS

Table 4.1 Demographic and socio-economic characteristics of respondents

Variable	Frequency (n=145)	Percentage (%)
Residence		
- Rural	61	42.1
- Urban	84	57.9
Religion		
- Christian	112	77.2
- Muslim	31	21.4
- Traditionalist	1	0.7
- Others	1	0.7
Education		
- Primary	36	24.8
- JHS/MSLC	18	12.4
- SHS/Vocation	40	27.6
- Tertiary	19	13.1
- No formal education	32	22.1
Occupation		
- Fully employed	47	32.4
- Self-employed	94	64.8
- Student	2	1.4
- Unemployed	2	1.4
Marital status		
- Married	102	70.3
- Single	18	12.4
- Divorced	12	8.3
- Co-habiting	3	2.1
- Widow/widower	10	6.9

(*) JHS-Junior High School, MSLC-Middle School Leaving Certificate, SHS- Senior High School

4.1 Demographic and socio-economic characteristics of respondents

A total of 145 participants were included in the study out of which (72%) were males and females (28%). The age range was between 20 and 86 years. The mean age (standard deviation) of respondents was 46.5. More than half (54.5%) of all respondents were between the ages of 40– and 60 years. About one-quarter of 40 (27.6%) of respondents had up to secondary/vocational level education, 36 (24.8%) of respondents completed primary level education, and 19 (13.1%) respondents had up to tertiary level education. Less than one-quarter of 18 (12.4%) of respondents had junior School level education while 32 (22.1%) of respondents had no formal education. More than half 94 (64.8%) of respondents were self-employed. About one-quarter 44(30.3%) of all respondents were fully employed while 2 (1.4%) of respondents were part-time employees. 102 respondents representing 70.3% were married, and 18 (12.4%) respondents were single as detailed in table 4.1 and Figure 4.1 and 4.2 below.

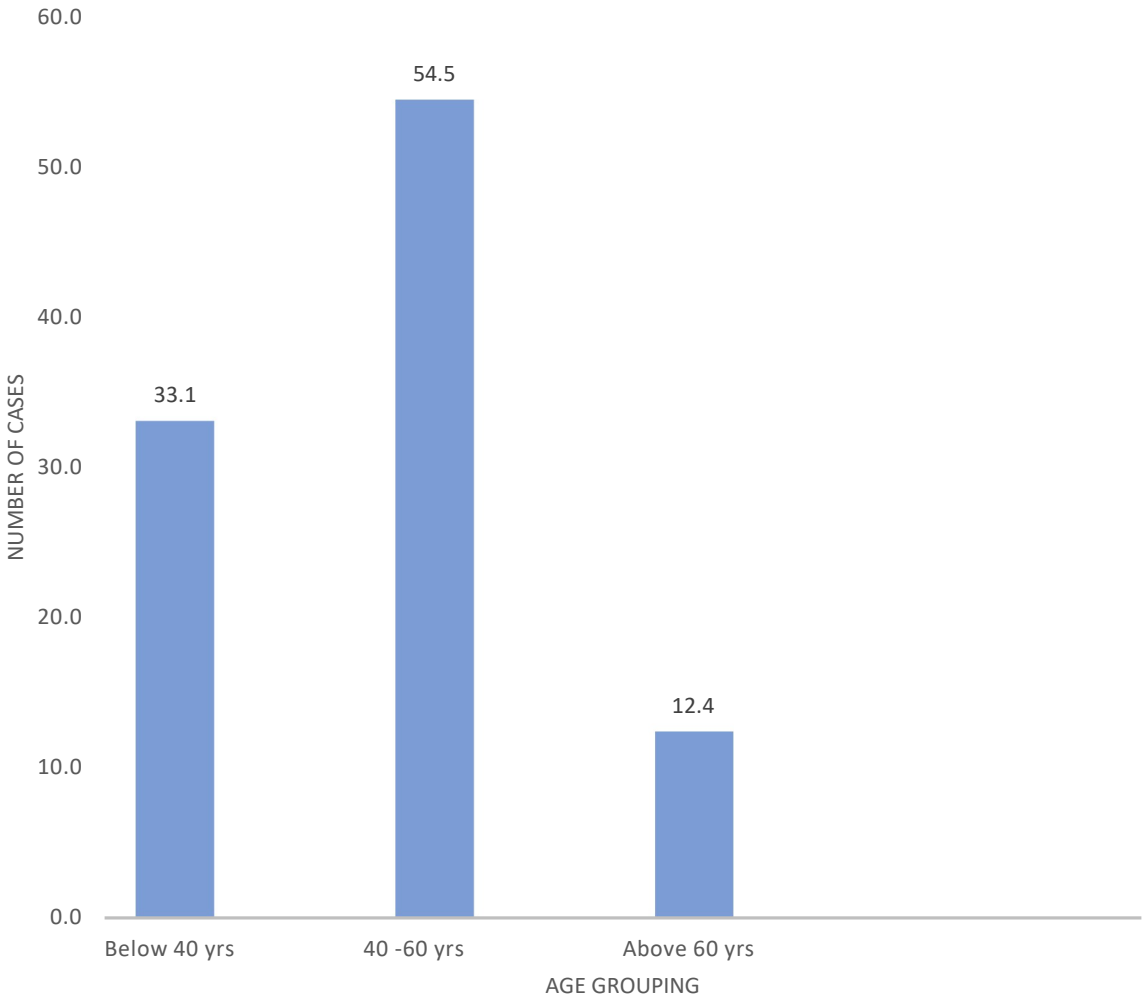

Figure 4. 1: Age distribution of respondents

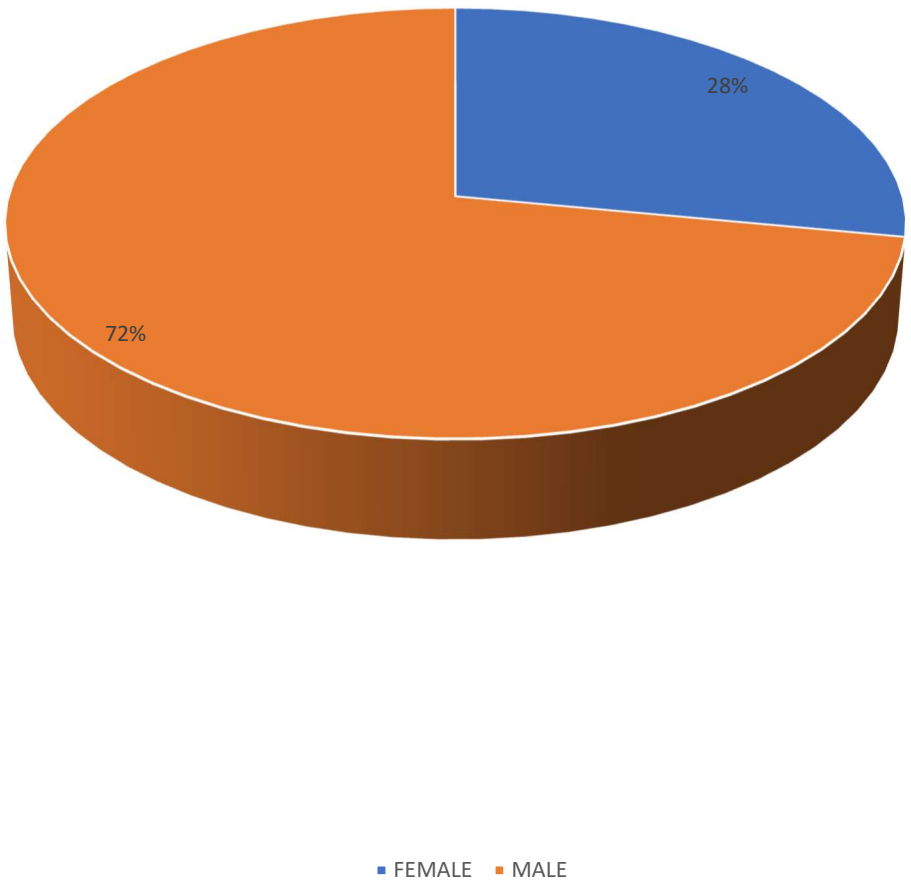

Figure 4. 2:Sex distribution of respondents

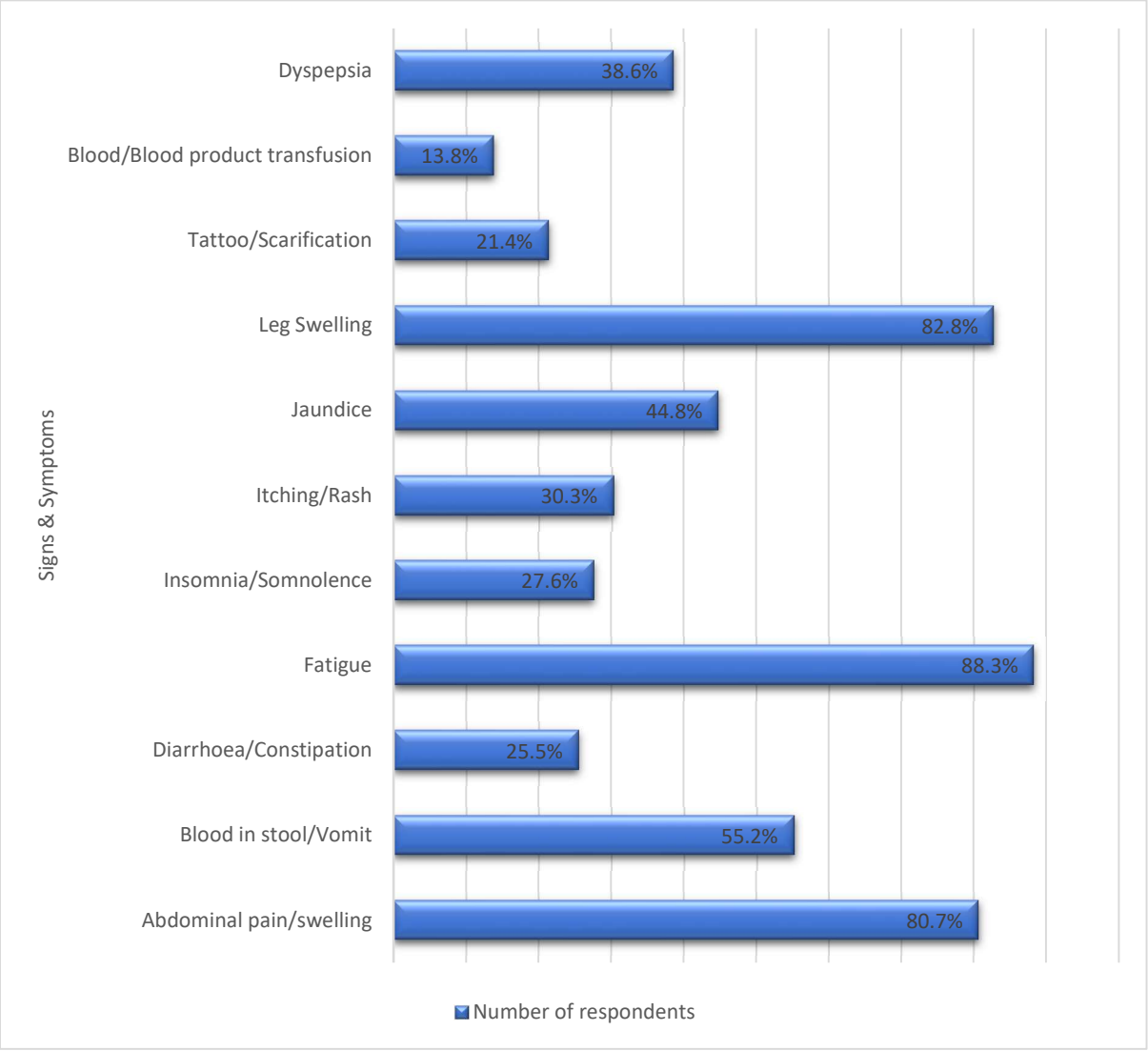

Figure 4. 3:Clinical information (signs and symptoms)

4.2 Clinical information (symptoms) of respondents

Figure 4.3 below shows a detailed description of the clinical presentation of respondents. The majority (80.7%) of respondents presented with abdominal pain/swelling. More than half, (55.2%) of respondents had blood in stool/vomit, and one-quarter (25.5%) of respondents presented with diarrhoea/constipation. Fatigue was experienced among (88.3%) of respondents, and (27.6%) of respondents reported having insomnia/solemnness. Also, about (82.8%) of respondents presented with leg swelling. (44.8%) of respondents presented with jaundice.

Table 4. 2: The social history of respondents

Variable	Frequency	Percentage (%)
Tattoo/Body piercing (n=145)		
- Yes	10	6.9
- No	135	93.1
Currently drink alcohol (n=145)		
- Yes	51	35.2
- No	94	64.8
Number of drinks per day (n=51)		
- 1 – 3 drinks	23	45.1
- 4 – 6 drinks	24	47.1
- 7 drinks and above	4	7.84
Number of drinks per week (n=51)		
- 1 day	12	23.5
- 2 – 4 days	10	19.6
- 5 – 7 days	29	56.9
Type of alcohol (n=51)		
- Gin/spirit	30	58.8
- Beer	14	27.5
- Locally brewed wine (Pito)	2	3.9
- All types	5	9.8
When was your last drink? (n=94)		
- Never	39	41.5
- Less than 1 year	3	3.2
- More than 1 year	15	16
- Can't tell	37	39.4
Alcohol negatively influences your work or personal life (n=51)		
- Yes	23	45.1
- No	28	54.9

Table 4. 2: The social history of respondents continued

Ever tried to cut down on alcohol consumed (n=51)		
- Yes	34	66.7
- No	17	33.3
Ever felt angry when asked about drinking (n=47)		
- Yes	20	39.2
- No	31	60.8
Ever felt guilty about drinking (n=47)		
- Yes	31	60.8
- No	20	39.2
Ever had an eye-opener drink (n=51)		
- Yes	18	35.3
- No	33	64.7
Ever used drugs (Narcotics) (n=145)		
- Yes	6	4.14
- No	139	95.9
Ever snorted drugs		
- Yes	10	7.0
- No	135	93.1

4.3 The social history of respondents

Respondents' social history was assessed and presented in table 4.2 About three in every 10 respondents consumed alcohol at the time of enrolment (35.2%, n=51). Among respondents who took alcohol, more than half 29 (56.9%) took a drink at least 5 - 7 days per week. Only 6 (4.1%) respondents had a history of illicit drug use (narcotic drugs). Also, less than 10 (7.0%) of the study respondents snorted drugs, and 10 (6.9%) of respondents had tattoo/body piercing as detailed below.

Table 4. 3: Drug history of respondents

Variable	Frequency	Percentage (%)
Tattoo/Body piercing (n=145)		
- Yes	10	6.9
- No	135	93.1
Currently drink alcohol (n=145)		
- Yes	51	35.2
- No	94	64.8
Number of drinks per day (n=51)		
- 1 – 3 drinks	23	45.1
- 4 – 6 drinks	24	47.1
- 7 drinks and above	4	7.84
Number of drinks per week (n=51)		
- 1 day	12	23.5
- 2 – 4 days	10	19.6
- 5 – 7 days	29	56.9
Type of alcohol (n=51)		
- Gin/spirit	30	58.8
- Beer	14	27.5
- Locally brewed wine (Pito)	2	3.9
- All types	5	9.8
When was your last drink? (n=94)		
- Never	39	41.5
- Less than 1 year	3	3.2
- More than 1 year	15	16
- Can't tell	37	39.4
Alcohol negatively influences your work or personal life (n=51)		
- Yes	23	45.1
- No	28	54.9

Table 4. 3: Drug history of respondents continued

Ever tried to cut down on alcohol consumed (n=51)		
- Yes	34	66.7
- No	17	33.3
Ever felt angry when asked about drinking (n=47)		
- Yes	20	39.2
- No	31	60.8
Ever felt guilty about drinking (n=47)		
- Yes	31	60.8
- No	20	39.2
Ever had an eye-opener drink (n=51)		
- Yes	18	35.3
- No	33	64.7
Ever used drugs (Narcotics) (n=145)		
- Yes	6	4.14
- No	139	95.9
Ever snorted drugs		
- Yes	10	7.0
- No	135	93.1

4.4 Drug history of respondents

Table 4.3 below shows a detailed drug history of respondents. More than one-quarter, 11 (28.2%) respondents reported using birth control pills, and less than 5 per cent, 4 (2.8%) of all respondents had a history of using bodybuilding drugs. Only a few 2 (1.4%) respondents had a history of steroid use. About 60 (41%) of all respondents have used herbal drugs in previous years. Among respondents who used herbal medication, most of the respondent,56 (93.3%), preferred oral herbal preparation.

Table 4.4: History of liver disease

Variable	Frequency	Percentage (%)
Ever been diagnosed with liver disease(n=145)		
- Yes	119	82.1
- No	26	17.9
Type of liver disease as reported by patients (n=119)		
- Hepatitis B	81	68.1
- Hepatitis C	3	2.5
- Hepatitis B & C co-infection	28	23.5
- NAFLD	2	1.7
- AFLD	3	2.5
- Cannot tell	2	1.7

(*) NAFLD- Non-Alcoholic Fatty Liver Disease, AFLD-Alcoholic Fatty Liver Disease

4.5 History of liver disease

Overall, 119 (82.1%) of respondents had previously been diagnosed with liver disease. The majority, 81 (68.1%), were diagnosed with hepatitis b infection. Hepatitis b and c co-infection accounted for 28 (23.5%) of liver diseases. A few respondents had a history of non-alcoholic fatty liver disease, 2 (1.7%) and alcoholic fatty liver disease, and 3 (2.5%) with alcoholic fatty liver disease. Hepatitis c infection was previously diagnosed in 3 (2.5%) respondents. These are shown in Table 4.4 above.

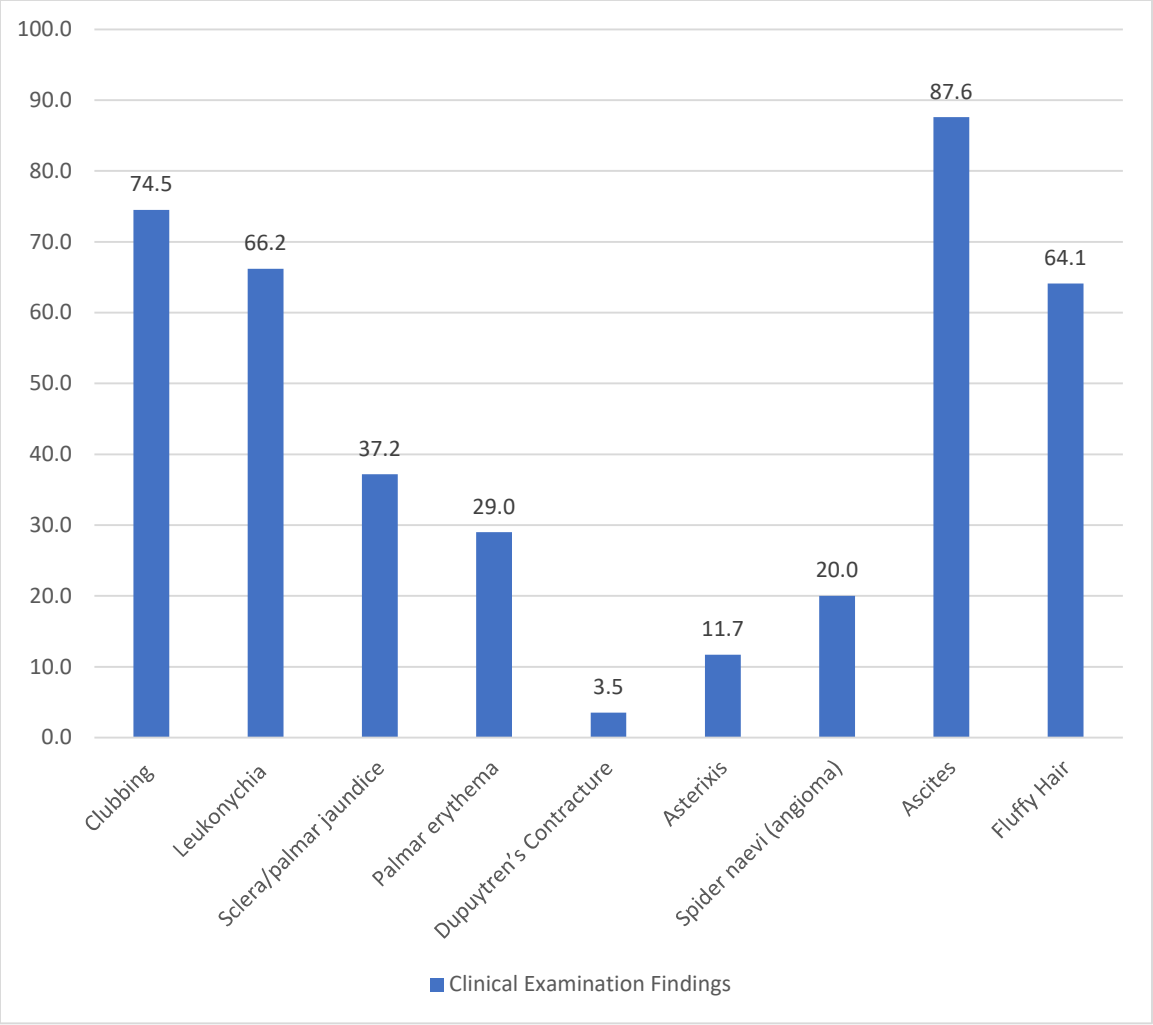

Figure 4. 4:Clinical examination findings

4.6 Examination findings

Figure 4.4 below shows a detailed description of the respondent's examination findings. Clubbing was observed in three-quarters of 74.5% of respondents, whereas more than half 66.2% of all respondents presented with Leukonychia. Sclera/palmar jaundice was observed in 37.2% of respondents. The majority, 87.6% of respondents presented with ascites while 64.1% of respondents had fluffy hair. Palmar erythema was observed in 29% of respondents. 11.7% and 3.5% of respondents presented with asterixis and Dupuytren's contracture respectively.

Table 4. 5 Disease severity

Variable	Frequency (n=145)	Percentage (%)
Ascites		
- None	20	13.8
- Small/diuretic controlled	87	60.0
- Tense	34	26.2
Hepatic encephalopathy		
- Absent	119	82.1
- Mild	24	16.6
- Significant	2	1.4

4.7 Disease severity

The severity of liver disease was assessed and presented in table 4.5 below. More than half 87 (60.0%) of respondents presented with small/diuretic-controlled ascites. tensed ascites were observed in one-quarter of 34(26.2%) of respondents, whereas 20 (13.8%) of respondents had no ascites. Majority of respondents 119(82.1%) had no overt hepatic encephalopathy, 24(16.1%) had mild and only 2 (1.4%) had significant Hepatic encephalopathy.

Table 4. 6: Laboratory investigation (n=145)

Variable	Frequency (n=145)	Percentage (%)
INR		
- <1.1	23	15.9
- >1.1	122	84.1
Albumin		
- Normal	10	6.9
- Low	155	93.1
Bilirubin		
- Normal	72	49.7
- High	73	50.3
Hepatitis B virus infection		
- Positive	109	75.2
- Negative	36	24.8
Hepatitis C Virus infection		
- Positive	30	20.7
- Negative	115	79.3
Haemoglobin		
- Normal	18	12.4
- **Low**	127	87.6
Platelet		
- Normal	37	25.5
- Low	108	74.5

(*) INR- International Normalised Ratio

4.8 Laboratory Investigation

Table 4.6 above shows a description of laboratory investigations. About three-quarters of respondents 109 (75.2%) tested positive for hepatitis B infection while 30 (20.7%) were positive for hepatitis C infection. Approximately 84.1% of respondents had INR greater than 1.1 and 15.9% of respondents had INR less than 1.1. Most of the respondents', 93.1%, had low albumin. 41 (50.3%) of. respondents had an elevated bilirubin level above 21 micrommoles per litre. Most of

the respondents' had had anaemia with haemoglobin levels less than 11g/dL while the majority 74.5% had low platelet count.

Table 4.7: Ultrasound findings (n=145)

Variable	Frequency (n=145)	Percentage (%)
Liver size		
- Average	64	44.1
- Enlarged	44	30.3
- Shrunken	37	25.5
Coarse liver echo pattern		
- Yes	133	91.7
- No	12	8.3
Bulbous edge (Cirrhosis)		
- Yes	141	97.2
- No	4	2.8
Portal vein dilatation		
- Yes	43	29.7
- No	102	70.3
Hepatic vein dilatation		
- Yes	13	9.0
- No	132	91.0
Splenic vein dilatation		
- Yes	4	2.8
- No	141	97.2
Spleen size		
- Average	70	48.3
- Enlarged	73	50.3
- Shrunken	2	1.38
Ascites		
- None	21	14.5
- Mild	29	20.0
- Moderate	30	20.7
- Marked (Gross)	16	11.0
- Tumour/masses	49	33.8

4.9: Ultrasound Findings

Table 4.7 below provides a summary of ultrasound findings among respondents. Shrunken liver was found in one-quarter 37 (25.5%) of respondents. Enlarged liver was observed in 44 (30.3%) of respondents, while 64 (44.1%) of respondents had an average liver size. Coarse liver echo patterns and bulbous edge liver was observed in the majority 133 (91.7%) and 141 (97.2%) respectively. Portal vein dilatation which is denoted by a diameter of more than 13 mm was observed in 43(29.7%) of respondents. 66 (50.0%) had an enlarged spleen. Hepatic vein dilatation denoted by a diameter of more than 6m m and splenic vein dilatation, with a diameter of more than 10mm was observed in 13 (9%) and 4 (2.8%) of respondents respectively. Ultrasound findings revealed tumour/masses in the background of liver cirrhosis in 49 (33.8%) of respondents. The majority of the respondents had clinically significant ascites 75(51.7%), most of whom were of the mild and moderate forms.

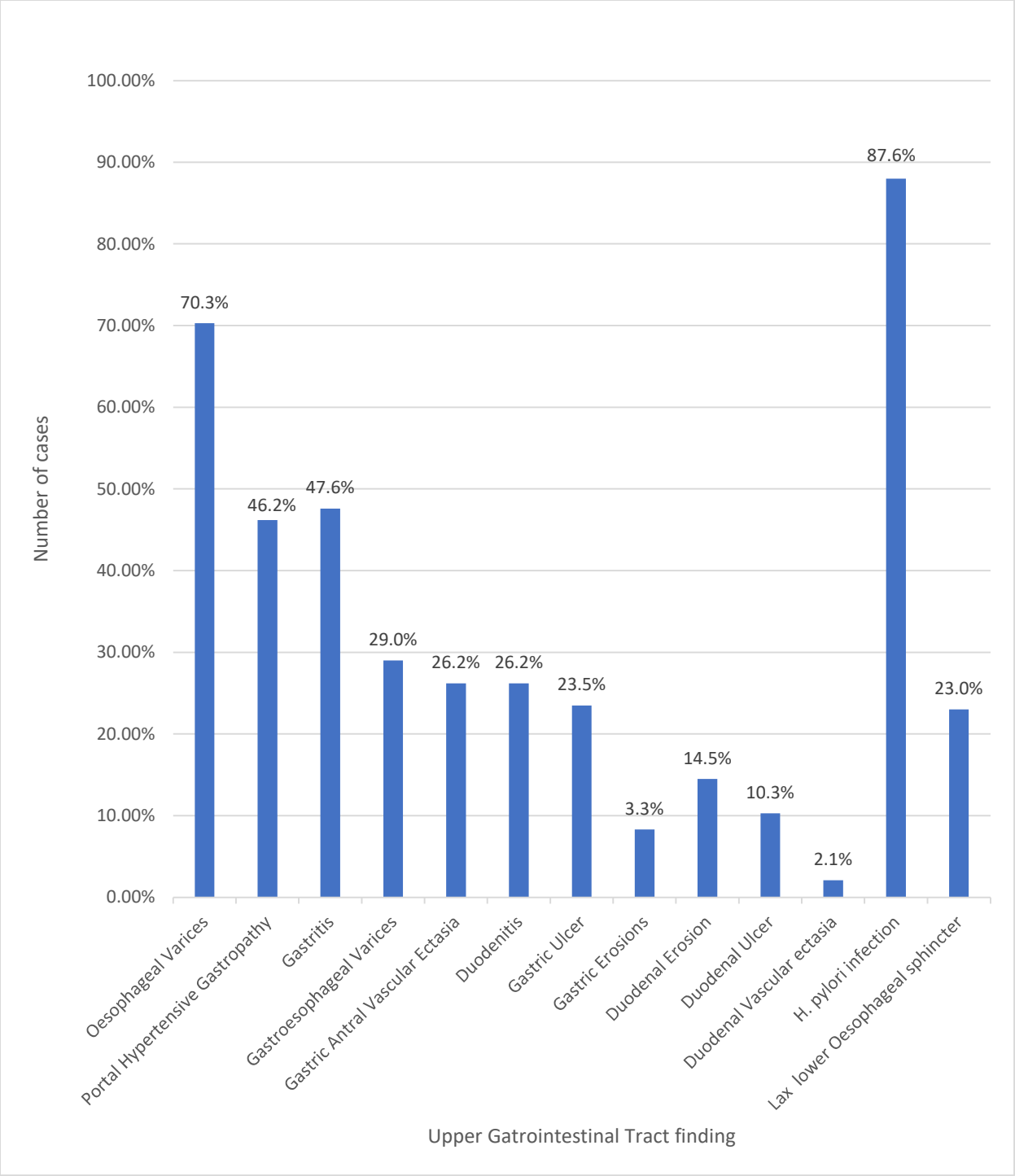

Figure 4. 5: Upper Gastrointestinal Tract findings in patients with Liver

4.10 Endoscopy Finding

Figure 4.5 below shows a detailed description of respondents' endoscopy finding esophageal varices were observed in 70.3%. 23.0% of respondents had lax oesophageal junction. 14.5% of respondents were found to have Gastroesophageal varices GOV-1 and GOV-2 were observed respectively. Gastric antral vascular ectasia (GAVE) was found in 26.2 % of the respondents when endoscopy of the stomach was assessed. Portal hypertensive gastropathy (PHG) was observed in 46.2% of respondents. Gastritis was seen in 46.2 % of all respondents, while 23.5% of respondents had stomach ulcers. Duodenum endoscopy showed that 14.5% of respondents had portal hypertensive duodenopathy. Duodenitis was reported in approximately one-quarter of 26.2% of the respondents. Duodenal ulcer and erosion were observed in 10.3% and 14.5% respectively, while duodenal vascular ectasia was observed in 2.1 % of respondents. The majority 87.6% tested positive for helicobacter pylori infection.

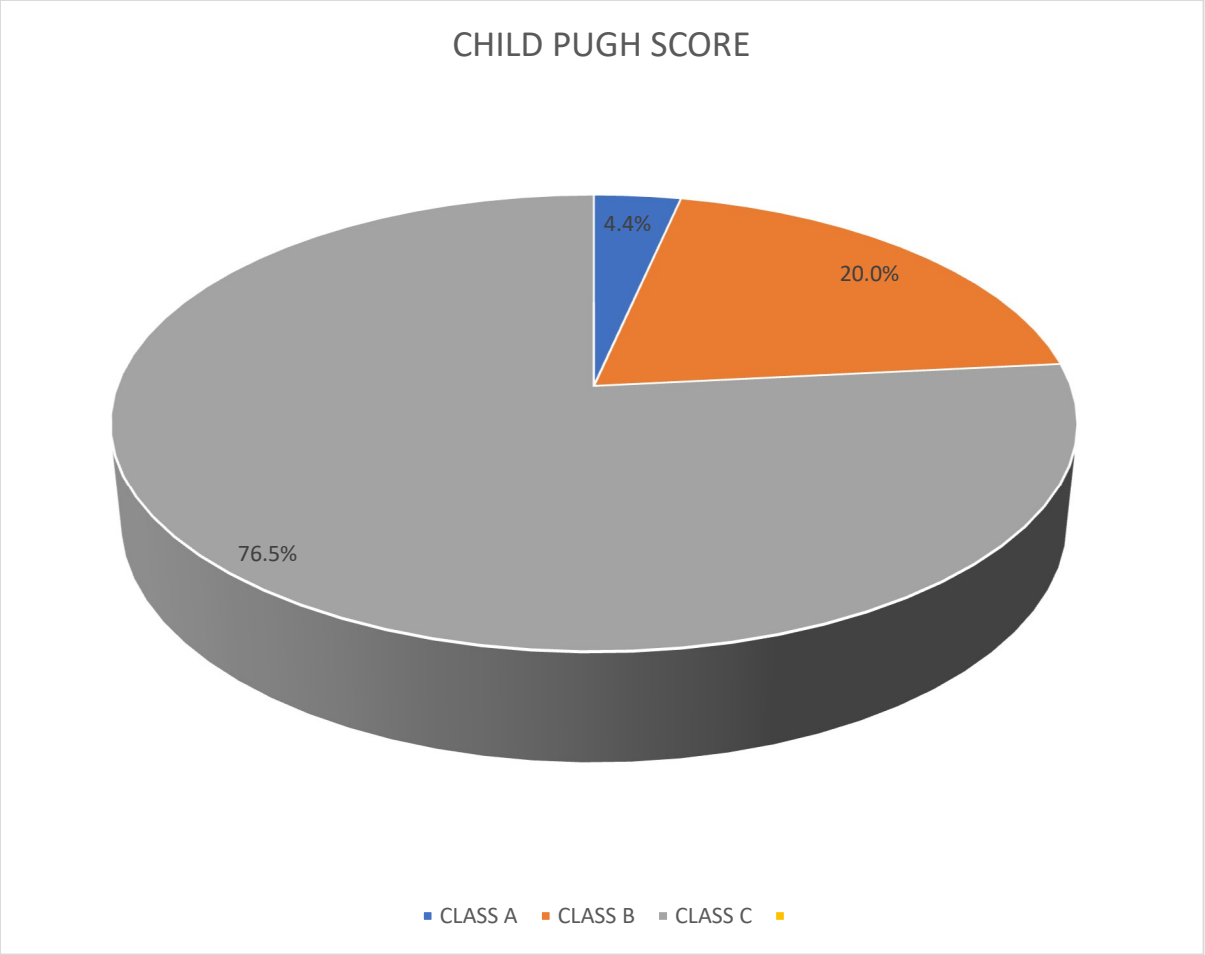

Figure 4. 6: Child-Turcotte-Pugh Score

Table 4.8: Relationship between socio-demographic characteristics and severity of the liver disease.

Variable	Child-Pugh Score			P-value
	Class A (%)	Class B (%)	Class C (%)	
Age				
- 20 – 40 years	3 (60.0)	9 (31.0)	36 (32.4)	
- 41 – 60 years	2 (40.0)	19 (65.5)	58 (52.3)	0.285
- 61 years and above	0 (0.0)	1 (3.5)	17 (15.3)	
Sex				
- Female	0 (0.0)	5 (17.2)	34 (30.6)	0.156
- Male	5 (100.0)	24 (82.8)	77 (69.4)	
Residence				
- Rural	1 (20.0)	14 (48.3)	46 (41.4)	0.523
- Urban	4 (80.0)	15 (51.7)	65 (58.6)	
Education				
- Primary	4 (80.0)	5 (17.2)	27 (24.3)	
- JHS/MSLC	0 (0.0)	3 (10.3)	15 (13.5)	
- Secondary/Vocation	0 (0.0)	12 (41.4)	28 (25.2)	
- Tertiary	1 (20.0)	4 (13.8)	14 (12.6)	0.184
- Post Tertiary	0 (0.0)	1 (3.7)	0 (0.0)	
- No formal education	0 (0.0)	5 (17.2)	27 (24.3)	
Occupation				
- Fully employed	1 (20.0)	12 (41.4)	31 (27.9)	
- Part time employed	0 (0.00)	2 (7.4)	3 (3.0)	
- Self employed	4 (80.0)	17 (58.6)	73 (65.8)	
- Student	0 (0.0)	0 (0.0)	2 (1.8)	0.823
- Retired	0 (0.0)	0 (0.0)	3 (2.7)	
- Unemployed	0 (0.0)	0 (0.0)	2 (1.8)	
Marital status				
- Married	4 (80.0)	20 (69.0)	78 (70.3)	0.869
- Single	1 (20.0)	4 (13.8)	13 (11.7)	
- Divorced	0 (0.0)	4 (13.8)	8 (7.2)	
- Co-habiting	0 (0.0)	0 (0.0)	3 (2.1)	
- Widow/widower	0 (0.0)	1 (3.5)	9 (8.1)	

(*) P-value less than 0.05

4.12. Relationship of socio-demographic characteristics and severity of the liver disease.

Respondents' socio-demographic characteristics and severity of liver disease were assessed and presented in table 4.8 below. When socio-demographic characteristics and severity of liver disease were compared, no significant association was observed.

Table 4.9: Respondents clinical information that influences the severity of liver disease

Variable	Child-Pugh score			P-value
	Class A (%)	Class B (%)	Class C (%)	
Abdominal pain/swelling				
- Yes	3 (60.0)	22 (75.9)	92 (82.9)	0.224
Blood in stool/vomit				
- Yes	1 (20.0)	16 (55.2)	63 (56.8)	0.323
			48 (43.2)	
Diarrhoea/Constipation				
- Yes	2 (40.0)	10 (34.5)	25 (22.5)	0.283
- No	3 (60.0)	19 (65.5)	86 (77.5)	
Fatigue				
- Yes	3 (60.0)	23 (79.3)	102 (91.9)	0.026*
- No	2 (40.0)	6 (20.7)	9 (8.1)	
Insomnia/Somnolence				
- Yes	3 (60.0)	9 (31.0)	28 (25.2)	0.206
- No	2 (40.0)	20 (69.0)	83 (74.8)	
Itching/Rash				
- Yes	2 (40.0)	3 (10.3)	39 (35.1)	0.016*
- No	3 (60.0)	26 (89.7)	72 (64.9)	
Jaundice				
- Yes	1 (20.0)	11 (37.9)	53 (47.8)	0.364
- No	4 (80.0)	18 (62.1)	58 (52.3)	

Table 4.9: Respondents clinical information that influences the severity of liver disease continued

Leg swelling				
- Yes	0 (0.0)	23 (79.3)	97 (87.4)	<0.001*
- No	5 (100.0)	6 (20.7)	14 (12.6)	
Tattoo/Scarification				
- Yes	1 (20.0)	7 (24.1)	23 (20.7)	0.917
- No	4 (80.0)	22 (75.9)	88 (79.3)	
Blood/Blood product transfusion				
- Yes	0 (0.0)	9 (31.0)	11 (9.9)	0.016*
- No	5 (100.0)	20 (69.0)	100 (90.1)	
Dyspepsia				
- Yes	2 (40.0)	12 (41.4)	42 (37.8)	0.941
- No	3 (60.0)	17 (58.6)	69 (62.2)	

(*) P-value less than 0.05

4.13 Respondents' Clinical characteristics influenced by the severity of liver cirrhosis.

Respondents' clinical characteristics that influence the severity of liver diseases were assessed and presented in table 4.9 below. The determining factors that were found to be influenced by disease severity were fatigue (p=0.026), itching or rash (p=0.016), leg swelling (p=<0.001) and blood product transfusion (p=0.016).

Table 4.10: Respondent Social history that influenced the severity of the liver disease

Variable	Child-Pugh score			P-value
	Class A (%)	Class B (%)	Class C (%)	
Tattoo/Body piercing	0 (0.0)	2 (6.9)	8 (7.2)	1.000
Currently drink alcohol				
- Yes	1 (20.0)	13 (44.8)	37 (33.3)	0.437
- No	4 (80.0)	16 (55.2)	74 (66.7)	
Ever used drugs				
- Yes	1 (20.0)	2 (6.9)	3 (2.7)	0.077
- No	4 (80.0)	27 (93.1)	108 (97.3)	
Ever snorted drugs				
- Yes	0 (0.0)	0 (0.0)	10 (9.0)	0.228
- No	5 (100.0)	29 (100.0)	101 (91.0)	

(*) P-value less than 0.05

4.14 Respondent Social history that influenced the severity of the liver disease.

Respondent's social history and severity of liver diseases were assessed and presented in table 4.10 below. When social history and severity of liver disease were compared, no significant association was observed.

Table 4.11 Respondent's drug history that influenced the severity of liver disease

Variable	Child-Pugh score			P-value
	Class A (%)	Class B (%)	Class C (%)	
- Birth control pills	0 (0.0)	1 (3.5)	10 (9.0)	0.638
- Bodybuilding drugs	0 (0.0)	0 (0.0)	4 (3.6)	0.636
- Steroid	0 (0.00)	0 (0.00)	0 (0.0)	1.000
- Herbal Preparation	1 (20.0)	12 (41.4)	47 (42.3)	0.710
Type of herbal medication used (n=56)				
- Oral	1 (100.0)	11 (91.7)	44 (93.6)	
- Topical	0 (0.0)	0 (0.0)	1 (2.1)	0.634
- Enema	0 (0.0)	1 (8.3)	2 (4.3)	
Frequency of use				
- Daily	0 (0.0)	2 (16.7)	1 (2.3)	0.147
- Intermittent	1 (100.0)	10 (83.3)	46 (97.9)	
Duration of used				
- 3 months	1 (100.0)	8 (66.7)	11 (23.4)	
- 6 months – year	0 (0.0)	0 (0.0)	8 (17.0)	0.019*
- For more than a year	0 (0.0)	4 (33.3)	28 (59.6)	

(*) P-value less than 0.05

4.16 Respondent's drug history that influenced the severity of liver disease

The respondent's drug history and severity of liver disease were assessed and presented in table 4.11 below. The determining factor that was found to influence disease severity was the duration of herbal medication use (p=0.019).

Table 4.12: History of risk factors for liver disease that influenced the severity of liver disease

Variable	Child-Pugh score			P-value
	Class A (%)	Class B (%)	Class (%)	
Ever been diagnosed with liver disease	4 (80.0)	21 (72.4)	94 (84.7)	0.222
Type of liver disease (n=110)				
- Hepatitis B	3 (75.0)	15 (71.5)	63 (67.0)	
- Hepatitis C	0 (00.0)	2 (9.5)	1 (1.1)	
- Hepatitis B&C co-infection	1 (25.0)	2 (9.5)	25 (26.6)	
- NAFLD				
- AFLD/chronic alcohol	0 (00.0)	0 (0.0)	2 (2.1)	0.073
- Can't tell	0 (0.0)	0 (0.0)	3 (3.2)	
	0 (00.0)	2 (9.5)	0 (0.0)	
Lifetime sexual partners				
- Less than 10 partners	5 (100.0)	25 (86.2)	75 (67.6)	
- 10 – 20 partners	0 (0.0)	4 (13.8)	25 (22.5)	
- 21 – 50 partners	0 (0.0)	0 (0.0)	9 (8.1)	0.380
- More than 50 partners	0 (0.0)	0 (0.0)	2 (1.8)	

4.17 History of risk factors for liver disease that influences the severity of liver disease

Respondents' history of risk factors for liver diseases that influence the severity of liver disease was assessed and presented in table 4.12 below. When the history of liver disease and severity of liver disease was compared, no significant association was observed.

Table 4. 13: Examination findings that influence the severity of liver cirrhosis.

Variable	Child-Pugh score			P-value
	Class A(%)	Class B (%)	Class C (%)	
Clubbing	0 (0.0)	17 (58.6)	91 (82.0)	<0.000*
Leukonychia	0 (0.0)	16 (55.2)	80 (72.1)	0.002*
Sclera/palmar jaundice	1 (20.0)	9 (31.0)	44 (39.6)	0.611
Palmar erythema	0 (0.00)	5 (17.2)	37 (33.3)	0.092
Dupuytren's Contracture	0 (0.0)	0 (0.0)	5 (4.5)	0.651
Asterixis	0 (0.0)	3 (10.3)	14 (12.6)	1.000
Spider naevi (angioma)	0 (0.0)	2 (6.9)	27 (24.3)	0.060
Ascites	2 (40.0)	17 (58.6)	108 (97.3)	<0.000*
Silky Hair	0 (0.0)	14 (48.3)	79 (71.2)	<0.000*

(*) P-value less than 0.05

4.18 Examination findings that influence the severity of liver cirrhosis.

Examination findings that influence the severity of liver disease were assessed and presented in table 4.13 below. The determining factors that were found to be influenced by the severity of liver disease were clubbing (p= <0.001), leukonychia (p= 0.001), ascites (p=<0.002) and silky hair (p=0.001).

Table 4.14: Clinical symptoms/signs that are influenced by the severity of liver cirrhosis.

Variable	Child-Pugh score			P-value
	Class A (%)	Class B (%)	Class C (%)	
Ascites				
- None	3 (60.0)	13 (44.8)	4 (3.6)	
- Small/diuretic	2 (40.0)	12 (41.4)	73 (65.7)	0.001
controlled	0 (0.0)	4 (13.8)	34 (30.6)	
- Tense				
Hepatic encephalopathy				
- Absent	5 (100.0)	26 (89.6)	88 (79.3)	
- Mild	0 (0.0)	2 (6.9)	22 (19.8)	
- Significant	0 (0.0)	1 (3.45)	1 (0.9)	0.225

(*) P-value less than 0.05

4.19 Clinical symptoms/signs that are influenced by the severity of liver cirrhosis.

Clinical symptoms/signs that influence the severity of liver cirrhosis were assessed and presented in table 4.14 below. The determining factor that was found to be influenced by the severity of the liver cirrhosis was ascites (p=<0.001)

Table 4.15; Ultrasound findings that influence the severity of liver cirrhosis.

Variable	Child-Pugh score			P-value
	Class A (%)	Class B (%)	Class C (%)	
Liver size				
- Average	4 (80.0)	16 (55.2)	44 (39.6)	0.326
- Enlarged	1 (20.0)	7 (24.1)	36 (32.4)	
- Shrunken	0 (0.0)	6 (20.7)	31 (27.8)	
Coarse liver echo pattern	4 (80.0)	22 (75.9)	107 (96.4)	<0.001*
Bulbous edge (Cirrhosis)	4 (80.0)	27 (93.10)	110 (99.1)	0.021*
Portal vein dilatation	0 (0.00)	8 (25.6)	35 (31.5)	0.408
Hepatic vein dilatation	0 (0.00)	4 (13.8)	9 (8.1)	0.671
Splenic vein dilatation	0 (0.00)	2 (6.9)	2 (1.8)	0.297
Spleen size				
- Average	5 (100.00)	12 (41.4)	53 (47.8)	0.143
- Enlarged	0 (0.00)	17 (58.6)	56 (50.5)	
- Shrunken	0 (0.00)	0 (0.00)	2 (1.8)	
Ascites				
- None	4 (80.0)	9 (31.0)	8 (7.2)	<0.001
- Mild	0 (0.00)	7 (24.1)	22 (19.8)	
- Moderate	0 (0.00)	4 (13.8)	26 (23.4)	
- Marked (Gross)	0 (0.00)	2 (6.9)	14 (12.6)	

(*) P-value less than 0.05

4.20 Ultrasound findings that were influenced by the severity of liver cirrhosis.

Respondent's ultrasound findings that were influenced by the severity of liver disease were assessed and presented in table 4.15 below. The determining factors that were found to be influenced by the severity of liver disease were coarse liver echo patterns (p= <0.001), bulbous edge (p=0.021) and ascites (p=<0.001).

Table 4.16 Endoscopy findings influenced by the severity of liver cirrhosis

Variable	Child-Pugh score			P-value
	Class A (%)	Class B (%)	Class C (%)	
Oesophageal varices				
- Small	1 (20.0)	5 (11.2)	11 (9.9)	
- Medium	0 (0.0)	5 (17.2)	39 (35.1)	
- Large	1 (20.0)	4 (13.8)	35 (31.5)	0.009*
- Large	0 (0.0)	0 (0.0)	1 (0.9)	
Lax Gastroesophageal Sphincter	4 (80.0)	9 (31.0)	2(20.7)	0.012*
Gastroesophageal varices (GOV-1)	0 (0.0)	2 (6.9)	3 (2.7)	
Gastroesophageal varices (GOV-2)	0 (0.0)	3 (10.3)	1(0.9)	0.066
Gastric antral vascular ectasia	0 (0.0)	4 (13.8)	34 (30.6)	0.088
Portal hypertensive gastropathy	1 (20.0)	12 (41.4)	54 (48.7)	0.441
Gastritis	2 (40.0)	15 (51.7)	52 (46.9)	0.894
Gastric erosions	0 (100.0)	3 (10.3)	9 (8.1)	0.815
Gastric ulcer	0 (100.0)	7 (24.1)	27 (24.3)	0.725
Isolated Gastric varices (IGV-1)	0 (0.0)	2 (6.9)	3 (2.7)	
Isolated Gastric varices (IGV-2)	0 (0.0)	3 (10.3)	1(0.9)	0.066
Portal Hypertensive Duodenopathy	0 (0.0)	5 (17.2)	16 (14.4)	0.896
Duodenal vascular Ectasia	0 (0.0)	0 (0.0)	3 (2.7)	1.000
Duodenal Erosion	0 (0.0)	3 (10.3)	18 (16.2)	0.711
Duodenitis	0 (0.0)	4 (13.8)	34 (30.6)	0.088
Duodenal Ulcer	0 (0.0)	2 (6.9)	13 (11.7)	0.849
H. pylori Infection	4 (80.0)	25 (86.2)	98 (88.3)	0.669

(*) P-value less than 0.05

4.21 Endoscopy findings influenced by the severity of liver cirrhosis

Respondents' endoscopy findings that were influenced by the severity of liver disease were assessed and presented in table 4.16 below. The determining factors that were found to be influenced by the severity of liver disease were Lax Gastroesophageal sphincter (p= 0.012) and Oesophageal varices (p=0.009)

Table 4.17: Multivariate logistic regression model for factors that influence the severity of liver cirrhosis

Variable	Number of respondents (%) of the total in every group)	OR (95% CI)	P-value	aOR (95% CI)	P-value
Fatigue	128 (88.3)	3.7 (1.3 – 10.4)	0.013	1.9 (0.4 – 8.3)	0.395
Itching/Rash	44 (30.3)	3.0 (1.1 – 8.3)	0.037	3. 4 (0.8 – 14.4)	0.094
Leg swelling	120 (82.8)	4.3 (1.7 – 10.9)	0.002	1.3 (0.2 – 6.5)	0.774
Blood/Blood product transfusion	20 (13.8)	0.4 (0.1 – 0.9)	0.032	0.3 (0.1 – 1.2)	0.774
Clubbing	108 (74.5)	5.2 (2.2 – 11.8)	<0.001	7.7 (1.2 - 49.8)	0.032
Leukonychia	96 (66.2)	3.2 (1.4 – 7.0)	0.004	0.2 (0.0 - 1.5)	0.102
Ascites	127 (87.6)	23.1 (7.3 -72.8)	<0.000	3.7 (0.1- 121.6)	0.469
Fluffy Hair	93 (64.1)	3.8 (1.7 – 8.4)	0.001	1.3 (0.3- 5.2)	0.69
Ascites					
- Small/diuretic controlled	20 (13.8)	17.6 (5.8 – 53.7) 2	<0.001	2.7 (0.1 – 89.9)	0.575
- Tense	87 (60.0)	9.3 (7.14 -1204)	<0.001	3.2 (0.1 – 129.8)	0.536
- None	34 (16.2)	1			
Oesophageal varices					
- Grade 1	17 (11.7)	1.3 (0.4 – 4.1)	0.645	1.1 (0.2 – 6.2)	0.943
- Grade 2	44 (30.3)	5.7 (1.9 – 17.3)	0.002	1.7 (0.4 – 8.2)	0.513
- Grade 3	40 (27.6)	5.0 (1.6 -15.2)	0.005	2.2 (0.5 – 10.1)	0.329
- Grade 4	1 (0.7)	-	-	-	-
Coarse liver echo pattern	133 (91.7)	6.8 (2.2 – 21.2)	0.001	1.8 (0.3 – 12.9)	0.550
Bulbous edge	141 (97.0)	11.0 (1.6 -77.1)	0.016	12.5(0.8– 200.7)	0.071
Ascites					
- Mild	29 (20.0)	13. 5 (2.4 – 75.7)	0.003	2.1 (0.1 – 25.0	0.545
- Moderate	30 (20.7)	6.2 (1.8 – 20.9)	0.003	1.5 (0.3 – 8.7	0.649
- Marked (Gross)	16 (11.0)	12.6 (3.2 – 49 -5)	<0.001	1.5 (0.2 – 10.7	0.706
- Tumour/masses	49 (33.8)	9.7 (3.1 – 31.0)	<0.001	1.1 (0.2 – 6.1)	0.897
Lax (LES)	36 (24.8)	0.023 (0.17 – 0)	0.023	0.6 (1.2 – 2.2)	0.453

(*) P-value less than 0.05, OR-Crude Odds Ratio, aOR- Adjusted Odds Ratio, CI- Confidence Interval

4.22 Multivariate logistic regression model for factors that influence the severity of liver cirrhosis

Ordinal regression analysis of factors that could be influenced by the severity of liver cirrhosis was done and reported in table 4.17 below.

All variables with a p-value <0.05 in the chi-square analysis between the severity of liver disease and its determining factors were added to the ordinal regression model. To test for association. It was further adjusted with all variables that could be influenced by the severity of liver cirrhosis to address confounders.

The risk of patients who experienced fatigue was 3 times higher among patients with severe liver cirrhosis (OR=3.7, 95% CI=1.3 – 10.4, p=0.013) compared to those with mild and moderate liver cirrhosis. Itching/rashes were 3 times more likely found in patients with severe liver disease (OR=3.0, 95% CI=1.1 – 8.3, p=0.037). The risk of developing leg swelling was increased by 4 folds among patients with severe liver disease (OR=4.3, 95% CI=0.2 – 6.5, p=0.002). Finger Clubbing was 5 times more likely to develop in respondents with severe liver disease (OR=5.2, 95% CI=2.2 - 11.8, p=0.001). Leukonychia was 3 times more likely to develop in patients with severe liver disease (OR=3.2, 95% CI=1.4 – 7.0, p=0.004). The of risk developing ascites increased by 23 folds in respondents who had severe liver disease (OR=23.1, 95% CI=0.1 – 121.6, p=,0.001). The risk of developing silky hair was 4 times higher in respondents with severe liver disease (OR=3.8, 95% CI=1.7 – 8.4, p=0.001). The risk of respondents with oesophageal varices grade II and III increased by more than 5 folds in patients with severe liver disease, (95% CI=1.9–17.3, p=0.002) and (OR=5.0, 95% CI=1.6 – 15.2, p=0.005). Also, respondents with severe liver disease were 6 times more likely to develop a coarse liver echo pattern (OR=6.8, 95% CI=2.2 – 21.2, p=0.001) while increasing the risk of having a liver with a bulbous edge by 11 folds (OR=11.0, 95% CI=1.6 – 77.1, p=0.016). Adjusting for other variables, respondents with severe liver cirrhosis were 8 times more likely to develop clubbing (OR=7.8, 95% CI=1.2 – 49.8).

Table 4.18: Correlation between clubbing and endoscopy findings

Variable	Clubbing		χ 2	P-value
	Yes (%)	No (%)		
Esophageal varices	86 (83.5)	17 (16.5)	15.2	<0.001
Lax Lower Esophageal Sphincter	20 (55.6)	16 (44.4)	9.0	0.004
Gastroesophageal varices				
- Gastroesophageal varices (GOV-1)	18 (85.7)	3 (14.3)	5.9	0.053
- Gastroesophageal varices (GOV-2)	19 (90.5)	2 (9.5)		
Gastric antral vascular ectasia (GAVE)	75 (70.1)	32 (29.9)	4.1	0.042
Portal hypertensive gastropathy (PHG)	56 (83.6)	11 (16.4)	5.4	0.020
Gastritis	50 (72.5)	19 (27.5)	0.3	0.703
Gastric erosions	2 (16.7)	10 (83.3)	23.0	<0.001
Gastric ulcer	33 (97.1)	1 (2.9)	11.9	<0.001
Isolated gastric varices (IGV-1)	4 (80.0)	1 (20.0)	0.1	1.000
Isolated gastric varices (IGV-2)	3 (75.00)	1(25.0)		
Portal Hypertensive Duodenopathy	12 (57.1)	9 (42.9)	3.9	0.049
Duodenal vascular Ectasia	2 (66.7)	1 (33.3)	0.1	0.754
Duodenal Erosion	15 (71.4)	6 (28.6)	0.1	0.728
Duodenitis	7 (18.4)	31 (81.6)	1.4	0.243
Duodenal Ulcer	9 (60.0)	6 (40.0)	1.8	0.174
Helicobacter pylori positive	95 (74.8)	32 (25.2)	0.1	8.814

(*) P-value less than 0.05

4.23 Correlation between clubbing and endoscopy findings

Table below shows a detailed description of clinical characteristics that influence endoscopy finding of cirrhosis patients. When clubbing was correlated with endoscopy findings a significant statistical association was observed in patients with esophageal varices ($\chi 2$ =15.2, p=<0.001), lax lower esophageal sphincter ($\chi 2$ =9.0, p=<0.004), gastroesophageal varices ($\chi 2$ =5.9, p=<0.053), Gastric antral vascular ectasia ($\chi 2$ =4.1, p=<0.042), portal hypertensive gastropathy ($\chi 2$ =5.4, p=<0.020), gastric erosion ($\chi 2$ =23.0p=<0.001), gastric ulcer ($\chi 2$ =11.9, p=<0.001) portal hypertensive gastropathy ($\chi 2$ =0.1, p=8.814) and portal hypertensive duodenopathy ($\chi 2$ =3.9, p=<0.049)

Table 4.19: correlation between Leukonychia and endoscopy findings

Variable	Leukonychia		χ 2	P-value
	Yes (%)	No (%)		
Esophageal varices	15 (35.7)	27 (64.3)	24.6	<0.001
Lax Lower oesophageal Sphincter	82 (75.2)	27 (24.8)	16.0	<1.001
Gastroesophageal junction				
- Gastroesophageal varices (GOV-1)	17 (81.0)	4 (19.1)	10.5	0.005
- Gastroesophageal varices (GOV-2)	19 (90.5)	2 (90.5)		
Gastric antral vascular ectasia (GAVE)	29 (76.3)	9 (23.7)	2.4	0.125
Portal hypertensive gastropathy (PHG)	53 (79.10)	14 (20.90)	9.3	0.002
Gastritis	42 (60.87)	27 (39.13)	1.7	0.195
Gastric erosions	2 (16.7)	10 (83.3)	14.4	<0.001
Gastric ulcer	32 (94.1)	2 (5.9)	15.5	<0.001
Isolated gastric varices (IGV-1)	4 (80.0)	1 (20.0)	0.6	0.741
Isolated gastric varices (IGV-2)	3 (75.0)	1 (25.0)		
Portal Hypertensive Duodenopathy	10 (47.62)	11 (52.38)	3.8	0.051

Table 4.19: correlation between Leukonychia and endoscopy findings continued

Duodenal vascular Ectasia	1 (33.3)	2 (66.7)	1.5	0.224
Duodenal Erosion	12 (57.1)	9 (42.9)	0.9	0.342
Duodenitis	29 (76.30	9 (23.7)	2.4	0.125
Duodenal Ulcer	9 (60.0)	6 (40.0)	0.3	0.591
Helicobacter pylori positive	86 (67.7)	41 (32.3)	1.0	0.307

(*) P-value less than 0.05

4.24 Correlation between Leukonychia and endoscopy findings

When leukonychia was correlated with endoscopy findings a significant statistical association was observed in patients with esophageal varices, ($\chi2$= 24.6, p=<0.001), Lax lower esophageal sphincter($\chi2$=16.0,p=<0.001),gastroesophageal varices,($\chi2$= 10.5, p=<0.005), Portal hypertensive gastropathy ($\chi2$= 9.3, p=<0.002), gastric erosion ($\chi2$= 14.4, p=<0.001), gastric ulcer ($\chi2$= 15.5, p=<0.001), and portal hypertensive duodenopathy ($\chi2$= 3.8,
p=<0.051).

Table 4.20: Correlation between Sclera jaundice and endoscopy findings

Variable	Sclera		χ 2	P-value
	Yes (%)	No (%)		
Esophageal varices	**18(42.9)**	**24(57.1)**	**0.8**	**0.372**
Lax Lower Esophageal Sphincter	17(47.2)	19(52.8)	2.0	0.153
Gastroesophageal junction				
- Gastroesophageal varices (GOV-1)	8(38.1)	13(61.9)	0.8	0.672
- Gastroesophageal varices (GOV-2)	6(28.6)	15(71.4)		
Gastric antral vascular ectasia (GAVE)	17(44.7)	21(55.3)	1.2	0.266
Portal hypertensive gastropathy (PHG)	24(35.8)	43(64.2)	0.1	0.743
Gastritis	23(33.3)	46(66.7)	0.9	0.354
Gastric erosions	4(33.3)	8(66.7)	0.1	0.770
Gastric ulcer	2(5.9)	32(94.1)	18.7	<0.001
Isolated gastric varices (IGV-1)	2(40.0)	3(60.0)	0.3	0.871
Isolated gastric varices (IGV-2)	1(25.0)	3(75.0)		
Portal Hypertensive Duodenopathy	9(42.9)	12(57.1)	0.3	0.565
Duodenal vascular Ectasia	1(33.3)	2(66.7)	0.0	0.887
Duodenal Erosion	6.(28.6)	15(71.4)	0.8	0.374
Duodenitis	8(21.1)	30(78.9)	5.8	0.016
Duodenal Ulcer	6(40.0)	9(60.0)	0.1	0.815
Helicobacter pylori positive	43(33.9)	84(66.1)	5.0	0.025

(*) P-value less than 0.05

4.25 Correlation between Sclera jaundice and endoscopy findings

When sclera jaundice was correlated with endoscopy findings, a significant association was observed among subjects with gastric ulcer ($\chi 2$= 18.7, p=<0.001), Duodenitis ($\chi 2$= 5.8, p=<0.016), and helicobacter pylori infection ($\chi 2$= 5.0, p=<0.025)

Table 4.21: Correlation between Palmer erythema and endoscopy findings

Variable	Palmar erythema		χ 2	P-value
	Yes (%)	No (%)		
Esophageal varices	4(9.5)	38(90.5)	10.9	<0.001
Lax Lower Esophageal Sphincter	1(2.8)	35(97.2)	15.9	<0.001
Gastroesophageal junction				
- Gastroesophageal varices (GOV-1)	8(38.1)	13(61.9)	0.8	0.672
- Gastroesophageal varices (GOV-2)	6(28.6)	15(71.4)		
Gastric antral vascular ectasia (GAVE)	17(44.7)	21(55.3)	1.2	0.266
Portal hypertensive gastropathy (PHG)	24(35.8)	43(64.2)	0.1	0.743
Gastritis	23(33.3)	46(66.7)	0.9	0.354
Gastric erosions	4(33.3)	8(66.7)	0.1	0.770
Gastric ulcer	2(5.9)	32(94.1)	18.7	<0.001
Isolated gastric varices (IGV-1)	2(40.0)	3(60.0)	0.3	0.871
Isolated gastric varices (IGV-2)	1(25.0)	3(75.0)		
Portal Hypertensive Duodenopathy	9(42.9)	12(57.1)	0.3	0.565
Duodenal vascular Ectasia	1(33.3)	2(66.7)	0.0	0.887
Duodenal Erosion	6(28.6)	15(71.4)	0.8	0.374
Duodenitis	8(21.1)	30(78.9)	5.8	0.016
Duodenal Ulcer	6(40.0)	9(60.0)	0.1	0.815
Helicobacter pylori positive	43(33.9)	84(66.1)	5.0	0.025

(*) P-value less than 0.05

4.26 Correlation between Palmer erythema and endoscopy findings

When palmer erythema was correlated with endoscopy findings, a significant association was observed among patients with Oesophageal varices ($\chi 2$= 10.0, p=<0.0001), Lax Lower Oesophageal Sphincter ($\chi 2$= 15.9, p=<0.0001), gastric ulcer ($\chi 2$= 18.7, p=<0.0001), duodenitis ($\chi 2$= 5.8, p=0.016) and helicobacter pylori positive ($\chi 2$= 5.0, p=<0.025),

Table 4.22: Correlation between Dupuytren's Contracture and endoscopy findings

Variable	Dupuytren's Contracture		χ 2	P-value
	Yes (%)	No (%)		
Esophageal varices	0 (0.0)	42 (100.0)	2.1	0.146
Lax Lower Esophageal Sphincter	0 (0.0)	36 (100.0)	1.7	0.191
Gastroesophageal junction				
- Gastroesophageal varices (GOV-1)	1 (4.8)	20 (95.2)	9.4	0.009
- Gastroesophageal varices (GOV-2)	3 (14.3)	18 (85.7)		
Gastric antral vascular ectasia (GAVE)	2 (5.3)	36 (94.8))	0.5	0.475
Portal hypertensive gastropathy (PHG)	4 (6.0)	63 (94.0)	2.4	0.123
Gastritis	1 (1.5)	68 (98.6)	1.6	0.209
Gastric erosions	0 (0.0)	12 (100.0)	0.5	0.494
Gastric ulcer	1 (2.9)	33 (97.10	0.0	0.853
Isolated gastric varices (IGV-1)	0 (0.0)	5 (100.0)	0.3	0.843
Isolated gastric varices (IGV-2)	0 (0.0)	4 (100.0)		
Portal Hypertensive Duodenopathy	0 (0.0)	21 (100.0)	0.9	0.349
Duodenal vascular Ectasia	0 (0.0)	3 (100.0)	0.1	0.741
Duodenal Erosion	0 (0.0)	21 (100.0)	0.9	0.349
Duodenitis	1 (2.6)	37 (97.3)	0.1	0.748
Duodenal Ulcer	1 (6.7)	14 (93.3)	0.5	0.471
Helicobacter pylori positive	3 (3.4)	124 (97.6)	2.6	0.057

(*) P-value less than 0.05

4.27 Correlation between Dupuytren's Contracture and endoscopy findings

When Dupuytren's contracture was correlated with endoscopic findings, a significant association was observed among patients with Gastroesophageal varices ($\chi 2 = 9.4$, $p = <0.009$),

Table 4.23: Correlation between Asterixis and endoscopy findings

Variable	Asterixis		χ 2	P-value
	Yes (%)	No (%)		
Esophageal varices	7 (16.7)	35 983.3)	1.4	0.237
Lax Lower Esophageal Sphincter	5 (13.9)	97 (86.1)	0.2	0.641
Gastroesophageal junction				
- Gastroesophageal varices (GOV-1)	3 (14.3)	18 (85.7)	0.2	0.891
- Gastroesophageal varices (GOV-2)	2 (9.5)	19 (90.5)		
Gastric antral vascular ectasia (GAVE)	8 (21.1)	30 (79.0)	4.3	0.037
Portal hypertensive gastropathy (PHG)	8 (11.9)	59 (88.1)	0.0	0.940
Gastritis	5 (7.3)	64 (92.8)	2.6	0.110
Gastric erosions	3 (25.0)	9 (75.0)	2.2	0.136
Gastric ulcer	0 (0.0)	34 (100.0)	5.9	0.015
Isolated gastric varices (IGV-1)	0 (0.0)	5 (100.0)	1.3	0.529
Isolated gastric varices (IGV-2)	0 (0.0)	4 (100.0)		
Portal Hypertensive Duodenopathy	6 (28.6)	15 (71.4)	6.7	0.009
Duodenal vascular Ectasia	0 (0.0)	3 (100.0)	0.4	0.524
Duodenal Erosion	3 (14.3)	18 (85.7)	0.2	0.693
Duodenitis	3 (7.9)	35 (92.1)	0.7	0.393
Duodenal Ulcer	3 (20.0)	12 (80.0)	1.1	0.293
Helicobacter pylori positive	12 (9.5)	115 (90.5)	5.1	0.024

(*) P-value less than 0.05

4.28 Correlation between Asterixis and endoscopy findings

When clinical presentation asterixis was correlated with endoscopy findings, a significant association was observed among patients with Gastric antral vascular ectasia ($\chi2$= 4.3, p=0.037), gastric ulcer ($\chi2$= 5.9, p=0.015), portal hypertensive duodenopathy ($\chi2$= 6.7, p=<0.009) and Helicobacter pylori infection. ($\chi2$= 5.1, p=<0.024)

Table 4.24: Correlation between Spider naevi (angioma) and endoscopy findings

Variable	Angioma		χ 2	P-value
	Yes (%)	No (%)		
Esophageal varices	2(4.8)	40(95.2)	8.6	0.003*
Lax Lower Esophageal Sphincter	1(2.8)	35(97.2)	8.9	0.003*
Gastroesophageal junction				
- Gastroesophageal varices (GOV-1)	8(38.1)	13(61.9)	9.3	0.010*
- Gastroesophageal varices (GOV-2)	7(33.3)	14(66.7)		
Gastric antral vascular ectasia (GAVE)	12(31.6)	26(68.4)	4.3	0.038*
Portal hypertensive gastropathy (PHG)	18(26.9)	49(73.1)	3.7	0.055*
Gastritis	9(13.0)	60(87.0)	3.9	0.046
Gastric erosions	0(0.0)	12(100.0)	3.3	0.071
Gastric ulcer	6(17.7)	28(82.3)	0.2	0.695
Isolated gastric varices (IGV-1)	1(20.0)	4(80.0)	1.0	0.598
Isolated gastric varices (IGV-2)	0(0.0)	4(100.0)		
Portal Hypertensive Duodenopathy	5(23.8)	16(76.2)	0.2	0.637
Duodenal vascular Ectasia	1(33.3)	2(66.7)	0.3	0.560
Duodenal Erosion	1(4.8)	20(95.2)	3.6	0.059
Duodenitis	7(18.4)	31(81.6)	0.1	0.777
Duodenal Ulcer	1(6.7)	14(93.3)	1.9	0.173
Helicobacter pylori positive	21(16.5)	106(83.5)	7.7	0.006*

(*) P-value less than 0.05

4.29 Correlation between Spider naevi (angioma) and endoscopy findings

When clinical finding spider naevi (angioma) was correlated with endoscopy findings, a significant association was observed among patients with esophageal varices ($\chi2$= 8.6, p=<0.003), Lax Lower Esophageal Sphincter ($\chi2$= 8.9, p=<0.003) Gastroesophageal varices ($\chi2$= 9.3, p=0.010), gastritis ($\chi2$= 3.9, p=<0.046) and Helicobacter pylori infection ($\chi2$= 7.7, p=<0.006),

Table 4.25: Correlation between Ascites and endoscopy findings

Variable	Ascites		χ 2	P-value
	Yes (%)	No (%)		
Esophageal varices	33(78.6)	9(21.4)	4.4	0.036*
Lax Lower Esophageal Sphincter	26(72.2)	10(27.8)	10.4	0.001*
Gastroesophageal junction				
- Gastroesophageal varices (GOV-1)	21(100.0)	0(0.0)	5.7	0.058
- Gastroesophageal varices (GOV-2)	20(95.2)	1(4.8)		
Gastric antral vascular ectasia (GAVE)	36(95.7)	2(5.3)	2.4	0.120
Portal hypertensive gastropathy (PHG)	62(92.5)	5(7.5)	2.8	0.094
Gastritis	57(82.6)	12(17.4)	2.9	0.083
Gastric erosions	8(66.7)	4(33.3)	5.3	0.022*
Gastric lcer	30(88.2)	4(11.8)	0.0	0.896
Isolated gastric varices (IGV-1)	4(80.0)	1(20.0)	0.8	0.660
Isolated gastric varices (IGV-2)	4(100.0)	0(0.0)		
Portal Hypertensive Duodenopathy	17(80.9)	4(19.1)	0.9	0.319
Duodenal vascular Ectasia	3(100.0)	0(0.0)	0.4	0.510
Duodenal Erosion	18(85.7)	3(14.3)	0.1	0.778
Duodenitis	36(94.7)	2(5.3)	2.4	0.120
Duodenal Ulcer	14(93.3)	1(6.7)	0.5	0.476
Helicobacter pylori positive	113(89.0)	14(11.0)	1.8	0.178

(*) P-value less than 0.05

4.30 Correlation between Ascites and endoscopy findings

When ascites was correlated with endoscopy findings, a significant association was observed among subjects with Oesophageal varices ($\chi 2$= 4.4, p=<0.036), Lax Lower Esophageal Sphincter ($\chi 2$= 10.4, p=<0.001) and gastric erosions ($\chi 2$= 5.3, p=<0.022),

Table 4.26: Correlation between Silky Hair and endoscopy findings

Variable	Silky Hair		χ 2	P-value
	Yes (%)	No (%)		
Esophageal varices	16(38.1)	26(61.9)	17.4	<0.001*
Lax Lower Esophageal Sphincter	14(38.9)	22(61.1)	13.3	<0.001*
Gastroesophageal junction				
- Gastroesophageal varices (GOV-1)	16(76.2)	5(23.8)	5.5	0.065
- Gastroesophageal varices (GOV-2)	17(80.9)	4(19.1)		
Gastric antral vascular ectasia (GAVE)	27(71.1)	11(28.9)	1.1	0.301
Portal hypertensive gastropathy (PHG)	47(70.2)	20(29.8)	1.9	0.162
Gastritis	41(59.4)	28(40.6)	1.3	0.259
Gastric erosions	2(16.7)	10(83.3)	12.8	<0.001*
Gastric ulcer	30(88.2)	4(11.8)	11.2	<0.001*
Isolated gastric varices (IGV-1)	4(80.0)	1(20.0)	0.8	0.670
Isolated gastric varices (IGV-2)	3(75.0)	1(25.0)		
Portal Hypertensive Duodenopathy	10(47.6)	11(52.4)	2.9	0.088
Duodenal vascular Ectasia	2(66.7)	1(33.3)	0.0	0.926
Duodenal Erosion	14(66.7)	7(33.3)	0.1	0.794
Duodenitis	28(73.7)	10(26.3)	2.0	0.153
Duodenal Ulcer	9(60.0)	6(40.0)	0.1	0.724
Helicobacter pylori positive	80(63.0)	52(37.0)	0.6	0.445

(*) P-value less than 0.05

4.31 Correlation between Silky Hair and endoscopy findings

When silky hair was correlated with endoscopy findings, a significant association was observed among patients with Oesophageal varices ($\chi 2$= 17.4, p=<0.0001), Lax Lower Esophageal Sphincter ($\chi 2$= 13.3, p=<0.0001), gastric erosions ($\chi 2$=12.8, p=<0.001) and gastric ulcer ($\chi 2$= 11.2, p=<0.001).

Table 4.27: Multivariate logistic regression model for patient characteristics that influence endoscopic findings.

Variable	Number of respondents (% of the total in every group)	OR (95% CI)	P-value	AOR (95% CI)	P-value
Esophageal varices	55 (37.9)	0.5 (0.2 – 1.2)	0.123	0.7 (0.1- 6.60	0.757
Lax Lower Esophageal Sphincter	36 (24.8)	0.4 (0.1 – 2.0)	0.271	0.6 (0.0–9.0)	0.699
Gastroesophageal Varices	42 (29.0)	2.5 (0.3 – 21.7)	0.396	0.9 (0.5-15.2)	0.944
Gastric antral vascular ectasia	38 (26.2)	2.2 (0.3 – 18.9)	0.473	2.7 (0.6-47.6)	0.493
Portal hypertensive gastropathy	67 (46.2)	2.2 (0.4 – 11.9)	0.349	1.8 (0.1 – 24.6)	0.668
Gastritis	69 (47.6)	0.7 (0.1 – 3.1)	0.606	1.4 (0.2 - 11.3)	0.749
Gastric erosions	12 (8.3)	0.1 (0.0 – 0.5)	0.005	0.1 (0.0 - 6.9)	0.024*
Isolated Varices	9 (6.21)	0.4 (0.0 – 3.4)	0.382	0.6 (0.1 – 16.9)	0.811
Portal Hypertensive Duodenopathy	12 (14.5)	0.4 (0.1 – 2.2)	0.292	0.2 (0.0 – 2.8)	0.219
Duodenal Erosion	21 (14.5)	1.0 (0.1 – 8.9)	0.988	3.9(0.1– 218.4)	0.508
Duodenitis	38 (26.2)	2.2 (0.3 – 18.9)	0.473	2.5 (0.2 – 30.5)	0.468
Duodenal Ulcer	15 (10.3)	0.7 (0.1 – 6.0)	0.727	1.5 (0.1 – 24.0)	0.758
Helicobacter pylori positive	127 (87.6)	3.1 (0.5 – 17.0)	0.204	3.5 (0.4 – 32.9)	0.276

(*) P-value less than 0.05, OR-Crude Odds Ratio, aOR- Adjusted Odds Ratio, CI- Confidence Interval

4.32 Multivariate logistic regression model for stigmata that influenced endoscopy findings

Multivariate logistic regression analysis of stigmata that could influence endoscopic findings in liver cirrhosis patients was assessed and presented in table 4.27 below. All variables with a p-value <0.05 in the chi-square analysis between stigmata of liver cirrhosis and endoscopy findings were added to the multivariate regression model to test for association. It was further adjusted with all variables that could be influenced by clinical findings to address co-founders.

The risk of developing gastric erosions was reduced by 99% among respondents with stigmata compared to those who did not have stigmata (OR=0.1, 95% CI= 0.0 – 0.5, p=0.005).

CHAPTER FIVE

DISCUSSION

5.1 AGE

A total of 145 participants were included in this study. The mean age of the respondents was 46.5 ± 12.14 years; similar age groups have been reported by studies in Ghana and other African countries. Duah et al and Blankson et al recorded a median age of 45 ± 12.28.[207] years and 46.0 years[27] respectively in Ghana. Studies done in other African countries also had similar age cohorts, Alema et al recorded 42 years ± SD 15.88 at the Lacor hospital in Uganda similar to the 45.5± SD 13.8 years recorded by Akere et al in Nigeria.[208,104] However, the mean ages of studies done in western countries were higher 52.0 years by Zaman et al in Portland, Oregon, USA,[209] and 51.84±12.26 years by Chaudhary et al in Nepal.[9]

The mean age of most respondents belongs to the very productive group in Ghana. This is very significant considering the impact on the socio-economic activities in our country.

The differences in the mean age in different geographic regions are likely to be related to differences in the aetiologies particularly the prevalence of hepatitis viruses in the populations.

5.2 SEX

Out of the 145 participants included in this study, there were 106 (73.1%) were males and female 39 (26.9%). This mirrors the gender /sex distribution in a study by Duah et al in Ghana, where the majority of patients were male patients 116 (77.9%) to female patients 33(22.1%) in a ratio of 4:1.[207] A similar male predominant gender distribution was also observed in other parts of Africa in a study by Alema et al at the Lacor hospital in Uganda with 113 (50.4%) males and 111 (49.6%) females.[208] Again, in a study in West Africa by Akere et al in Nigeria, a similar gender/sex distribution of 43 (76.8%) males to 13 (23.2%) females was observed.[104] A male to female ratio of 3.7:1 and 2.6:1 were observed in a study by Chaudhary et al in Nepal in Asia and Zaman et al in the USA respectively.[9,210] In Ghana, males are the main breadwinners in most families, based on the above distribution, it is apparent that the overall socio-economic status of the country is likely to be affected negatively.

5.3 MARITAL STATUS

Most respondents', 102(70.3%) were married. 18(12.4%) were single, 12(8.3%) Divorced, 10(6.9%) widowed while 3(2.1%) were co-habiting. This follows from the above information that most respondents were predominantly males who are married and belong to the working class in Ghana. Again, a negative socio-economic impact is likely to be felt by most families in Ghana and the country at large.

5.4 EDUCATIONAL BACKGROUND

A significant number of respondents, 32(22.1%) had no formal education, 36(24.8%) had Basic education, and 18(12.4%) had either Junior High school or Middle school leaving certificate education. 40(27.6%) had either a secondary school education or went into vocational training. Only 19(13.1%) had tertiary education. This is of significance in terms of how information about the causes and risk factors of liver cirrhosis, its complications including the various upper GIT lesions, how to recognize early signs and symptoms as well as preventive measures against the causes and risk factors, would be disseminated.

5.5 RELIGION

Most respondents are Christians 112(77.2%), 31(21.4%) Muslims, 1(0.7%) traditionalist and 1(0.7%) belonged to other religions. The above distribution may be very useful in utilizing the role religion may play in dealing with the causes of liver cirrhosis.

5.6 OCCUPATION

Out of a total of 145 respondents, 141(97.2%) were employed. Most of them were, 94(64.8%) were self-employed while 47(32.3%) were employed by someone. Students and the unemployed accounted for 4(2.8%) of the respondents. This information reiterates the fact that most respondents belong to the working class in Ghana which could have a negative implication for the country.

5.7 LABORATORY INVESTIGATIONS

Chronic hepatitis B and C were the main causes of liver cirrhosis, with frequencies of (75.2%) and (20.7%) respectively. There were no HBV and HCV co-infections detected by laboratory investigation. However, 2(1.7%) of respondents who had a history of liver disease had hepatitis B

and C co-infection despite a significant prevalence of HBV (13%) and HCV (3.0%) in Ghana.[211,212] This finding is also in keeping with those in the literature from West Africa and other hepatitis B endemic countries.[39,213] Ayele et al. in Ethiopia also reported HBV and HCV as the major causes of liver cirrhosis.[214] Alcohol use was found in 35.3% of respondents, out of which 45.1% took 1-3 drinks per day, of which 58.8% were gin/spirits. Over half of respondents who currently used alcohol have significant alcohol intake and dependence by way of the CAGE questions in table 3. In Sudan, alcohol abuse and HBV were the common causes.[215]Alcohol use may likely play a significant role in the aetiology of liver cirrhosis in this study, This is in keeping with findings from a study in KBTH where alcohol was the second and a significant cause of liver cirrhosis.[207] Non-Alcoholic Fatty Liver (NAFLD) was a cause of Liver cirrhosis in 2.5% of respondents who gave a history of liver disease, this is relatively low compared to the United States of America where NAFLD is a major cause of liver cirrhosis.[216]

The overall spectrum of causes of liver cirrhosis is the same globally but the percentage of individual causes varies from one country to another country. NAFLD was not an important cause of cirrhosis in this study, but it is increasingly becoming an important cause of cirrhosis globally. This may be due to the increasing rate of obesity in western countries and Asia compared to African countries[217]. It was also realised that Majority of patients in this study, 93.1%, had low albumin, 50.3% had an elevated bilirubin level above 21 micrommoles per litre. 87.6% had anaemia with haemoglobin levels less than 11g/dL while the majority 74.5% had low platelet count. This is possible considering the high prevalence of upper GI findings including oesophageal varices, Peptic ulcer, portal hypertensive gastropathy which may lead to blood occult and overt blood loss and by extension anaemia

Additionally, majority have very low platelet count, thus about 74.5% which points to portal hypertension. Portal hypertension may eventually lead to GI mucosal compromise and hence increased mucosal injury from non-variceal lesions.

5.7 PREVALENCE OF UPPER GIT ENDOSCOPIC FINDINGS

Oesophageal varix is the most predominant finding in this study with a prevalence of 70.3%, this prevalence is higher than the global estimates of approximately 50% of patients who have liver cirrhosis but below that reported in KBTH[207] (90.6%) with relatively similar sample size. The majority of patients from the study in KBTH involved only patients who presented with upper GIT

bleeding to the hospital, hence likely to be decompensated, whereas this study included all patients with either compensated or decompensated liver cirrhosis, with or without upper GIT bleeding. This study also included both old patients who were already being managed at the GIT unit and might have had improvement or resolution of signs and symptoms as well as new patients presenting for the first time. This may have accounted for the difference in prevalence.
The prevalence in this study was much higher than the 53.6% prevalence reported by Ajayi et al in Nigeria.[218] Although the sample size was higher in this study, the marked difference in the prevalence of oesophageal varices could be explained by the fact that only grade 2 to 4 varices were included in their study, whereas our study included grades 1 to grade 4 varices.

The prevalence of oesophageal varices in this study was lower than the 75% reported by Achinge et al, the difference observed in the prevalence could be because only newly diagnosed patients with liver cirrhosis were recruited in their study, whereas this study included newly diagnosed patients in addition to those who had been on treatment for portal hypertension and hence varices. This prevalence was also much higher than that reported in other parts of the world. In a study by Giannini et al in Italy with much bigger sample size, the prevalence of oesophageal varices was 61%.[219] Their study was retrospective compared to a cross-sectional type in this study. The lower prevalence in their study could be explained by the stringent inclusion criteria employed because patients with active GI bleeding at admission, those who had previously undergone one form of treatment or the other for oesophageal varices, and those who were on primary prophylaxis for variceal bleeding were excluded from their study.
In a study by Nebel lower oesophageal sphincter pressure (LESP) in patients with cirrhosis only was not different from that of control subjects but was found to be significantly higher than the LESP recorded in patients with cirrhosis and ascites. It was also observed that the LESP significantly increased after the drainage of ascitic fluid[220]

Most patients had severe liver cirrhosis by way of the Child-Pugh class C (76.5%), oesophageal varices (72.7%) and ascites (87.1%) in this study; these could explain the high prevalence of laxity of the Lower oesophageal sphincter (LES) observed in our study.
Another mechanism that aids reduction in LESP in cirrhosis has to do with plasma vasoactive peptides and neurotensin, which are known to reduce LESP and are elevated in patients with liver cirrhosis.[221] Oesophageal candidiasis was observed in none of our patients although a retrospective

study by Ou et al recorded a prevalence of 0.8%.[222] The large sample size, as well as the category of patients studied, might have contributed to the difference in the prevalence. While they studied human immunodeficiency virus (HIV)-infected subjects among whom 3,017 had liver cirrhosis, we studied only patients with liver cirrhosis. However, it is possible that some of our patients had underlying HIV or other immunosuppressive conditions since none of our patients was screened for these conditions. Although it is known that oesophageal candidiasis is common in immunocompromised states such as HIV infection or as a result of iatrogenic immunosuppression.[223,224] Liver cirrhosis has also been found to lower immunity and as such predispose to bacterial and fungal infections. Reasons for this include reduced antibody production, increased production of immunosuppressive cytokines, reduced leukocyte function, reduced opsonization, and disturbances of complement.[225–227] In this study, the prevalence of gastric varices was 6.1%, which is far lower than that reported by Mumtaz et al which was 15%.[228] While their study included patients with other causes of portal hypertension, this present study recruited only patients with liver cirrhosis as the cause of portal hypertension. Another observation is that 86% of their patients with gastric varices had hepatitis C virus (HCV) infection as the aetiology of the liver disease, whereas only 2.7% of our patients had HCV infection. These two factors might explain the difference in the prevalence of gastric varices.
In this study, IGV1 and IGV2 were not observed. This finding is similar to that recorded by Mumtaz et al.[99]

In a study by Sarin et al, IGV2 were reported to predominantly arise after oesophageal variceal ligation. This may explain the absence of IGV2 in our patients since none of them had variceal band ligation before the study.[229] In the study by Schechter et al, the prevalence of gastric varices was 8%, which was higher than in the present study.[230] This may be explained by the fact that most of their patients had less severe clinical presentation compared to our patients. in another study by sarin et al the prevalence of gastric varices was higher than was found in this study. GOV-1 was the most common type they observed in their patient populations as was found in this study. The relatively higher prevalence may be explained by the fact that their patients included both cirrhotic and non-cirrhotic portal hypertension whereas this study only included patients with cirrhosis.

Gastric and duodenal ulcers were seen in 24.2% and 10.6% of our patients respectively, this finding is of importance in the sense that this may be a source of upper gastrointestinal bleeding (UGIB)

in some of these patients. This is paramount so as not to attribute every case of UGIB in patients with liver cirrhosis to variceal bleeding alone. In a study by Gado et al, in Giza, Egypt, peptic ulcer was found in 60% of their patients with liver cirrhosis who had acute non-variceal UGIB and was the commonest cause of bleeding in this category of patients.[123] Also, in their patients with acute variceal UGIB, peptic ulcer was diagnosed in 17% of them. Their study recruited patients with only liver cirrhosis and acute UGIB, whereas our study recruited patients with liver cirrhosis who have had UGIB as well as those who have not bled. This might explain the higher prevalence of peptic ulcers recorded in their study compared to what we found in our study.

However, the prevalence of peptic ulcers in this present study is comparable to that reported in other studies.[121,231,232] The presence of peptic ulcers in cirrhotic patients may be associated with some ulcerogenic factors that are specific to patients with liver cirrhosis. Among the proposed factors is hypergastrinemia, decreased gastric prostaglandin E2 levels, and the observed portosystemic shunting in liver cirrhosis, which may prevent ulcerogenic factors from being cleared by the liver.[233,234] Also, it has been observed that the presence of portal hypertension and PHG may predispose the gastric mucosa and duodenal mucosa to damage by the ulcerogenic factors as well as impair the ability of these to repair the damage.[235]In this present study, PHG was observed in 48.5% of our patients, and this may explain the high prevalence of gastroduodenal ulcers observed. Duodenal varices were not seen in any of our patients although these lesions are said to be of low prevalence in the general population, however, there is an about 3.71-fold increase in their prevalence in males with liver cirrhosis from chronic active hepatitis due to HBV, alcoholism and Primary sclerosing cholangitis.[236]

5.8 CORRELATION BETWEEN PATIENT CHARACTERISTICS AND ENDOSCOPIC FINDINGS WITH SEVERITY OF LIVER CIRRHOSIS

The only upper GI tract endoscopic finding that was found to have a positive correlation with the severity of liver cirrhosis was lax lower oesophageal sphincter ($\chi 2 = 6.40$, $p= 0.041$), this is in keeping with a study by Nebel where LESP in patients with cirrhosis only, was not different from that of control subjects, but was found to be significantly lower than the LESP recorded in patients with worsening cirrhosis and ascites.[220] It was also observed that the LESP significantly increased after the drainage of ascitic fluid. Another mechanism that aids reduction in LESP in worsening cirrhosis has to do with plasma vasoactive peptide and neurotensin, which are known

to reduce LESP and these are elevated in patients with liver cirrhosis.[221] Patients' clinical characteristics that were influenced by the worsening severity of liver disease were itching or rash (p=0.02), leg swelling (p=<0.001), and blood product transfusion (p=0.007).
Finger clubbing ($\chi 2$ = 21.04, p= <0.001), leukonychia ($\chi 2$ 13.41, p= 0.001), ascites ($\chi 2$ =41.28, p=<0.001) and silky hair ($\chi 2$ = 14.66, p=0.001) were found to have no correlation with worsening disease severity. \
Various stigmata of liver cirrhosis were also determined and analysed for statistically significant associations with the various endoscopic findings, it was found that oesophageal varices and lax LES occurred most frequently and were strongly associated with patients who had finger clubbing, leukonychia, silky hair, ascites, palmar erythema as well as spider naevi. Gastric ulcers were predominant in patients who had finger clubbing, leukonychia, asterixis, sclera jaundice and silky hair whereas gastric erosions were seen in those with finger clubbing, leukonychia, silky hair, ascites, and palmer erythema.

Portal Hypertensive Gastropathy and GOV-2 were more common after gastric ulcer and gastric erosion. PHG was associated with clubbing, asterixis and silky hair while GOV-2 showed association with patients who presented with leukonychia, palmer erythema and Dupuytren's contracture.
Additionally, PHG and GAVE followed with the same frequency, with PHG occurring in patients with leukonychia and palmer erythema while GAVE in those presenting with asterixis and palmer erythema.

Gastroesophageal varix-1, Duodenal ulcer and Gastritis occurred only in patients who had Palmer erythema as a stigma of their underlying cirrhosis of the Liver.
Liver cirrhosis is often associated with a hyperdynamic circulatory syndrome, with high cardiac output and reduced systemic vascular resistance and arterial pressure. The hyperdynamic circulatory syndrome is due to arterial vasodilation that mainly occurs in the splanchnic circulation, while vascular resistance in the other circulatory districts is normal or increased, according to the degree of portal hypertension, liver impairment and activation of the renin-aldosterone and sympathetic nervous system.[237] The above explanations could explain the presence of clubbing, palmer erythema, and spider naevi in the various endoscopic findings with a worsening child-Pugh score. Additionally, advanced cirrhosis is associated with a decrease in

plasma albumin.[65] Patients with cirrhosis have impaired hepatocellular function and reduced albumin synthesis, which can reach a 60-80% reduction in advanced cirrhosis.[238] The low albumin level leads to leukonychia, ascites formation and silky hair, hence their association with the endoscopic findings which tend to be prevalent with a worsening child-Pugh score.

5.9 HELICOBACTER pylori INFECTION AND LIVER CIRRHOSIS

H. pylori was found in most respondents (87.6%) in this study, this is in keeping with the significance of this bacterium in liver cirrhosis but with a much higher prevalence compared to one of the first studies performed in patients with chronic liver injury. This first study pointed to the presence of Helicobacter genus bacteria in the liver tissue in 26% of patients.[239] Current studies in patients infected with HBV, HCV, and patients with chronic noninfectious liver conditions point to much higher prevalence of H. pylori in the liver tissue. Infections are thought to occur in effect of disturbances in patients' immune functions.[240] Both experimental and clinical studies demonstrate unfavorable effect of H. pylori infection onto the course of liver injury, especially exacerbated fibrosis. One of the reasons for this is the influence of infection onto metabolic changes connected with carbohydrate turnover, synthesis of high energy compounds (mainly ATP), and increased concentration of proinflammatory cytokines. Despite a very high prevalence of H. pylori in this study, there was no positive correlation with severity of liver cirrhosis. This is a sharp contrast to that of some studies that point to a positive correlation with worsening disease severity,[200] and the high importance of the cytopathological effect of H. pylori on hepatocytes.[198]

LIMITATIONS OF THE STUDY

1. The diagnosis of liver cirrhosis was limited to a transabdominal ultrasound scan. Liver tissue biopsy which gives a more accurate diagnosis of liver cirrhosis was not readily available. Because Liver cirrhosis was not accurately diagnosed with histopathology, other non-liver causes of upper GIT endoscopic findings could have been included in this study.
2. This study is hospital-based, and the findings may not be generalizable to the community.
3. The use of an antispasmodic, hyoscine butyl bromide during the endoscopic procedure could have affected the laxity of the Lower oesophageal sphincter
4. The measurement of the length of the oesophagus endoscopically from the upper incisors to the gastroesophageal junction only does not give the accurate length of the oesophagus.
5. Liver Biopsy was not done due to the invasive nature of the procedure, and the chronic shortage of blood and blood products at the blood Bank, should bleeding occur.0

CONCLUSIONS

1. The most prevalent endoscopic finding in this study was oesophageal varices, most being medium and large oesophageal varices, as well as a significant number of patients with peptic ulcers. This underscores the importance of screening endoscopy for varices and the diagnosis of other additional lesions as complications may arise from them if they are not detected and treated early.
2. Oesophageal varices and lax LES showed a positive correlation with severity of the liver cirrhosis as assessed by Child-Turcotte-Pugh score.
3. Various stigmata of liver cirrhosis had strong associations with the various endoscopic findings with various frequencies of occurrence:

   (a) Oesophageal varices and lax LES occurred most frequently and were strongly associated with patients who had finger clubbing, leukonychia, silky hair, ascites, palmar erythema and spider naevi

   (b) Gastric ulcer was predominant in patients who had finger clubbing, leukonychia, asterixis, sclera jaundice and silky hair

   (c) Gastric erosions were seen in those with finger clubbing, leukonychia, silky hair, ascites and palmer erythema.

   (d) PHG was associated with clubbing, asterixis and silky hair

   (e) GOV-2 showed association with leukonychia, palmer erythema and Dupuytren's

   (f) PHG was associated with leukonychia and palmer erythema while GAVE was associated with asterixis and palmer erythema.
4. Most patients with liver cirrhosis were middle-aged men with chronic HBV infection being the leading underlying cause. HCV viral infection was the second commonest cause of liver cirrhosis.
5. NAFLD was not a major cause of liver cirrhosis in this study.
6. Herbal medication may also play a role in the aetiology of liver cirrhosis.
7. H. pylori was observed in most respondents but, there was no association with the severity of liver cirrhosis.

RECOMMENDATIONS

1. A large proportion of patients with liver cirrhosis at the KATH have oesophageal varices and Peptic ulcers during the endoscopic screening. This calls for systems that will strengthen health care facilities to be able to perform an endoscopic assessment for all patients with cirrhosis.
2. Interventions aimed at screening and early detection of liver cirrhosis and its associated risk factors should be instituted. Given the fact oesophageal varices and lax LES show a positive correlation with severity of the liver cirrhosis by way of the Child-Pugh score, screening for liver cirrhosis and upper GIT endoscopic at an early state will prevent complications that may arise from late diagnosis.
3. The various associations may be very useful in predicting likely endoscopic findings in a patient with a particular clinical presentation. In a resource-poor environment, such as ours, this will help health care providers to institute preliminary treatment before patients are referred to tertiary centers.
4. Universal testing for HBV and HCV infection and HBV vaccination at birth and access to treatment should be intensified. Most respondents had HBV and HCV as the cause of their liver cirrhosis and belong to the very productive group in Ghana. This is very significant considering the impact on the socio-economic activities in our country.
5. A similar study should be done on a larger scale country-wide in multiple centers and regions to get a well-balanced prevalence of these upper GI tract lesions as well as a more accurate association between the various stigmata and the UGIT endoscopic findings.

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APPENDIX I: PARTICIPANTS INFORMATION SHEET

PARTICIPANTS INFORMATION SHEET

This study aimed at evaluating the prevalence and significance of various forms of upper gastrointestinal tract mucosal findings in patients at the Directorate of internal medicine with liver cirrhosis, correlating them with the severity of liver disease and evaluating patients' characteristics that predict the presence of these lesions.

The procedure of the research

Clinical history and physical examination findings will be obtained from patients and patient records. Upper gastrointestinal endoscopy will be done for each patient.

Risk

All the procedures that will be done during the study will be dictated by the attending physician/endoscopist as part of their normal patient care and not for the study. The risks associated with the study are those that all outpatients encounter at the endoscopy unit and nothing peculiar to the study.

Confidentiality

All efforts will be taken to maintain the confidentiality of patients' information. All patients' records will be anonymized with a study number, which will be used in the data entry. Information about patients will be kept confidential with access to the investigator and the supervisors only.

Cost to participants

Patients enrolled on this study will not incur any extra costs.

Benefits

There may be no direct benefits to the study participants. However, the results of the study will help improve the management of liver cirrhosis patients. The study will also provide local data that will inform policy and support the development of protocols and guidelines for the better management and control of people living with liver cirrhosis. In addition, it will provide data, which will be the basis for the future research hypothesis.

Voluntariness

Patients' participation in this study is entirely voluntary.

Alternatives to participation

If a patient chooses not to participate in the study it will not affect their management in the hospital in any way.

Consequences of participants' decision to withdraw from the research

Patients can also choose to withdraw from the research at any time and all the data collected on them will be destroyed.

APPENDIX II: QUESTIONNAIRE

Demographic data

Study number: .....

Name: ..... Date: -------/------/----------

Date of birth: ----/----/---- Age [ ] years Gender: M [ ] F [ ] Height ……

Residential Address: .....

Religion: Christian [ ] Moslem [ ] Others [ ] specify……..

Educational level: None [ ] Primary [ ] Secondary [ ] Tertiary [ ]

Occupation: .....

Marital status: Single [ ] Divorced [ ] Widow / Widower [ ]
Married [ ] Separated [ ] Co-habitation [ ]

Clinical information

History of presenting complaints

a. Have you had, or do you have any of the following? Please circle Yes or No

Symptom	CODE	CODE
Abdominal pain/swelling	Yes [1]	No [2]
Blood - in stool/vomit	Yes [1]	No [2]
Diarrhoea/constipation	Yes [1]	No [2]
Fatigue	Yes [1]	No [2]
Insomnia / somnolence	Yes [1]	No [2]
Itching / Rash	Yes [1]	No [2]

Jaundice	Yes [1]	No [2]
Leg swelling	Yes [1]	No [2]
Tattoo/ scarifications	Yes[1]	No[2]
Blood/blood products transfusion	Yes[1]	No[2]
Dyspepsia (Bloating/Heartburns/indigestion)	Yes[1]	No[2]

b. Have you ever taken any of the following?

Social History	code	code
Do you have any tattoos/body piercings?	Yes [1] No [2]	No [
Do you currently drink alcohol (including low-alcohol beverages)?	Yes [1] No [2]	

Number of drinks per day_____ Number of days per week_____Type_____

If No, when was your last drink? _____ month(s)/yrs ago

Have you ever had alcohol negatively influence your work or personal life?	Yes [1] No [2]
Have you ever tried to cut down on the amount that you were drinking?	Yes [1] No [2]
Have you ever felt annoyed when people asked about your drinking?	Yes [1] No [2]
Have you ever felt guilty about your drinking?	Yes [1] No [2]
Have you ever had an “eye-opener” drink, first thing in the morning?	Yes [1] No [2]

Street Drugs

Have you ever used drugs? (Cocaine, marijuana, uppers, downers, LSD, etc.)	Yes [1] No [2]
Have you ever snorted drugs?	Yes [1] No [2]
Have you ever used IV needles? (non-medical injections)	Yes [1] No [2]

If yes, what was the first date used?

If yes, what was the last date used?

When was your last experience with any drugs? Date:

Drug history

☐Birth Control Pills Yes [1] No [2]

☐Body Building Drugs Yes [1] No [2]

☐Steroids Yes [1] No [2]

☐ Oral Herbal Preparations use Yes [1] No [2]

if Yes,

Type of preparation: ……

Approximate Duration of use: ……..

Duration of Usage: ……..

Other Medications (if applicable, list all medications you are currently taking and the doses (include injectable, vitamins, herbs, alternative and over-the-counter products)

code code

c. Have you ever been diagnosed of having Liver disease? Yes [1] No [2]

if Yes, which type ……..

Duration of Diagnosis

d. Sexual partners in your lifetime

Number (Check Box below) code code

☐<10 Yes [1] No [2]

☐10-20 Yes [1] No [2]

☐20-50 Yes [1] No [2]

☐>50 Yes [1] No [2]

Sexual preference code code

☐Male Yes [1] No [2]

☐Female Yes [1] No [2]

☐Both Yes [1] No [2]

Examination findings

a). Stigmata of Liver Disease code code

Finger clubbing Yes [1] No [2]

Leukonychia	Yes [1] No [2]
Sclera/palmar jaundice	Yes [1] No [2]
Palmar erythema	Yes [1] No [2]
Dupuytren's Contracture	Yes [1] No [2]
Asterixis	Yes [1] No [2]
Spider naevi (angioma)	Yes [1] No [2]
Ascites	Yes [1] No [2]
Fluffy hair	Yes [1] No [2]

(b) Severity of Liver Disease

Ascites	code
None	[1]
Small/diuretic controlled	[2]
Tense	[3]

Hepatic encephalopathy	code
Absent	[1]
Mild	[2]
Significant	[3]

Laboratory investigations

Haemoglobin level	code
	< 11 [1]
	11-16 [2]
	>16 [3]

Platelet Count	Code

<140 k/μL	[1]
140-400k/μL	[2]
>400k/μL	[3]

P T / (INR)	code
< 1.7	[1]
1.7 – 2.2	[2]
> 2.2	[3]

ALBUMIN (g/L)	code
> 35	[1]
28 – 35	[2]
< 28	[3]

BILIRUBIN (μmol/L)	code
< 34.2	[1]
34 - 51	[2]
> 51.4	[3]

PLATELET

HAEMOGLOBIN

code code

c). Hepatitis B virus infection: Positive [1] Negative [2]

code code

d). Hepatitis C virus infection: Positive [1] Negative [2]

e) ULTRASOUND FINDINGS

LIVER SIZE	code code
Enlarged	Yes [1] No [2]
Average	Yes [1] No [2]
Shrunken	Yes [1] No [2]
COARSE LIVER ECHOPATTERN	Yes[1] No [2]
BULBOUS EDGE (CIRRHOSIS)	Yes [1] No [2]
PORTAL VEIN DILATATION	Yes [1] No [2]
HEPATIC VEIN DILATATION	Yes [1] No [2]
SPLENIC VEIN DILATATION	Yes [1] No [2]
SPLEEN SIZE	
Enlarged	Yes [1] No [2]
Average	Yes [1] No [2]
Shrunken	Yes [1] No [2]
ASCITES	
None	Yes [1] No [2]
Mild	Yes [1] No [2]
Moderate	Yes [1] No [2]
Marked (Gross)	Yes [1] No [2]
Tumours/masses	Yes [1] No [2]

f). Endoscopic findings

OESOPHAGUS	
LENGTH	----------
Centimetres	
VARICES	
Absent	Yes [1] No [2]
Small	Yes [1] No [2]
Medium	Yes [1] No [2]
Large	Yes [1] No [2]
GASTROESOPHAGEAL JUNCTION	(LAX) (NORMAL)
VARICES	
Absent	Yes [1] No [2]
Gastroesophageal varices (GOV-1)	Yes [1] No [2]
Gastroesophageal varices (GOV-2)	Yes [1] No [2]
STOMACH	
Gastric antral vascular ectasia (GAVE)	Yes [1] No [2]
Portal hypertensive gastropathy (PHG)	Yes [1] No [2]
Gastritis	Yes [1] No [2]
Erosions	Yes [1] No [2]
Ulcer	Yes [1] No [2]
VARICES	
Absent	Yes [1] No [2]
Isolated gastric varices (IGV-1)	Yes [1] No [2]
Isolated gastric varices (IGV-2)	Yes [1] No [2]
DUODENUM	
Portal Hypertensive Duodenopathy	Yes [1] No [2]
Duodenal vascular Ectasia	Yes [1] No [2]
Erosion	Yes [1] No [2]

Duodenitis Yes [1] No [2]

Ulcer Yes [1] No [2]

HELICOBACTER pylori TEST POSITIVE [1] NEGATIVE[2]

APPENDIX III: CONSENT FORM

GENERAL CONSENT FORM

I am conducting a study at the Directorate of Medicine, Komfo Anokye Teaching Hospital to determine the prevalence and significance of various forms of upper gastrointestinal tract findings in patients with liver cirrhosis correlating them with the severity of liver disease and evaluate patient characteristics that predict the presence of these lesions amongst patients on admission.

If you agree to participate in the study, you will be asked questions about yourself, and your disease condition and examined. An endoscopy will be done on you.

Failure to agree to participate in this study will not affect your clinical management in any way. You can also pull out of the study at any point in time if you so wish.

Thank you for agreeing to participate in this study.

Yours faithfully,

DR BRIGHT OPPONG

Name and affiliation of researcher applicant

This study is to be conducted by DR BRIGHT OPPONG of the Directorate of Medicine Komfo Anokye Teaching Hospital.

Statement of the person obtaining informed consent

I have fully explained this research to ..... and have given sufficient information including information about risks and benefits to make an informed decision.

Date.....

Name.....

Signature.....

Statement of the person giving consent

The description of this study has been explained to me in a language that I understand. I do know that my participation is voluntary. I know enough about the purpose, methods, risks and benefits of the research study to judge that I want to take part in it. I understand that I may freely stop being part of this study at any time.

Date.....

Name.....

Signature.....

Witness' signature (if applicable).....

Witness' name (if applicable).....

UPPER GIT CONSENT FORM

Study Identification:

Name:

Address:

Date of birth:

Gender: M/ F

Interpreter or an Interpreter Service required? Yes No

If yes, is a qualified Interpreter present? Yes No

Condition and treatment

The doctor has explained that you have the following condition: (Doctor to document in patient's own words)

.....

.....

..... This condition requires the following procedure. (Doctor to document - include site and/or side were relevant to the procedure)

.....

.....

..... An upper gastrointestinal (GI) endoscopy is where the doctor uses an instrument called an endoscope to look at the inside lining of your oesophagus (food pipe), stomach and duodenum (first part of the small intestine). This is done to look at reasons why you may have swallowing problems, nausea, vomiting, reflux, bleeding, indigestion, abdominal pain or chest pain. This procedure may or may not require sedation.

Preparation for the procedure

Your stomach must be empty for the procedure to be safe and thorough, so you will not be able to eat or drink anything for at least six hours before the procedure.

What if the doctor finds something wrong?

Your doctor may take a biopsy (a very small piece of the stomach lining) to be examined in Pathology. Biopsies are used to identify many conditions even if cancer is not thought to be the problem

Risks of an upper gastrointestinal endoscopy +/- sedation

There are risks and complications with this procedure. They include but are not limited to the following. Common risks and complications include:

- Nausea and vomiting.
- Faintness or dizziness, especially when you start to move around.
- Headache.
- Pain, redness or bruising at the sedation injection site (usually in the hand or arm). • Muscle aches and pains.

- Allergy to medications given at the time of the procedure. Uncommon risks and complications include
- About 1 person in every 1,000 will experience bleeding from the oesophagus (food pipe), stomach and duodenum where a lesion or polyp was removed. This is usually minor and can usually be stopped through the endoscope. Rarely, surgery is needed to stop bleeding.
- Heart and lung problems such as heart attack or vomit in the lungs causing pneumonia. Emergency treatment may be necessary.
- Damage to your teeth or jaw due to the presence of instruments in your mouth.
- An existing medical condition that you may have got worse. Rare risks and complications include:
- Missed polyps or growths.
- About 1 person in every 5,000 will accidentally get a hole (perforation) in the oesophagus, stomach or duodenum. This can cause a leak of stomach contents into the abdomen. If a hole is made, you will be admitted to the hospital for further treatment which may include surgery.
- Your procedure may not be able to be finished due to problems inside your body or because of technical problems.
- Bacteraemia (infection in the blood). This will need antibiotics.
- 'Dead arm' type feeling in any nerve, due to positioning with the procedure – usually temporary.
- Anaphylaxis (severe allergy) to medication given at the time of the procedure.

• Death as a result of complications to this procedure is rare. D. Significant risks and procedure options (Doctor to document in space provided.

.....

.....

.....

.....

What can I expect after this procedure?

You will remain in the recovery area for about 2 hours until the effect of the sedation wears off. Your doctor will tell you when you can eat and drink. Most times this is straight after the procedure. Your throat may feel sore and you might have some cramping pain or bloat because of the air entering the stomach during the procedure. You will be told what was found during the examination or you may need to come back to discuss the results and to find out the results of any biopsies that may have been taken.

What are the safety issues? Sedation will affect your judgment for about 24 hours. For your safety and in some cases legally;

• Do NOT drive any type of car, bike or other vehicle. You must be taken home by a responsible adult person

• Do NOT operate machinery including cooking implements.

• Do NOT make important decisions or sign a legal document.

• Do NOT drink alcohol, take other mind-altering substances, or smoke. They may react to the sedation drugs.

• Have an adult with you on the first night after your surgery.

Notify the hospital Emergency Department straight away if you have;

• Severe ongoing abdominal pain

• Trouble swallowing

• A fever

• Sharp chest or throat pain

• Have redness, tenderness or swelling for more than 48hours where you had the injection

Patient consent

I acknowledge that the doctor has explained;

- my medical condition and the proposed procedure, including additional treatment if the doctor finds something unexpected. I understand the risks, including the risks that are specific to me.
- The anaesthetic/sedation required for this procedure. I understand the risks, including the risks that are specific to me.
- other relevant procedure/treatment options and their associated risks. • my prognosis and the risks of not having the procedure.
- that no guarantee has been made that the procedure will improve my condition even though it has been carried out with due professional care.
- the procedure may include a blood transfusion.
- if immediate life-threatening events happen during the procedure, they will be treated based on my discussions with the doctor or my Acute Resuscitation Plan.
- a doctor other than the Consultant may conduct the procedure. I understand this could be a doctor undergoing further training. I have been given the following Patient Information Sheet/s: Upper Gastrointestinal Endoscopy
- I was able to ask questions and raise concerns with the doctor about my condition, the proposed procedure and its risks, and my treatment options. My questions and concerns have been discussed and answered to my satisfaction.
- I understand I have the right to change my mind at any time, including after I have signed this form but, preferably following a discussion with my doctor.
- I understand that image/s or video footage may be recorded as part of and during my procedure and that these image/s or video/s will assist the doctor to provide appropriate treatment. Based on the above statements, I request to have the procedure

Name of Patient:.....

Signature: .....

Date:.....

.

Interpreter's statement

I have given a sight translation in

(language)…….....

of the consent form and assisted in the provision of any verbal and written information given to the patient/parent or guardian/substitute decision-maker by the doctor.

Name

Interpreter:.....

Signature:.....

Date:.....

Appendix IV

STUDY TIMELINE

	2018			**2019**												**2020**		
ACTIVITY/DATE	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M
PROPOSAL DEVELOPMENT																		
GCPS APPROVAL																		
ETHICAL APPROVAL																		
DATA COLLECTION AND ENTRY																		
DATA CLEAN UP AND STATISTICAL ANALYSIS																		
MANUSCRIPT WRITING																		

BUDGET AND RESOURCES

Project working currency (Ghana Cedi)

Duration of research project (6 months):

BUDGET SUMMARY

Budget category	**Month 1** 22 patients	**Month 2** 22 patients	**Month 3** 22 patients	**Month 4** 22 patients	**Month 5** 22 patients	**Month 6** 22 patients	**Total** 132 patients
Patient's Transportation (GHC 50 PER PATIENT)	1,100.00	1,100.00	1,100.00	1,100.00	1,100.00	1,100.00	6,600.00
Laboratory Evaluation (FULLY DISCOUNTED)	-	-	-	-	-	-	
Discounted Endoscopic expense (FULLY DISCOUNTED)	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Ultrasound investigation (FULLY DISCOUNTED)	-	-	-	-	-	-	
Total in project currency	1,100.00	1,100.00	1,100.00	1,100.00	1,100.00	.00	**6,600.00**

BUDGET CERTIFICATION

We hereby certify that this budget proposal and all its accompanying detailed budget submission forms, correctly and fairly reflect the financial plan of the proposed project.

Name of principal researcher: DR. BRIGHT OPPONG	Job title: PHYSICIAN		Signature:
	Date:		

- 145 Patients will undergo Elective Gastroscopy over a period of 6 months 17 patient every month for 4 Consecutive months and 18 patients for the 2 remaining months).
- Each Endoscopic procedure will be fully discounted at GHC 00.00
- All patients in the cohort will have Ultrasound scan of the abdomen, Albumin, Bilirubin as well as and Prothrombin Time (PT).
- Each patient would be given a stipend of GHC 50 for transportation for the elective Upper GIT endoscopy.

Kwame Nkrumah
University of Science
and Technology, Kumasi

College of Health Sciences
SCHOOL OF MEDICINE AND DENTISTRY

COMMITTEE ON HUMAN RESEARCH, PUBLICATION AND ETHICS

Our Ref: CHRPE/AP/159/22

29th April 2022.

Dr. Bright Oppong
Directorate of Medicine
Komfo Anokye Teaching Hospital
Post Office Box 1934
KUMASI.

Dear Sir,

LETTER OF APPROVAL

Protocol Renewal: ***"Evaluation of Upper Gastrointestinal Tract Findings in Patients with Liver Cirhossis in the Directorate of Medicine, Komfo Anokye Teaching Hospital."***

Proposed Site: ***Directorate of Medicine, Komfo Anokye Teaching Hospital.***

Sponsor: ***Principal Investigator.***

Your submission to the Committee on Human Research, Publication and Ethics on renewal to protocol No. CHRPE/AP/045/19 dated 19th February, 2019 refers.

The Committee reviewed the following documents:

- A notification letter of 17th January, 2019 from the Komfo Anokye Teaching Hospital (study site) indicating approval for the conduct of the study at the Hospital.
- A Completed CHRPE Application Form.
- Participant Information Leaflet and Consent Form.
- Research Protocol.
- Questionnaire.
- Amendment: Increasing the sample size from 132 participants to 145 participants.

The Committee has considered the ethical merit of your proposed renewal and amendment and approved it. The approval is for a fixed period of one year, beginning **29th April 2022 to 28th April 2023** renewable thereafter. The Committee may however, suspend or withdraw ethical approval at any time if your study is found to contravene the approved protocol.

Data gathered for the study should be used for the approved purposes only. Permission should be sought from the Committee if any amendment to the protocol or use, other than submitted, is made of your research data.

The Committee expects a report on your study annually or at the close of the project, whichever one comes first. It should also be informed of any publication arising from the study.

Thank you, Sir for your application.

Yours faithfully,

Rev. Prof. John Appiah-Poku.
Honorary Secretary
FOR: CHAIRMAN

Room 7, Block L, School of Medicine and Dentistry, KNUST, University Post Office, Kumasi, Ghana
Tel: +233 (0) 3220 63248 **Mobile:** +233 (0) 20 5453785 **Email:** chrpe.knust.kath@gmail.com/chrpe@knust.edu.gh

KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY
COLLEGE OF HEALTH SCIENCES
SCHOOL OF MEDICAL SCIENCES / KOMFO ANOKYE TEACHING HOSPITAL
COMMITTEE ON HUMAN RESEARCH, PUBLICATION AND ETHICS

Our Ref: CHRPE/AP/045/19 19th February, 2019.

Dr. Bright Oppong
Directorate of Medicine
Komfo Anokye Teaching Hospital
Post Office Box 1934
KUMASI.

Dear Sir,

LETTER OF APPROVAL

Protocol Title: ***"Evaluation of Upper Gastrointestinal Tract Findings in Patients with Liver Cirhossis in the Directorate of Medicine, Komfo Anokye Teaching Hospital."***

Proposed Site: ***Directorate of Medicine, Komfo Anokye Teaching Hospital.***

Sponsor: ***Principal Investigator.***

Your submission to the Committee on Human Research, Publications and Ethics on the above-named protocol refers.

The Committee reviewed the following documents:

- A notification letter of 17th January, 2019 from the Komfo Anokye Teaching Hospital (study site) indicating approval for the conduct of the study at the Hospital.
- A Completed CHRPE Application Form.
- Participant Information Leaflet and Consent Form.
- Research Protocol.
- Questionnaire.

The Committee has considered the ethical merit of your submission and approved the protocol. The approval is for a fixed period of one year, beginning 19th February, 2019 to 18th February, 2020 renewable thereafter. The Committee may however, suspend or withdraw ethical approval at any time if your study is found to contravene the approved protocol.

Data gathered for the study should be used for the approved purposes only. Permission should be sought from the Committee if any amendment to the protocol or use, other than submitted, is made of your research data.

The Committee should be notified of the actual start date of the project and would expect a report on your study, annually or at the close of the project, whichever one comes first. It should also be informed of any publication arising from the study.

Yours faithfully,

Osomfo Prof. Sir J. W. Acheampong MD, FWACP
Chairman

Room 7 Block J, School of Medical Sciences, KNUST, University Post Office, Kumasi, Ghana
Phone: +233 3220 63248 Mobile: +233 20 5453785 Email: chrpe.knust.kath@gmail.com / chrpe@knust.edu.gh