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كلية الطب البشري

HEALTH RELATED QUALITY OF LIFE AMONG CHRONIC LIVER DISEASES PATIENTS AT PUBLIC HOSPITALS IN SANA'A CITY 2022

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Dedication

- We dedicate our research to our parents who did for us more than we can did for ourselves.

-To our family members who believed in us more than we believed in ourselves.

- To our first love, Yemen

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List of Abbreviations

AFLD	Alcoholic Fatty Liver Disease
AIH	Autoimmune Hepatitis
ALD	Alcoholic Liver Disease
AMA	Antimitochondrial Antibodies
AST	Aspartate Aminotransferase
CLD	Chronic Liver Disease
DNA	Deoxyribonucleic Acid
ECM	` Extracellular Matrix
HAV	Hepatitis A Virus
HBV	Hepatitis B Virus
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C Virus
HDV	Hepatitis D Virus
HEV	Hepatitis E Virus
HHC	Hereditary Haemochromatosis
HPCs	Hepatic Progenitor Cell
IBD	Inflammatory Bowel Disease
MEOS	Microsomal Ethanol-Oxidising System
NAD	Nicotinamide Adenine Dinucleotide
NAFLD	Non-Alcoholic Fatty Liver Disease
NASH	Nonalcoholic Steatohepatitis
NHANES	National Health and Nutrition Examination Survey
PBC	Primary Biliary Cirrhosis
PNPLA3	Phospholipase Domain-Containing 3
PSC	Primary Sclerosing Cholangitis
RNA	Ribonucleic Acid

Abstract

Background: Chronic liver disease is a leading cause of mortality and morbidity across the world. It is the 11th leading cause of death and 15th leading cause of morbidity. Health related quality of life is a multidimensional construct that includes the psychological, social, and functional aspects of an illness as well as its physical aspects.

Aim of the study: The aim of the study was to evaluate health related quality of life among patients with chronic liver diseases at public hospitals in Sana'a city.

Methodology: A hospital-based, descriptive cross-sectional study was used. The sample size was 197 patients. The sample was approached at the public hospitals in the medical wards and out-patients departments .The data collection tools were consisted of two parts: the healthy related quality of life questionnaires and the clinical data cheet.The data was analyzed by SPSS program.

Results: The mean age of the patients was more than 55 years, 75.9% of them are males, 45.4% of them are free workers. 91.4% of the patients complain of fatigue, and 73.0% have right hypochondrium pain and ascites. Positive autoantibody represents 41.3% of the causes of CLD. About 48.3% the patients are in class B followed by class C according to the Child-Pugh Score and the mean ± SD Score of the MELD score is16.3 ± 11.27 for the disease severity. 41.4 %of patients have slight problem in mobility and 43.7% in usual activity, and half of them have problems in self-care, and approximately one third of them have slight problems associated with pain

and disomfort while one third have no problem with anxiety or depression. The majority of patients suffer from the jaundice and loss of appetite .

Conclusion: The overall LDSI is low in the hindrance of the patient regarding daily activities and social life. There are statistically significant differences among patients' EQ-5D- 5L scores regarding the age, the level of education, the occupation, the monthly income and the yearly income. There are also statistically significant differences among patients' Child-Pugh scores regarding the liver disease symptom index LDSI, while there are no statistically significant differences among patients' Child-Pugh scores regarding the EQ-5D-5L scores.

الملخص

الخلفية: مرض الكبد المزمن هو سبب رئيسي للوفيات والمراضة في جميع أنحاء العالم. إنه السبب الحادي عشر للوفاة والسبب الرئيسي الخامس عشر للمراضة. نوعية الحياة المتعلقة بالصحة (HRQL)هي بناء متعدد الأبعاد يشمل الجوانب النفسية والاجتماعية والوظيفية للمرض بالإضافة إلى جوانبه الجسدية.

الهدف من الدراسة: كان الهدف من الدراسة هو تقييم نوعية الحياة المتعلقة بالصحة HRQOLبين مرضى أمراض الكبد المزمنة في المستشفيات العامة في مدينة صنعاء.

المنهجية: تم استخدام دراسة مقطعية وصفية قائمة على المستشفى. كان حجم العينة ١٩٧ مريضا. تم الاتصال بالعينة في المستشفيات العامة في الأجنحة الطبية وأقسام العيادات الخارجية للمرضى. تتكون أدوات جمع البيانات من جزأين: استبيانات جودة الحياة المتعلقة بالصحة وصحيفة البيانات السريرية. تم تحليل البيانات بواسطة برنامج.SPSS

النتائج: كان متوسط عمر المرضى أكثر من ٥٥ سنة ٧٥.٩٪ منهم ذكور و٤٥.٤٪ عامل حر. ٩١.٤٪ من المرضى يشكون من التعب و٧٣.٠٪ يعانون من ألم المراق الأيمن والاستسقاء. يمثل الجسم المضاد الإيجابي ٤١.٣٪ من أسباب .CLD حوالي ٤٨.٣ ٪ من المرضى في الفئة B متبوعًا بالفئة C وفقًا لدرجة Child-Pugh ومتوسط SD ± من درجة MELD هو ١٦.٣ ± ١١.٢٧ لشدة المرض. يعاني ٤١.٤٪ من المرضى من مشكلة طفيفة في الحركة و٤٣.٧٪ في النشاط المعتاد، ونصفهم يعانون من مشكلة في الرعاية الذاتية، وحوالي ثلثهم يعانون من مشاكل طفيفة في الألم وعدم الراحة بينما لا يعاني ثلثهم من القلق أو الاكتئاب. يعاني غالبية المرضى من اليرقان وانخفاض الشهية.

الخلاصة: إن LDSI الكلي منخفض في إعاقة أنشطة المريض اليومية والحياة الاجتماعية. توجد فروق ذات دلالة إحصائية بين درجة EQ-5D-5L للمرضى فيما يتعلق بالعمر ومستوى التعليم والمهنة والدخل الشهري والدخل السنوي. تم العثور على فروق ذات دلالة إحصائية بين

درجة Child-Pugh للمرضى فيما يتعلق بمؤشر أعراض أمراض الكبد LDSI، بينما لا توجد فروق ذات دلالة إحصائية بين درجة Child-Pugh للمرضى فيما يتعلق بنتيجة EQ-5D-5L.

CHAPTER ONE
INTRODUCTION

1.1 Background

Chronic liver diseases are a set of disease characterized by decreased hepatic function as a result of chronic inflammation or insult to the liver. Chronic liver diseases (CLD) are considered a major public health burden at a global level (Gazineo et al., 2021).

The burden of liver disease is increasing, largely due to the combined impact of alcohol related to liver disease (ARLD), non-alcoholic fatty liver disease (NAFLD), and viral hepatitis). Liver disease is often sub- clinical until more advanced disease is established, resulting in an increasing incidence of cirrhosis in many countries (Orr et al., 2014).

A significant increase in morbidity and mortality of CLDs has been observed worldwide over the last decades in contrast to the decrease in a cardiovascular diseases, which instead constituted the main critical health challenge in many industrialized countries during the second half of twentieth century (Gazineo et al., 2021).

The main causes of cirrhosis and liver cancer in Europe are viral hepatitis B and C, alcohol consumption and metabolic syndrome (Gazineo et al., 2021).

Over the last few decades, assessing the quality of life (QoL) of individuals with diseases has become common clinical practice. as a consequence of increase in survival of patients with chronic diseases (Gomes, Lima, Bueno, Araújo, & Souza, 2015).

The term health related quality of life (HRQoL) reflects the impact of the disease upon person's quality of life. It is a subjective, multidimensional concept addressing various aspects of the individual's life such as age, gender, socioeconomic status, type of illness, and treatment that should be considered during patient evaluation (Gomes et al., 2015).

CLD has a negative impact on HRQoL since patients often present asthenia, indisposition, abdominal, muscle, and or joint pain or discomfort, loss of appetite, insomnia, and complications related to liver cirrhosis, such as ascites, variceal bleeding in the stomach and esophagus, and hepatic encephalopathy. Moreover, CLD is linked to job loss, impaired functioning, mood swings, anxiety, low self-esteem, depression, and other emotional problems that severely affect QoL and well-being (Gomes et al., 2015).

1.2 Significant

Chronic liver disease (CLD) is one of the leading causes of morbidity and mortality in today's world. It is increasingly becoming more prevalent, and part of this rise can be attributed to improved detection and opportunistic screening. Medical researchers are trying continuously to analyze this problem and searching for factors that aid in its prevention (Banait, Jin, Campos, & Pérez-Prado, 2021).

Chronic liver disease is a leading cause of mortality and morbidity across the world. It is the 11th leading cause of death and 15th leading cause of morbidity, accounting for 2.2% of deaths and 1.5% of disability-adjusted life years worldwide in 2016 (Banait et al., 2021).

CLD caused 1.32 million deaths in 2017, approximately two-thirds men and one-third among women (Cheemerla & Balakrishnan, 2021).

Health-related quality of life (HRQL) is a multidimensional construct that includes the psychological, social, and functional aspects of an illness as well as its physical aspects. HRQL is usually assessed with the help of self-reported measures, which reflect the patient's appraisal of his or her own illness and its accompanying impairments (Schulz, Kroencke, Ewers, Schulz, & Younossi, 2008).

CLDs have been long recognized and associated with depression with an occurrence reported 15% of patients waiting for a liver transplant and 57% of patients with cirrhosis. Depressive symptoms have been associated with reduced HRQOL and worsened cognitive function. CLDs severity is normally considered by physicians an important prognostic factor, and previous studies found that CLDs severity has an impact on patient's HRQOL, affecting both physical and psycho-social aspects. However, to the best of our knowledge, few studies have been conducted, especially in the Italian context, on how CLDs severity influences both physical and psycho-social aspects of HRQOL, such as self-care, daily life activities, and depression. (Gazineo D, et al, 2021) Therefore, the aim of the present study was to evaluate if CLD severity may influence the HRQOL and lead to the development of depressive symptoms. It is expected that the severity of disease may be related to a little perception of HRQOL and to an increased incidence of depressive symptoms. The results of this study could be used to develop the interventions and policies aiming to improve the quality of life for CLD patients.

1.3 Objectives of the Study

1.3.1 General objective:

The general objective of the study was to evaluate Health Related Quality of life HRQOL among patients with Chronic Liver Diseases at Public Hospitals in Sana'a City.

1.3.2 Specific objective:

1. To identify the HRQOL level among CLD patients.
2. To determine the differences of the HRQoL scores between demographic groups among CLD patients.
3. To identify the association between disease severity and HRQoL.

CHAPTER TWO

LITERATURE REVIEW

2.1 Definition of Chronic liver disease:

Is a progressive deterioration of liver functions for more than six months. Liver functions include the production of clotting factors and other proteins, detoxification of harmful products of metabolism, and excretion of bile. This is a continuous process of inflammation, destruction, and regeneration of liver parenchyma leading to fibrosis and cirrhosis. Cirrhosis is a final stage of chronic liver disease that results in disruption of liver architecture, the formation of widespread nodules, vascular reorganization, neo-angiogenesis, and deposition of an extracellular matrix. The underlying mechanism of fibrosis and cirrhosis at a cellular level is the recruitment of stellate cells and fibroblasts that cause fibrosis, while parenchymal regeneration relies on hepatic stem cells. (Sharma & Nagalli, 2021).

2.2 Epidemiology of Chronic Liver Disease

-Chronic liver disease (CLD) and cirrhosis account for >44,000 deaths in the United States and 2 million deaths worldwide each year, in addition to a high burden of disability and increased health care utilization (Moon, Singal, & Tapper, 2020).

-Globally, 1.5 billion persons had CLD in 2017, most commonly resulting from NAFLD (60%), HBV (29%), HCV (9%), and ALD (2%)(Moon et al., 2020).

-Globally, 71 million people are infected with chronic HCV, with 51% concentrated in six countries: India, China, Egypt, Russia, United States, and Pakistan. (Sharma & Nagalli, 2021).

-NAFLD has a 24% estimated global prevalence rate, and it is >30% in the Middle East and South America. Up to 59% of NAFLD cases are of the nonalcoholic steatohepatitis (NASH) phenotype, the main disease subtype with risk for fibrotic progression to cirrhosis(Sharma & Nagalli, 2021).

-Worldwide, 257 million (3.5%) people had chronic HBV infection in 2015. Western Pacific nations (6.2%) and Africa (6.1%) had the highest prevalence of HBV and accounted for more than two thirds of all cases. A recent survey from the National Health and Nutrition Examination Survey (NHANES) estimated the US prevalence of chronic HBV as 840,000 (0.35%) overall in 2011 to 2016, varying from 3.85% among Asian immigrants and 0.79% among American-born Asians. (Sharma & Nagalli, 2021)

2.3 Pathophysiology

The liver is the largest organ in the body, comprising about 1/50 of adult body weight. It fulfills diverse vital functions, including protein, fat, and carbohydrate metabolism; vitamin and mineral storage; digestion of food; detoxification of wastes; and pathogen and endotoxin clearance. Eighty percent of the liver volume is composed of hepatocytes, the

parenchymal cells responsible for the metabolic and detoxifying functions. Other cell types, including endothelial, hepatic stellate (HSC), and Kupffer cells (KC) closely interact to participate in immune defense and nutrient storage as well as in maintaining the liver histological structure. Long-term and continuous damage as well as sustained inflammation lead to unbalanced homeostasis and progressive loss of liver function. These events are the hallmark of chronic liver disease, whereby repeated cycles of hepatocyte death, inflammation, and compensatory proliferation may lead to hepatic fibrosis. Fibrosis is a reversible wound-healing response characterized by the accumulation of extracellular matrix (ECM). When the insult is acute or self-limited, these changes are transient, and liver architecture is restored. However, when the injury is maintained over time, chronic inflammation and accumulation of ECM persist, leading to a progressive substitution of liver parenchyma by scar tissue and a loss of endothelial cell fenestrations. Such alterations lie at the basis of the disturbances in solute exchange between blood and hepatocytes in liver.1 This process results in cirrhosis, the final consequence of progressive fibrosis, considered irreversible and characterized by a distortion of the liver parenchyma and vascular architecture. Notably, cirrhosis is the ninth leading cause of death in the Western world (Cohen, Horton, & Hobbs, 2011).

Another cause of chronic liver damage is non-alcoholic fatty liver disease (NAFLD), which consists of a range of related disorders, from simple steatosis to steatohepatitis, that affects a third of adults in Western countries.7 The earliest stage of this disease is hepatic steatosis, which is characterized by the deposition of triglycerides (TG) as lipid droplets in the

cytoplasm of hepatocytes. Hepatic steatosis is often self-limited, but it can progress to NASH (non-alcoholic steatohepatitis), characterized by the presence of hepatocyte injury (hepatocyte ballooning and cell death), an inflammatory infiltrate, and/or collagen deposition. NASH is associated with obesity, type 2 diabetes mellitus, and dyslipidemia. Recently, it has been recognized as a major cause of liver fibrosis, and between 10 and 29% of individuals with NASH develop cirrhosis within 10 years. (Mendez-Sanchez)

A third major cause of chronic liver injury is long-term and excessive alcohol consumption, which causes alcoholic liver disease (ALD), a major source of alcohol related morbidity and mortality. It is estimated that 10–15 % of alcoholics will develop cirrhosis. This observation suggests that other factors contribute to determining the evolution of alcohol-related liver disease, among these certain polymorphisms in alcohol metabolizing enzymes, obesity, exposure to other hepatotoxins, and HCV/ HBV infection. ALD consists of a spectrum of liver abnormalities, ranging from simple fatty liver (steatosis) to steatohepatitis, and cirrhosis that can eventually lead to liver cancer.11 The participation of alcohol metabolites, inflammatory cytokines, reactive oxygen/nitrogen species, and bacterial translocation from the gut are widely recognized as the combined cause of alcohol-induced hepatic damage. Thus, ALD involves a complex orchestration between activated HSCs, apoptotic hepatocytes, and KCs. In this regard, ethanol has a dual function in KC, depressing KC phagocytosis and the clearance of endobacteria, and increasing gut permeability to endotoxins. This potentiates inflammatory responses by KCs and subsequent damage (Armengol et al., 2013)

2.4 Etiology

Viral hepatitis This must be considered in anyone presenting with hepatitis liver blood tests (high transaminases).

Alcoholic liver disease Alcohol is one of the most common causes of chronic liver disease worldwide, with consumption continuing to increase in many countries. Patients with ALD may also have risk factors for other liver diseases (e.g., coexisting NAFLD or chronic viral hepatitis infection), and these may interact to increase disea

(Penman, Ralston, Strachan, & Hobson, 2022).

Toxic And Drug-Induced Hepatitis

- Dose-dependent (direct hepatotoxins) onset is within 48 h, predictable, necrosis around terminal hepatic venule—e.g., carbon tetrachloride, benzene derivatives, mushroom poisoning, acetaminophen, or microvascular steatosis (e.g., tetracyclines, valproic acid).

(Penman et al., 2022).

Primary Biliary Cirrhosis (PBC) PBC is a progressive nonsuppurative destructive intrahepatic cholangitis. Strong female predominance, median age of 50 years. Presents as asymptomatic elevation in alkaline phosphatase (better prognosis) or with pruritus, progressive jaundice, consequences of

impaired bile excretion, and ultimately cirrhosis and liver failure (Jameson et al., 2020).

- Inherited liver diseases

The inherited diseases are an important and probably underdiagnosed group of liver diseases. In addition to the ‘classical’ conditions, such as haemochromatosis and Wilson’s disease, the important role played by the liver in the expression of the inborn errors of metabolism should be remembered, as should the potential for genetic underpinning for intrahepatic cholestasis.

- Haemochromatosis

Haemochromatosis is a condition in which the amount of total body iron is increased; the excess iron is deposited in, and causes damage to, several organs, including the liver. It may be primary or secondary to other diseases.

Wilson’s disease (hepatolenticular degeneration) is a rare but important autosomal recessive disorder of copper metabolism caused by a variety of mutations in the ATP7B gene on chromosome 13. T

- Gilbert’s syndrome

Gilbert’s syndrome is by far the most common inherited disorder of bilirubin metabolism (Penman et al., 2022).

Autoimmune liver and biliary disease the liver is an important target for autoimmune injury. The clinical picture is dictated by the nature of the autoimmune process and, in particular, the target cell for immune injury. The disease patterns are quite distinctive for primary hepatocellular injury (in the context of autoimmune hepatitis) and biliary epithelial cell injury (primary biliary cholangitis and primary sclerosing cholangitis). Autoimmune hepatitis

(Penman et al., 2022).

Primary Biliary Cirrhosis Pathogenesis. Primary biliary cirrhosis is an idiopathic autoimmune disorder that occurs more often in middle-aged women. Bilirubin levels do not elevate until the disease is extremely far advanced, which is usually after 5 to 10 years. Primary biliary cirrhosis has a strong association with other autoimmune diseases, such as Sjögren syndrome, rheumatoid arthritis, and scleroderma (Marsano et al., 2016).

- ♦ Primary sclerosing cholangitis

Primary sclerosing cholangitis (PSC) is a cholestatic liver disease caused by diffuse inflammation and fibrosis;

- (Jameson et al., 2020).

2.5 Clinical features of chronic liver disease.

2.5.1 Symptoms:

The clinical presentation is highly variable. Some patients are asymptomatic and the diagnosis is made incidentally at ultrasound or at surgery. Others present with isolated hepatomegaly, splenomegaly, signs of portal hyper-tension or hepatic insufficiency. When symptoms are present, they are often non-specic and include weakness, fatigue, muscle cramps, weight loss, upper abdominal discomfort, abdominal distinction, anorexia, nausea, vomiting, diarrhea, vague right upper quadrant (RUQ) pain, fatigue, weakness fever, pruritus. amenorrhea, impotence, infertility, Osteoporosis and hypothyroidism are found in20to 30% of patients, (Penman et al., 2022).

jaundice: jaundice refers to yellowing of skin, sclerae, and mucosae when the plasma bilirubin exceeds 40 μmol/L (~2.5 mg/dL. (Jameson et al., 2020).

Cirrhosis will occasionally present because of shortness of breath due to a large right pleural effusion, or with hepatopulmonary syndrome: This condition is characterized by resistant hypoxemia (PaO_2 < 9.3 kPa (70 mmHg)), intrapulmonary vascular dilatation in patients with cirrhosis, and portal hypertension. Clinical features include finger clubbing, cyanosis and a characteristic reduction in arterial oxygen saturation on standing (orthodeoxia). The hypoxia is due to intrapulmonary shunting through direct arteriovenous communications. Nitric oxide (NO) overproduction may be important in pathogenesis (Wilkinson et al., 2017).

2.5.2 Signs

Hepatomegaly: is common when the cirrhosis is due to alcoholic liver disease or haemochromatosis: An inherited disorder of iron metabolism in which intestinal iron absorption leads to iron deposition in joints, liver, heart, pancreas, pituitary, adrenals, and skin. Middle aged men are more frequently and severely affected than women, in whom the disease tends to present ~10yrs later the Hepatocellular cancer develops in 15 to 20% of patients. Restrictive cardiomyopathy develops in approximately 15% of patients. Arthralgias, skin hyperpigmentation, diabetes, and hypogonadism are also common (Marsano et al., 2016).

Progressive hepatocyte destruction and fibrosis gradually reduce liver size as the disease progresses in other causes of cirrhosis. The liver is often hard, irregular and non-tender. Jaundice is mild when it first appears and is due primarily to a failure to excrete bilirubin. Palmar erythema (redness over the thenar and hypothenar eminences) can be seen early in the disease but is of limited diagnostic value, as it occurs in many other conditions associated with a hyper-dynamic circulation, including pregnancy, as well as being found in some healthy people. Spider telangiectasias (or spider naevi) occur and comprise a central arteriole (that occasion-ally raises the skin surface), from which small vessels radiate.

They blanch with pressure and refill from the center outwards, are usually found on the hands, face and upper chest. One or two small spider telangiectasias may be present in up to 15% of young healthy adults and may occur transiently in greater numbers in the third trimester of pregnancy, but otherwise multiple spider telangiectasias are a strong

indicator of liver disease. Florid spider telangiectasia and gynecomastia are most common in alcohol related cirrhosis, possibly related to phytoestrogens in alcoholic drinks. Pigmentation is most striking in haemochromatosis and in any cirrhosis associated with prolonged cholestasis. Clubbing of the fingers and toes is not a sign of cirrhosis but is seen in combination with hypoxia in hepatopulmonary syndrome. scleral icterus, parotid and lacrimal gland enlargement, Dupuytren's, hepatosplenomegaly, ascites, gastrointestinal bleeding (e.g., varices), associated with a worse prognosis (Jameson et al., 2020).

Esophagogastric Varices: common manifestation of chronic liver disease. the risk of a variceal bleed occurring within 2 years varies from 7% for small varices up to 30% for large varices. About one-third of pts with cirrhosis have varices, and one-third of pts with varices will develop bleeding. Bleeding is a life-threatening complication; risk of bleeding correlates with variceal size and location, the degree of portal hypertension (portal venous pressure >12 mmHg), and the severity of cirrhosis (Wilkinson et al., 2017).

Hepatic encephalopathy: is a neuropsychiatric syndrome caused by liver disease that occurs in 30%–40% of patients with cirrhosis. It causes a spectrum of symptoms ranging from mild fluctuating cognitive impairment to coma. The degree of encephalopathy can be graded from 1 to 4, and this is useful in assessing progression or response to therapy. The earliest features are very mild and easily overlooked, but as the condition becomes more severe, inability to concentrate, delirium, disorientation, drowsiness, slurring of speech and eventually coma develop. Seizures are rare.

Examination usually shows flapping tremor (asterixis), inability to perform simple mental arithmetic tasks or to draw objects such as a star (constructional apraxia, and, as the condition progresses, hyper-reflexia and bilateral extensor plantar responses. Hepatic encephalopathy rarely causes focal neurological signs; if these are present, other causes must be sought. Fetor hepaticus, a sweet musty odour to the breath, is usually present but is more a sign of liver failure and portosystemic shunting than of hepatic encephalopathy. Rarely, chronic hepatic encephalopathy (hepatocerebral degeneration) gives rise to variable combinations of cerebellar dysfunction, Parkinsonian syndromes, spastic paraplegia and dementia (Jameson et al., 2020).

ascites: Ascites means the accumulation of free fluid in the peritoneal cavity and is usually because of malignant disease, cirrhosis or heart failure; however, primary disorders of the peritoneum and visceral organs can produce ascites, even in a patient with chronic liver disease. Clinical findings in such patients are abdominal distension, shifting dullness, and a fluid wave. Tense ascites can lead to shortness of breath or early satiety. When the albumin level is low in the ascitic fluid, the gradient, or difference between the ascites and the serum, is high. When this gradient, or SAAG, is >1.1, portal hypertension, as from cirrhosis, is generally the cause. When the SAAG is <1.1, it means the ascitic fluid albumin level is high. Cancer and infections generally give a SAAG <1(Marsano et al., 2016).

Endocrine changes are noticed more readily in men, who show loss of male hair distribution and testicular atrophy. Gynecomastia is common and

can be due to drugs such as spironolactone, Leukonychia (white nails with lunulae undemarcated) from hypoalbuminemia, Terry's nails (white proximally but distal ⅓ reddened by telangiectasias) are a low albumin level, an elevated prothrombin time. The prothrombin time is prolonged because of the loss of ability to synthesize clotting factors and Spontaneous bacterial peritonitis, Anaemia is common and often multifactorial, due to a combination of chronic inflammation, bone marrow suppression, haemolysis or chronic blood loss (Wilkinson et al., 2017).

Chronic hepatitis B: Hepatitis B The Hepatitis B virus (HBV) of a core containing DNA and a DNA polymerase enzyme needed for virus replication, surrounded by surface protein. The virus and an excess of its surface protein (known as hepatitis B surface antigen, HBsAg) circulate in the blood. The virus replicates and assembles within hepatocytes but is not directly cytotoxic; hepatocyte damage occurs during immune-mediated clearance of infected hepatocytes. Hepatitis B is one of the most common causes of chronic liver disease and hepatocellular carcinoma worldwide. Approximately 250 million people have chronic HBV infection. There is large regional variation, with the highest rates seen in the Western Pacific and African regions. Hepatitis B can cause acute or chronic infection. The risk of developing chronic HBV infection depends on the source and timing of exposure. Infections may occur via a number of routes. In endemic areas, vertical transmission from mother to child in the perinatal period is the most common cause of infection and carries the highest risk of ongoing chronic infection (90%–95%). In contrast, exposure to HBV at an older age is much more likely to result in an acute hepatitis, with chronic infection developing in less than 5% of adult-acquired HBV. In perinatal infection, adaptive

immune responses to HBV may be absent initially, with apparent immunological tolerance. Although HBV specific T-cells are detectable in this setting, they are weak and functionally impaired. The mechanisms underlying this are incompletely understood. Chronic hepatitis can lead to cirrhosis or hepatocellular carcinoma, usually after decades of infection Chronic HBV infection is a dynamic process that can be divided into five phases these are not necessarily strictly sequential, however, and not all patients will go through all phases. Phases are considered as either ‘infection’ where circulating HBsAg is detectable but is not resulting in any current liver injury, or ‘hepatitis’ where this is accompanied by liver inflammation and fibrosis (Robinson, 2023).

Fatigue is a common symptom, and persistent or intermittent jaundice is a common feature in severe or advanced cases. Intermittent deepening of jaundice and recurrence of malaise and anorexia, as well as worsening fatigue, are reminiscent of acute hepatitis; such exacerbations may occur spontaneously, often coinciding with evidence of virologic reactivation; may lead to progressive liver injury; and, when superimposed on well-established cirrhosis, may cause hepatic decompensation. Complications of cirrhosis occur in end-stage chronic hepatitis and include ascites, edema, bleeding gastroesophageal varices, hepatic encephalopathy, coagulopathy, or hypersplenism. Occasionally, these complications bring the patient to initial clinical attention. Extrahepatic complications of chronic hepatitis B, similar to those seen during the prodromal phase of acute hepatitis B, are associated with deposition of circulating hepatitis B antigen–antibody immune complexes. These include arthralgias and arthritis, which are common, and the more rare purpuric cutaneous lesions (leukocytoclastic

vasculitis), immune-complex glomerulonephritis, and generalized vasculitis (polyarteritis nodosa) (Kasper et al., 2015).

Hepatitis C: This is caused by an RNA flavivirus. Acute symptomatic infection with hepatitis C is rare. Most individuals are unaware of when they became infected and are identited only when they develop chronic liver disease. Around 70% of individuals exposed to the virus become chronically infected and late spontaneous viral clearance is rare. It is estimated that around 70 million individuals have chronic hepatitis C worldwide, with the highest prevalence in the Eastern Mediterranean region. There is no active or passive protection against hepatitis C virus (HCV).

Hepatitis C infection is usually identited in asymptomatic individuals screened because they have risk factors for infection, such as previous injecting drug use or have incidentally been found to have abnormal liver blood tests. Although most people remain asymptomatic until progression to cirrhosis occurs, fatigue can complicate chronic infection and is unrelated to the degree of liver damage. If hepatitis C infection is left untreated, progression from chronic hepatitis to cirrhosis may occur, with 20% developing cirrhosis over 20 years. Risk factors for progression include male gender, immunosuppression (such as co-infection with HIV), prothrombotic states and heavy alcohol misuse. Once cirrhosis is present, 2%–5% per year will develop primary hepatocellular carcinoma, although this rate falls by around 75% following successful antiviral therapy (Penman et al., 2022).

Clinical features of chronic hepatitis C are similar to those described above for chronic hepatitis B. Generally, fatigue is the most common symptom; jaundice is rare. Immune complex-mediated extrahepatic complications of chronic hepatitis C are less common than in chronic hepatitis B (despite the fact that assays for immune complexes are often positive in patients with chronic hepatitis C), with the exception of essential mixed cryoglobulinemia (Chap. 360), which is linked to cutaneous vasculitis and membranoproliferative glomerulonephritis as well as lymphoproliferative disorders such as B-cell lymphoma and unexplained monoclonal gammopathy. In addition, chronic hepatitis C has been associated with extrahepatic complications unrelated to immune-complex injury. These include Sjögren's syndrome, lichen planus, porphyria cutanea tarda, type 2 diabetes mellitus, and the metabolic syndrome (including insulin resistance and steatohepatitis). Laboratory features of chronic hepatitis C are similar to those in patients with chronic hepatitis B, but aminotransferase levels tend to fluctuate more (the characteristic episodic pattern of aminotransferase activity) and to be lower, especially in patients with long-standing disease. An interesting and occasionally confusing finding in patients with chronic hepatitis C is the presence of autoantibodies. Rarely, patients with autoimmune hepatitis (see below) and hyperglobulinemia have false-positive immunoassays for anti-HCV. On the other hand, some patients with serologically confirmable chronic hepatitis C have circulating anti-LKM. These antibodies are anti-LKM1, as seen in patients with autoimmune hepatitis type 2 (see below), and are directed against a 33-aminoacid sequence of cytochrome P450 IID6. The occurrence of anti-LKM1 in some patients with

chronic hepatitis C may result from the partial sequence homology between the epitope recognized by anti-LKM1 and two segments of the HCV polyprotein. In addition, the presence of this autoantibody in some patients with chronic hepatitis C (Kasper et al., 2015).

Alcoholic liver Disease: Chronic and excessive alcohol ingestion is one of the major causes of liver disease. The pathology of alcoholic liver disease consists of three major lesions, with the progressive injury rarely existing in a pure form: (1) fatty liver, (2) alcoholic hepatitis, and (3) cirrhosis. Fatty liver is present in >90% of daily as well as binge drinkers. A much smaller percentage of heavy drinkers will progress to alcoholic hepatitis, thought to be a precursor to cirrhosis. The prognosis of severe alcoholic liver disease is dismal; the mortality of patients with alcoholic hepatitis concurrent with cirrhosis is nearly 60% at 4 years. Although alcohol is considered a direct hepatotoxin, only between 10 and 20% of alcoholics will develop alcoholic hepatitis. The explanation for this apparent paradox is unclear but involves the complex interaction of facilitating factors, such as drinking patterns, diet, obesity, and gender. There are no diagnostic tools that can predict individual susceptibility to alcoholic liver disease (Kasper et al., 2015).

Pathophysiology: Alcohol reaches peak blood concentrations after about 20 minutes, although this may be influenced by stomach contents. It is metabolised almost exclusively by the liver via one of two pathways Approximately 80% of alcohol is metabolised by alcohol dehydrogenase to acetaldehyde, and then by aldehyde dehydrogenase to acetate. This process converts NAD (nicotinamide adenine dinucleotide) to NADH, altering the

redox potential of the cell. Up to 20% of alcohol is metabolised by the microsomal ethanol-oxidising system (MEOS), predominantly through the inducible cytochrome p450 2E1, also generating acetaldehyde along with oxygen free radicals. The CYP2E1 enzyme also metabolises acetaminophen, and hence chronic alcoholics are more susceptible to hepatotoxicity from low doses of paracetamol. Acetaldehyde from either pathway is toxic and causes structural alterations of cellular proteins. This results in altered mitochondrial function and generation of reactive oxygen species, leading to oxidative stress. The altered ratio of reduced/oxidised NAD interrupts beta-oxidation of fatty acids and causes upregulation of sterol regulatory element-binding protein 1 (SREBP1), promoting fatty acid synthesis. Damage to hepatocytes leads to stimulation of immune cells via damage-associated molecular patterns (DAMPs) such as mitochondrial DNA or necrotic debris. Alcohol also affects the gut leading to dysbiosis and increased gut permeability, delivering pathogen-associated molecular patterns (PAMPs) such as lipopolysaccharide and bacterial DNA via the portal vein which stimulate immune cells, leading to release of tumour necrosis factor alpha (TNF-α) and interleukin (IL)-1, IL-2 and IL-8. All of these cytokines have been implicated in the pathogenesis of liver fibrosis. The pathological features of ALD are shown. The most common manifestation is accumulation of triglycerides within hepatocytes (hepatic steatosis), or alcohol-related fatty liver. This progresses in some patients to cause hepatocyte injury and inflammation, or steatohepatitis. This can present acutely with a clinical syndrome of rapid onset jaundice (alcoholic hepatitis) or can result in progressive fibrosis leading to cirrhosis; these two

presentations can coexist. Iron deposition is common and does not necessarily indicate haemochromatosis (Penman et al., 2022).

The clinical manifestations of alcoholic fatty liver are subtle and characteristically detected as a consequence of the patient's visit for seemingly unrelated matter. Previously unsuspected hepatomegaly is often the only clinical finding. Occasionally, patients with fatty liver will present with right upper quadrant discomfort, nausea, and, rarely, jaundice. Differentiation of alcoholic fatty liver from nonalcoholic fatty liver is difficult unless an accurate drinking history is ascertained. In every instance where liver disease is present, a thoughtful and sensitive drinking history should be obtained. Standard, validated questions accurately detect alcohol-related problems Alcoholic hepatitis is associated with a wide gamut of clinical features. Fever, spider nevi, jaundice, and abdominal pain simulating an acute abdomen represent the extreme end of the spectrum, while many patients will be entirely asymptomatic. Portal hypertension, , can occur in the absence of cirrhosis. Recognition of the clinical features of alcoholic hepatitis is central to the initiation of an effective and appropriate diagnostic and therapeutic strategy. It is important to recognize that patients with alcoholic cirrhosis often exhibit clinical features identical to other causes of cirrhosis (Kasper et al., 2015). Alcoholic cirrhosis Palmar erythema, Dupuytren's contracture (thickening of the palmar fascia) is associated with chronic alcohol excess, but is not predictive of underlying liver disease, spider naevi and gynecomastia are more common in alcoholic cirrhosis than in cirrhosis of other aetiologies. Alcoholic cirrhosis often presents with a serious complication, such as variceal haemorrhage or ascites, and only half of such patients will survive for 5 years from

presentation. However, most who survive the initial illness and who become abstinent will survive beyond 5 years (Robinson, 2023).

Nonalcoholic fatty liver disease (NAFLD):

Is the most common chronic liver disease in many parts of the world, including the United States. Population-based abdominal imaging studies have demonstrated fatty liver in at least 25% of American adults. Because the vast majority of these subjects deny hazardous levels of alcohol consumption (defined as greater than one drink per day in women or two drinks per day in men), they are considered to have NAFLD. NAFLD is strongly associated with overweight/obesity and insulin resistance. However, it can also occur in lean individuals and is particularly common in those with a paucity of adipose depots (i.e., lipodystrophy). Ethnic/racial factors also appear to influence liver fat accumulation; the documented prevalence of NAFLD is lowest in African Americans (~25%), highest in Americans of Hispanic ancestry (~50%), and intermediate in American whites (~33%). NAFLD encompasses a spectrum of liver pathology with different clinical prognoses. The simple accumulation of triglyceride within hepatocytes (hepatic steatosis) is on the most clinically benign extreme of the spectrum. On the opposite, most clinically ominous extreme, are cirrhosis (Chap. 365) and primary liver cancer (Chap. 111). The risk of developing cirrhosis is extremely low in individuals with chronic hepatic steatosis, but increases as steatosis becomes complicated by histologically conspicuous hepatocyte death and inflammation (i.e., nonalcoholic steatohepatitis (NASH)). NASH itself is also a heterogeneous condition; sometimes it improves to steatosis or normal histology, sometimes it

remains relatively stable for years, but sometimes it results in progressive accumulation of fibrous scar that eventuates in cirrhosis. Once NAFLD-related cirrhosis develops, the annual incidence of primary liver cancer is 1% (Kasper et al., 2015).

Patients with NASH have significantly higher rates of fibrosis progression than those with simple steatosis. Due to its increasing prevalence, NAFLD cirrhosis is predicted to become the main aetiology in patients undergoing liver transplantation during the next 5 years (Penman et al., 2022).

Clinical features NAFLD: NAFLD is frequently asymptomatic, although it may be associated with fatigue and mild right upper quadrant discomfort. It is commonly identied as an incidental biochemical abnormality during routine blood tests or as a fatty liver on abdominal imaging. Alternatively, patients may present late in the natural history of the disease with complications of cirrhosis and portal hypertension, such as variceal haemorrhage, or with hepatocellular carcinoma (Robinson, 2023).

Obesity is present in 50–90% of subjects. Most patients with NAFLD also have other features of the metabolic syndrome. Some have subtle stigmata of chronic liver disease, such as spider angiomata, palmer erythema, or splenomegaly. In a small minority of patients with advanced NAFLD, complications of end-stage liver disease (e.g., jaundice, features of portal hypertension such as ascites or variceal hemorrhage) may be the initial findings. The association of NAFLD with obesity, diabetes, hypertriglyceridemia, hypertension, and cardiovascular disease is well known. Other associations include chronic fatigue, mood alterations,

obstructive sleep apnea, thyroid dysfunction, and chronic pain syndrome. NAFLD is an independent risk factor for metabolic syndrome (Kasper et al., 2015).

Autoimmune hepatitis: Autoimmune hepatitis (AIH) is a disease of immune-mediated injury targeting hepatocytes, which can present either as an acute severe hepatitis or chronic hepatitis leading to cirrhosis. It is a lifelong disease which often runs a relapsing and remitting course. It can develop at any age, with peaks around the second and sixth decades. It is more common in women with a 5:1 predominance. It has a strong association with other autoimmune diseases:

- Autoimmune thyroiditis.
- Systemic lupus erythematosus.
- Rheumatoid arthritis.
- Primary sclerosing cholangitis.
- Coeliac disease.
- Type 1 diabetes.
- Dermatomyositis.
- Coombs-positive haemolyticanaemia Ulcerative colitis (Robinson, 2023).

Pathophysiology: AIH An inflammatory liver disease of unknown cause33 characterized by abnormal T-cell function and autoantibodies directed against hepatocyte surface antigens. AIH predominantly affects young or middle-aged women (bimodal, ie 10–30yrs—or >40yrs old). Up to 40% present with acute hepatitis and signs of autoimmune disease, eg fever, malaise, urticarial rash, polyarthritis, pleurisy, pulmonary infiltration,

or glomerulonephritis. The remainder present with gradual jaundice or are asymptomatic and diagnosed incidentally with signs of chronic liver disease. (Robinson, 2023))

Clinical features autoimmune hepatitis: Some patients may be asymptomatic, with a raised ALT detected on blood tests. The onset of symptoms is usually insidious, with fatigue, anorexia and arthralgia (Penman et al., 2022).

Autoimmune hepatitis has distinct features. Such patients are predominantly young to middle aged women with marked hyperglobulinemia and high-titer circulating ANAs. This is the group with positive lupus erythematosus (LE) preparations (initially labeled “lupoid “hepatitis) in whom other autoimmune features are common. malaise, amenorrhea, acne, arthralgias, and jaundice is common. Occasionally, arthritis, maculopapular eruptions (including cutaneous vasculitis), erythema nodosum, colitis, pleurisy, pericarditis, anemia, azotemia, and sicca syndrome (keratoconjunctivitis, xerostomia) occur. In some patients, complications of cirrhosis, such as ascites and edema (associated with portal hypertension and hypoalbuminemia), encephalopathy, hypersplenism, coagulopathy, or variceal bleeding may bring the patient to initial medical attention (Kasper et al., 2015).

Primary biliary cirrhosis: Pathogenesis. Primary biliary cirrhosis is an idiopathic autoimmune disorder that occurs more often in middle-aged women. Bilirubin levels do not elevate until the disease is extremely far advanced, which is usually after 5 to 10 years. Primary biliary cirrhosis has

a strong association with other autoimmune diseases, such as Sjögren syndrome, rheumatoid arthritis, and scleroderma (Marsano et al., 2016).

Clinical features PBC.

The patient Often asymptomatic and diagnosed after incidental finding increase ALP, Lethargy, sleepiness, and pruritus may precede jaundice by years. Signs: Jaundice; skin pigmentation; xanthelasma (Wilkinson et al., 2017).

systemic symptoms such as fatigue and generalised itch are common (Penman et al., 2022).

Primary sclerosing cholangitis: As in PBC, the cause of PSC remains unknown. PSC is a chronic cholestatic syndrome that is characterized by diffuse inflammation and fibrosis involving the entire biliary tree, resulting in chronic cholestasis. This pathologic process ultimately results in obliteration of both the intra and extrahepatic biliary tree, leading to biliary cirrhosis, portal hypertension, and liver failure. The cause of PSC remains unknown despite extensive investigation into various mechanisms related to bacterial and viral infections, toxins, genetic predisposition, and immunologic mechanisms, all of which have been postulated to contribute to the pathogenesis and progression of this syndrome. Pathologic changes that can occur in PSC show bile duct proliferation as well as ductopenia and fibrous cholangitis (pericholangitis). Often, liver biopsy changes in PSC are not pathognomonic, and establishing the diagnosis of PSC must involve imaging of the biliary tree. Periductal fibrosis is occasionally seen on biopsy specimens and can be quite helpful

in making the diagnosis. As the disease progresses, biliary cirrhosis is the final, end-stage manifestation of PSC. (Harjola et al., 2015)

Clinical features: The diagnosis is often made incidentally when persistently raised serum ALP is discovered in an individual with ulcerative colitis. Patients may present with episodes of biliary obstruction, or with symptoms of cirrhosis or portal hypertension. Common symptoms include fatigue, intermittent jaundice, weight loss, right upper quadrant abdominal pain and pruritus. Attacks of acute cholangitis are uncommon and usually follow biliary instrumentation (Penman et al., 2022).

2.6 Diagnosis

2.6.1 History:

Patient presents with signs and symptoms of chronic liver disease (e.g., alcohol abuse, risk of viral hepatitis, obesity) (Heidelbauch & Bruderly, 2006).

2.6.2 Physical examination:

Patient has hallmark findings consistent with chronic liver disease (Heidelbauch & Bruderly, 2006).

2.6.3 Laboratory evaluation

Complete blood count (CBC) with platelets, and a prothrombin time test should be performed (Heidelbauch & Bruderly, 2006).

2.6.4 Serological tests

Common tests in standard liver panels include the serum enzymes aspartate transaminase (AST), alanine transaminase (ALT), alkaline

phosphatase, and g glutamyl transferase; total, direct, and indirect serum bilirubin; and serum albumin. The ALT is thought to be the most cost-effective screening test for identifying metabolic or drug-induced hepatic injury, but like other liver function tests, it is of limited use in predicting degree of inflammation and of no use in estimating severity of fibrosis.

2.6.5 Radiological investigations

Although various radiographic studies may suggest the presence of cirrhosis, no test is considered a diagnostic standard. The major use of radiographic studies is to detect ascites, hepatosplenomegaly, hepatic or portal vein thromboses, and hepatocellular carcinoma, all of which strongly suggest cirrhosis (Heidelbauch & Bruderly, 2006).

Is one of the most common and affordable imaging studies in the case of chronic liver disease. Ultrasound detects the size, echogenicity nodularity of the liver, thereby diagnosing liver cirrhosis. (Sharma & Nagalli, 2021).

CT AND MRI

Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) generally are poor at detecting morphologic changes associated with early cirrhosis, but they can accurately demonstrate nodularity and lobar atrophic and hypertrophic changes, as well as ascites and varices in advanced disease. (Heidelbauch & Bruderly, 2006).

Transient elastography (TE) detects early stages of cirrhosis. It can also detect cardiovascular damage in patients with NAFLD. It works on two physical principles; strain displacement and shear wave imaging and

quantification. , TE is the most effective approach to diagnose cirrhosis in chronic liver disease.

Wedge hepatic venous pressure measures portal venous pressure in CLD.

Doppler scan can help in diagnosing Budd-Chiari and portal vein thrombosis.

EEG shows delta waves in hepatic encephalopathy.

An upper endoscopy can diagnose and treat esophageal varices. On endoscopy, we can measure the size of varices. Small varices are less than 5 mm, and large varices are greater than 5 mm (Sharma & Nagalli, 2021).

2.6.6 Liver biopsy

Obtaining liver tissue samples by liver biopsy (percutaneous, laparoscopic, surgical, transjugular) is obviously the most direct approach to the evaluation of hepatic fibrosis. Liver tissue samples can be used for assessing the topographical distribution of fibrosis by employing different stainings and, in addition, offer the possibility of performing molecular studies. (Pinzani, Rombouts, & Colagrande, 2005).

2.7 Preventive in Chronic Liver Disease

- Vaccination, recommendations for vaccination are outlined in the Centers for Disease Control and Prevention and Advisory Committee on Immunization Practices' guidelines, Follow-up testing is recommended for those who remain at risk of infection, (Terrault et al., 2018).

- Antiviral Prophylaxis Versus OnDemand Therapy, although many immunosuppressive and immunomodulating drugs have been associated with HBV reactivation (Terrault et al., 2018).

- Avoid alcohol of all types (beer, wine, liquor, mixed drinks) (T. R. Riley & Smith, 1999).

- Avoid the drug classes with known hepatotoxicity include antidepressants, nonsteroidal anti-inflammatory drug (Riley, T.R. et all 2001)

- iron overload must be distinguished from those with hereditary hemochromatosis, (T. Riley & Bhatti, 2001).

- Secondary prevention has as its aim the early diagnosis of excessive alcohol consumption (Silva et al., 2006).

Complication of chronic liver disease:

1.Nutrition:

is considered one of the most important prognostic factors in CLD. Malnutrition affects pre- and post-transplant survival, and nutritional assessment should be a priority in children with liver disease. It should be assumed that all children with CLD present with substrate and nutrient deficiencies for two reasons: impaired absorption or intake, and impaired hepatic homeostasis. (Tsouka & McLin, 2012).

2.Cirrhosis: -

Cirrhosis is characterised by diffuse hepatic fibrosis and nodule formation. It can occur at any age, has significant morbidity and is an important cause

of premature death. It is the most common cause of portal hypertension and its complications. Worldwide,

3.Hepatomegaly is common when the cirrhosis is due to alcoholic liver disease or haemochromatosis. Progressive hepatocyte destruction and fibrosis gradually reduce liver size as the disease progresses in other causes of cirrhosis. A reduction in liver size is especially common if the cause is viral hepatitis or autoimmune liver disease. The liver is often hard, irregular and non-tender.(Penman et al., 2022).

4.Portal hypertension: - One of the major complications of CLDs is Portal hypertension (PH), leads to the progression of portal vein-systemic collateral circulation that includes portal hypertensive gastropathy (PHG) and esophageal and gastric varices. A dreaded complication of portal hypertension is variceal bleeding.(Penman et al., 2022). A frequent reason behind disease and death in liver cirrhosis is upper gastrointestinal bleeding. Hemostasis is a central role of liver, by the synthesis of clotting factors, inhibitors of coagulation, and fibrinolytic proteins. (Arshad et al., 2020).

5.Hepatorenal syndrome: Cirrhosis also effects renal function which collectively leads toward many other complications. Renal dysfunction is most common among hospitalized cirrhotic patients. Cirrhotic patients face both acute and chronic liver failure. Sometimes both conditions are present simultaneously. Approximately 20% hospitalized cirrhotic patients are affected by acute renal failure. Acute renal failure is characterized by increased serum creatinine levels. (Arshad et al., 2020).

6.Ascites: is present when there is accumulation of free fluid in the peritoneal cavity. Small amounts of ascites are asymptomatic, but with larger accumulations of fluid (> 1 L) there is abdominal distension, fullness in the flanks, shifting dullness on percussion and, when the ascites is marked, a fluid thrill/fluid wave. Other features include eversion of the umbilicus, herniae, abdominal striae, divarication of the recti and scrotal oedema. Dilated superficial abdominal veins may be seen if the ascites is due to portal hypertension. (Penman et al., 2022).

7.Spontaneous bacterial peritonitis : is the most common bacterial infection in patients with cirrhosis, and results from translocation of bacteria from the intestine into ascites. It may present with abdominal pain or fever in a patient with obvious features of cirrhosis and ascites.(Penman et al., 2022).

8.Hepatocellular carcinoma: is the most common primary liver tumor. Cirrhosis is present in 75% to 90% of individuals with HCC and is an important risk factor. The risk is between 1% and 5% in cirrhosis caused by hepatitis B and C. Risk is also increased in cirrhosis because of haemochromatosis, alcohol, NASH and α1- antitrypsin deficiency. In northern Europe, 90% of HCC patients have underlying cirrhosis, compared with 30% in Taiwan, where hepatitis B is the main cause. (Penman et al., 2022).

2.8 Quality of life

Definitions and general information:

Quality of life has been defined by WHO as “individuals’ perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations and concerns.” This is a general definition, referring not only to quality of life related to individuals’ health status but to life in general. Overall quality of life is affected by health, but also by income, environment and freedom. Although income, freedom and environment may affect health, they are usually not the main focus of health policy measures. The current guidelines relate to “health-related quality of life” (HRQoL), or quality of life related to factors that affect an individual’s health. It is considered that the primary aim of a health care system is to maintain or improve health and HRQoL of the population, rather than overall quality of life or well-being. There is little agreement in literature about what constitutes HRQoL, even if the definition of HRQoL has as a common basis, being the definition of health given by the WHO. According to the definition of the WHO “health” is “a state of complete physical, mental and social well-being and not merely the absence of disease”.(EUnetHTA E, at all,2013).. Each domain (physical, psychological etc.) consists of several dimensions. Physical functioning refers to mobility, self-care, usual activities and other functional abilities. Psychological health includes elements like cognitive functioning, emotional distress and anxiety. Finally, social health refers to the quantity and quality of social contacts and interactions. (da Silva et al.)

2.9 Treatment / Management of chronic liver disease

Treatment and Prophylaxis.The treatment goal is to stop the progression of the disease and complications and require a multidisciplinary approach. The principle of management is mainly underlying cause correction, Portal hypertension management, and specific treatments for individual disease. (Liu, Herzschuh, Shen, Jiang, & Xiao, 2008)

General Management.Patients with chronic liver disease mostly present with one of the complications.

• Esophageal varices: Varices related bleeding are one of the deadly complications, and the treatment includes aggressive fluid resuscitation, vasopressors (octreotide, terlipressin), and endoscopy. (Davidson, 2006)

• Ascites: Essential treatment for ascites are diuretics (furosemide, spironolactone) and sodium restriction. Then for tense ascites, therapeutic paracentesis is done. Albumin infusion can also be considered. (Liu et al., 2008)

• SBP: Initially, broad-spectrum antibiotics are the treatment of choice for SBP and then specific antibiotics after culture. (Liu et al., 2008)

• Hepatic encephalopathy: The basic principle of treatment is to address the precipitating factors. Patients with hepatic encephalopathy usually improve with precipitating cause correction along with rifaximin and lactulose.Liver transplant is a curative treatment in patients with. hepatorenal syndrome. (Liu et al., 2008)

Hepatocellular carcinoma (HCC): Treatment is based on the Barcelona clinic liver Initial stage (single HCC lesion): cancer staging system in the management of HCC: Resection and ablation. Intermediate stage:

Transarterial chemoembolization and Sorafenib A el, al 2006)) radio-embolization. Metastatic disease: (Marrero et al., 2018). Transarterial chemoembolization (TACE) improves survival in selected patients It is recommended as first-line palliative therapy for nonsurgical patients with large or multifocal HCC who do not have vascular invasion or metastatic disease (Kudo et al., 2011).

Specific Treatment

• Viral Hepatitis: Continuous viral suppression with nucleoside and nucleotide analogs Direct-acting antivirals achieving HCV eradication Interferon-alpha.

Patients with decompensated cirrhosis can also be treated with oral antiviral agents, but liver transplantation may be required.-. U (Ballinger, 2011)

Autoimmune hepatitis: Corticosteroids and the immunosuppressive drugs Budesonide 3 mg × 2 or 3 daily has fewer side-effects than prednisolone and is now the preferred treatment.(Ballinger, 2011)

Alcohol treatment: All patients should stop drinking alcohol. (Ballinger, 2011)

- Fatty liver: The patient is advised to stop drinking alcohol; the fat will disappear and the liver biochemistry usually returns to normal. (Ballinger, 2011)
- Copper overload (Wilson disease): Copper chelators Lifetime treatment with penicillamine, 1–1.5 g daily, is effective in chelating copper. If treatment is started early, clinical and

biochemical improvement can occur. Trien tine (1.2–1.8 g/day) and zinc acetate (150 mg/day) have been used as maintenance therapy and for asymptomatic cases.(Ballinger, 2011)

• Drugs and toxins: Identify and stop the factor. (Kudo et al., 2011)

• Primary biliary cholangitis (PBC): Ursodeoxycholic acid (UDCA)

Ursodeoxycholic acid (10–15 mg/kg) improves bilirubin and aminotransferase levels. The lack of effective medical therapy has made PBC a major indication for liver. transplantation. (Ballinger, 2011)

• Primary sclerosing cholangitis: The only proven treatment is liver transplantation. (Ballinger, 2011)

CHAPTERTHREE

METHODOLOGY

3.1 Study design

This study was a hospital-based descriptive cross-sectional study to assess health related quality of life among patients with chronic liver disease in public hospitals in Sana'a city, Yemen.

3.2 Study setting

This study was conducted in three main public hospitals in Sana'a city, The hospitals include Al-Thawra Modern General Hospital Authority, Al-Kuwait University Hospital, and Republican Teaching Hospital Authority.

3.3 Study population

All Yemeni patients who have chronic liver disease and admitted to the selected hospitals or attended in the OPDs (233 pts. During 2022)

- Al-Thawra Modern General Hospital Authority (145)
- Al-Kuwait University Hospital (57)
- Republican Teaching Hospital Authority (31)

3.4 Sampling

3.4.1 Sampling method

The Convenience sampling method was used.

3.4.2 Sample size

Epi Info Program, version 7.2.3.1 (StatCalc for sample size and power for population survey or descriptive study) was used to calculate a sample size based on population size, with considering the following: Population size = 233, expected frequency =23.7 % ***(Mondal et al, 2022),*** acceptable

margin of error is 3 %; and level of confidence 95%. Based on these criteria, the required sample size is 179 patients.

The missing data and non-response rate =10% so the final sample size was 197 patients. The response rate was 88%.

Table 3.1: Total Patients' population and sample size according to the hospital.

Table 3- 1: Total Patients' population and sample size according to the hospital.

Name hospital	Total population	%	Sample size
Al-Thawra Modern General Hospital	145	62.23%	123
Al-Kuwait University Hospital	57	24.46%	48
Republican Teaching Hospital Authority	31	13.30%	26
Total	**233**	**100%**	**197**

The percentage of the patients in each hospital was calculated in relation to the total population of patients in the selected hospitals. Then the sample size was selected from each hospital according to that percentage. Details were shown in table (3.1).

3.4.3 Inclusion criteria

1. Patients who had chronic liver disease in Sana'a city.
2. Patients who are adult (more than 18 years old.
3. Patients who agree to participate in the study.
4. Stable patient.

3.4.4 Exclusion criteria

1. Patients who do not agree to participate in the study.
2. Patients who are in critical situation.
3. Pediatric patients.

3.5 Data Collection

3.5.1 Data collection method

The sample was conducted at the public hospitals in the medical wards and out-patients departments OPDs. The questionnaire was prepared in English language and translated from English into Arabic. All of the patients were received an Arabic version questionnaire. The questionnaire has taken from (15 – 30) minutes to be filled. Researchers gave a brief clarification of the study topic and objectives. Unclear questions were clarified by the researchers. The clinical data was collected by reviewing the patients records and direct physical examination.

3.5.2 Data collection instrument.

The data was collected by two instruments:

1. Standard structured questionnaire contains questions about the sociodemographic data of the patients and the following scales:

- The European Quality of life–5 Dimensions–5 levels (EQ-5D-5L)
- Original Liver Disease Symptom Index (LDSI)
- ***EQ-5D-5L***

EQ-5D is an instrument which evaluates the generic quality of life developed in Europe and widely used. The EQ-5D descriptive system is a preference-based HRQL measure with one question for each of the five dimensions that include mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The answers given to ED-5D permit to find 243 unique health states or can be converted into EQ-5D index a utility score anchored at 0 for death and 1 for perfect health. The EQ-5D questionnaire also includes a Visual Analog Scale (VAS), by which respondents can report their perceived health status with a grade ranging from 0 (the worst possible health status) to 100 (the best possible health status).

- ***LDSI***

The LDSI 2.0 consists of 18 items. It measures severity and hindrance that patients experience from nine symptoms: ‘itch’, ‘joint pain’, ‘pain in the right upper abdomen’, ‘sleepiness during the day’, ‘worry about family situation’, ‘decreased appetite’, ‘depression’, ‘fear of complications and ‘jaundice’. In this study, only the symptom severity scores were used. The LDSI 2.0 can be extended with six items considered to be important by the board of the NLV: ‘memory problems’, ‘change of personality’, ‘financial problem’, ‘daily time management’, ‘decreased sexual interest’, and ‘decreased sexual activity’. Scores are given on a five-point scale ranging from ‘no symptoms at all’1 to ‘symptoms to a high extent’.5

2. The clinical sheet which designed to assess the signs and symptoms as well as the etiology of the liver diseases. The clinical

sheet also contains the lab. Investigation and radiology (US and CT scan). The following scales were used to measure the disease severity:

- ***Child Pugh Classification (Table 3.2):***

Modified Child-Pugh classification of the severity of liver disease according to the degree of ascites, the serum concentrations of bilirubin and albumin, the prothrombin time, and the degree of encephalopathy. A total Child-Turcotte-Pugh score of 5 to 6 is considered Child-Pugh class A (well-compensated disease), 7 to 9 is class B (significant functional compromise), and 10 to 15 is class C (decompensated disease). These classes correlate with one- and two-year patient survival: class A: 100 and 85%; class B: 80 and 60%; and class C: 45 and 35%.

- ***Model of End-Stage Liver Disease (MELD) score (Table 3.3)***

The MELD score is a prospectively developed and validated chronic liver disease severity scoring system that uses a patient's laboratory values for serum bilirubin, serum creatinine, and the international normalized ratio (INR) for prothrombin time to predict three-month survival. In patients with cirrhosis, an increasing MELD score is associated with increasing severity of hepatic dysfunction and increased three-month mortality risk. Given its accuracy in predicting short-term survival among patients with cirrhosis.

Table 3- 2: Child Pugh Classification

Clinical and Lab Criteria	Points*		
	1	2	3
Encephalopathy	None	Mild to moderate (grade 1 or 2)	Severe (grade 3 or 4)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	< 2	2-3	>3
Albumin (g/dL)	> 3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
International normalized ratio	<1.7	1.7-2.3	>2.3
Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points) Class A = 5 to 6 points (least severe liver disease) Class B = 7 to 9 points (moderately severe liver disease) Class C = 10 to 15 points (most severe liver disease)			

Table 3- 3: Model of End-Stage Liver Disease (MELD) score.

Parameter	**Numerical score**		
	1	2	3
Ascites	None	Slight	Moderate-Severe
Encephalopathy	None	Slight-Moderate	Moderate-Severe
Bilirubin (mg/dL)	<2.0	2-3	>3.0
Albumin (g/dL	>3.5	2.8-3.5	<2.8
Prothrombin time (prolonged in seconds)	1-3	4-6	>6.0s

3.6 Pilot study

The pretest of the questionnaire was performed before data collection, a pilot study was done in the study setting on 19 patients (10%) of the sample to assess the reliability of the questionnaire also to test the feasibility of the study, recruitment of subjects, responses rate and research tool. The identification of the practical or local problems that might be potentially affect the research process was done. Some questions were omitted, some added and others rephrased. The pilot study samples were excluding from the study samples.

3.7 Reliability:

The reliability test was conducted for measuring the reliability of the different variables, either dependents or independents, included in this study. Reliability analysis measures the internal consistency of a group of items which accordingly reflects the quality of appreciativeness of the measure used in this study. Cronbach's alpha coefficient (α) is the most frequently used by the index of the reliability which reflects the average correlation among the items that constitute a scale. The results obtained from performing the reliability analysis which is shown in Table 3.4.

Table 3: Reliability Analysis for Variables

Number of Items	Variable	Alpha
24	Signs and symptoms of liver disease	93.4%
10	Symptoms of chronic liver disease	82.9%
14	Signs of chronic liver disease	84.2%
5	Clinical and lab criteria	78.7%
53	**All items**	**89.1%**

Table 3.6 shows the stability of the data collection tool and the credibility of answers, that the values of the Cronbach's alpha coefficient (α) for data collecting scale stability is (89.1%) which means a high degree of the credibility of the answers, and this means that the sample is homogeneous in responding to the questionnaire and greatly can depend on the results and generalize it to the study population.

3.8 Validity

The validity of the questionnaires was reviewed by two experts who determine the clarity and phrasing of the questionnaire.After that, all modifications were taken.

3.9 Data Analysis

The data was entered and analyzed by SPSS program version 25.The data was analyzed according to the study objectives. Frequencies and percentage were used for descriptive data. Regarding the differences, the statistical test was used according to the data type t-test and NOVA test were used for numerical data and chi-square was used for categorical data. For investigating the relation between the variables,the Correlations was used.

3.10Ethical consideration

- Ethical approval was obtained from research committee, University of 21 September, Faculty of medicine.

- permissions were obtained from the three public hospitals.

- Verbal consent was obtained from all participants after explaining the purpose of this study to them, they have right to withdraw at any time without any deprivation.Privacy and confidentiality were ensured by using coded questionnaire. The participant has right to benefit from the researcher knowledge and skills

- The patients who refused to participate in the study was exclude.

CHAPTER FOUR

RESULTs

4.1 Demographic Data

Table 4- 1: Distribution of the sample according to the demographic characteristics

Variable		N	%
Gender	Male	132	75.9%
	Female	42	24.1%
	Total	**174**	**100.0%**
Age	Less than 25 years	23	13.2%
	25-35 years	41	23.6%
	36-45 years	26	14.9%
	46-55 years	30	17.2%
	More than 55 years	54	31.0%
	Total	**174**	**100.0%**
Residency	Urban	97	55.7%
	Rural	77	44.3%
	Total	**174**	**100.0%**
Education level	Illiterate	44	25.3%
	can read & write	36	20.7%
	Secondary	19	10.9%
	High level	52	29.9%
	Postgraduate	22	12.6%
	Advanced studies	1	0.6%
	Total	**174**	**100.0%**
Occupation	Officer	24	13.8%
	No job	21	12.1%
	Businessman	6	3.4%
	Free worker	79	45.4%
	Student	18	10.3%
	Housewife	26	14.9%
	Total	**174**	**100.0%**
Monthly income level	Less than 30,000 YER	28	16.1%
	30,000-50,000 YER	59	33.9%
	50,000- 100,000YER	54	31.0%
	100,000- 150,000YER	20	11.5%
	More than 150,000 YER	13	7.5%
	Total	**174**	**100.0%**
Yearly income	Enough	26	14.9%
	Not enough	148	85.1%
	Total	**174**	**100.0%**

The above table shows the demographic characteristics of the patients, 75.9% of them are male and 31.0% are above 55 years old followed by 23.6% between 25 – 35 years old. While approximately the same percentage of the patient who live in urban and rural areas with 55.7% and 44.3%, respectively. Regarding the level of education, the illiterate, read and write; and high level have high percentage with 25.3%,20.7%,29.9%, respectively. Nearly the half of the patients 45.4% are free workers and 33.9% of them their monthly income was between 30,000-50,000 YER followed be 31% between 50,000-100,000 YER. Eighty five percent of them indicate that the yearly income of them is not enough.

4.2 Admission Status:

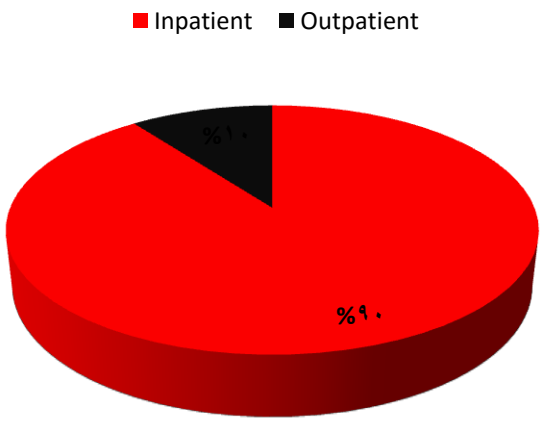

Figure 1: Distribution of the sample according to the admission status

The figure (4.1) reveals the percentage of inpatients versus outpatients. 90% of the patients are admitted to the medical wards while 10% of them attend in the outpatients' departments (OPDs)

4.3 Clinical Data:

4.3.1 Symptoms of chronic liver disease:

Table ٤٢ □: Distribution of the sample according to the Symptoms of chronic liver disease

Rank	Symptom	Yes		No	
		N	%	N	%
1.	Rt. hypochondrium pain	127	73.0%	47	27.0%
2.	Itching	86	49.4%	88	50.6%
3.	Fatigue	159	91.4%	15	8.6%
4.	Nausea	121	69.5%	53	30.5%
5.	Vomiting	86	49.4%	88	50.6%
6.	Anorexia	127	73.0%	47	27.0%
7.	Diarrhea	42	24.1%	132	75.9%
8.	Encephalopathy	71	40.8%	103	59.2%

The table (4.2) reveals that 91.4% complain of fatigue followed by Rt. hypochondrium pain and anorexia with 73% for both. Nausea takes 69.5% between the patients. And approximately half of the patients 49.4% suffer from itching and vomiting. Finally, 40.8% of them present with encephalopathy.

4.3.2 Signs of chronic liver disease:

Table 4٣□: Distribution of the sample according to the Signs of chronic liver disease.

Rank	Signs	Yes		No	
		N	%	N	%
1.	Ascites	128	73.6%	46	26.4%
2.	Clubbing	66	37.9%	108	62.1%
3.	Leukonychia	59	33.9%	115	66.1%
4.	Palmar erythema	54	31.0%	120	69.0%
5.	DuPuy Ren contracture	19	10.9%	155	89.1%
6.	Spider naevi	43	24.7%	131	75.3%
7.	Skin pigmentation	83	47.7%	91	52.3%
8.	Jaundice	112	64.4%	61	35.6%
9.	Anemia pallor	111	63.8%	63	36.2%
10.	Central cyanosis	41	23.6%	133	76.4%
11.	Fetor hepaticus	42	24.1%	132	75.9%
12.	Ankle edema	73	42.0%	101	58.0%
13.	Gynecomastia	23	13.2%	151	86.8%
14.	Scratch marker.	38	21.8%	136	78.2%

The above table illustrates that the patients present with ascites, jaundice and Anemia pallor with 73.6%, 64.4% and 63.8%, respectively. Also 47.7% of the patients have skin pigmentation and 42% of them present with ankle edema. Approximately one third of them have clubbing,

leukonychia and palmar erythema with 37.9%, 33.9% and 31%, respectively.

4.3.3 Cause of chronic liver disease:

Table 4٤ : Distribution of the sample according to the Cause of chronic liver disease

N	Cause	Yes		No	
		N	%	N	%
1.	Unknown:	110:	63.1%:		
	Positive autoantibody	72	41.3%	64	36.7%
	Negative autoantibody	38	21.8		
2.	Viral:	65	37.3%		
	Hepatitis B	36	20.7%	138	79.3%
	Hepatitis C	27	15.5%	147	84.5%
	Hepatitis B+D	2	1.1%	172	98.9%
3.					
4.	Primary biliary cholangitis	3	1.7%	171	98.3%
5.	Toxicity (Drug)	2	1.1%	172	98.9%
6.	Hemochromatosis	1	0.6%	173	99.4%
7.	Alpha-1 Antitrypsin deficiency	1	0.6%	173	99.4%
8.	Wilson's disease	0	0.0%	174	100%
9.	Alcoholic	0	0.0%	174	100%
10.	Primary sclerosing cholangitis	0	0.0%	174	100%

The table (4.4) describes the causes of chronic liver diseases. The autoimmune takes the highest percent with 41.4% of the patients followed by hepatitis B and hepatitis C with 20.7% and 15.5%, respectively. It is noticed that also 15.5% of the patients their causes are unknown.

4.3.4 U/S or CT Scan reports:

Table 4٥ : Distribution of the sample according to the U/S or CT Scan reports

N	Depend to U/S or CT Scan check of the following	Yes		No	
		N	%	N	%
DE1	Ascites	134	77.0%	40	23.0%
DE2	Hepatic focal lesion	55	31.6%	119	68.4%
DE3	Splenomegaly	106	60.9%	68	39.1%

The above table illustrates that the patients present with ascites represent 77%, splenomegaly60.9% and hepatic focal lesion 31.6% depending on the U/S or CT Scan reports.

4.4 Severity of the Liver Disease

4.4.1 Child – Pugh Score cirrhosis mortality:

Table 4٦□: Distribution of the sample according to the Child – Pugh Score.

N	Liver disease severity classification	N	%
1.	Class A	16	9.2%
2.	Class B	84	48.3%
3.	Class C	74	42.5%
	Total	١٧٤	100%

The table (4.7) illustrates the classification of the liver disease severity according to the Child – Pugh Score. Approximately half of the patients are in class B with 48.3% followed by class C with 42.5%.

1. Model of end stage liver disease (MELD) score:

Table 4٧□: Distribution of the sample according to the Model of End Stage Liver Disease Score (MELD).

	N	Minimum	Maximum	Mean	SD
MELD Score	173	6	123	16.3	11.27

The above table reveals the classification of the liver disease severity according to the Model of End Stage Liver Diseases Score MELD. The minimum score is 6 and the maximum score is 123 with mean (SD) equal 16.3 (11.27).

4.5 Health Related Quality of Life

4.5.1 The European Quality of Life–5 Dimensions–5 levels (EQ-5D-5L)

Table 4- 8: Distribution of the sample according to the EQ-5D-5L.

EQ – 5D – 5L	No problem		Slight problems		Moderate problems		Severe problems		Extreme problems	
	N	%	N	%	N	%	N	%	N	%
Mobility	50	28.7	72	41.4	40	23.0	12	6.9	0	0
Self -Care	89	51.1	41	23.6	24	13.8	14	8.0	6	3.4
Usual activities	21	12.1	76	43.7	41	23.6	29	16.7	7	4.0
Pain / Discomfort	24	13.8	55	31.6	59	33.9	30	17.2	6	3.4
Anxiety /Depression	60	34.5	47	27.0	43	24.7	16	9.2	8	4.6
Total	**244**	**28**	**291**	**33.4**	**207**	**23.8**	**101**	**11.6**	**27**	**3.1**

The table (4.10) illustrates the quality of life of the patients according to the European Quality of life–5 Dimensions–5 levels. Regarding the mobility, 41.4% of the patients have slight problems and 51.1% with no problems in self-care. Less than half of the patients (43.7%) have slight problems with the usual activities. Pain and discomfort represent slight problems with 31.6% of the patients and moderate problem with 33.9% of them. Approximately one third (34.5%) of the patients have no problem with anxiety or depression.

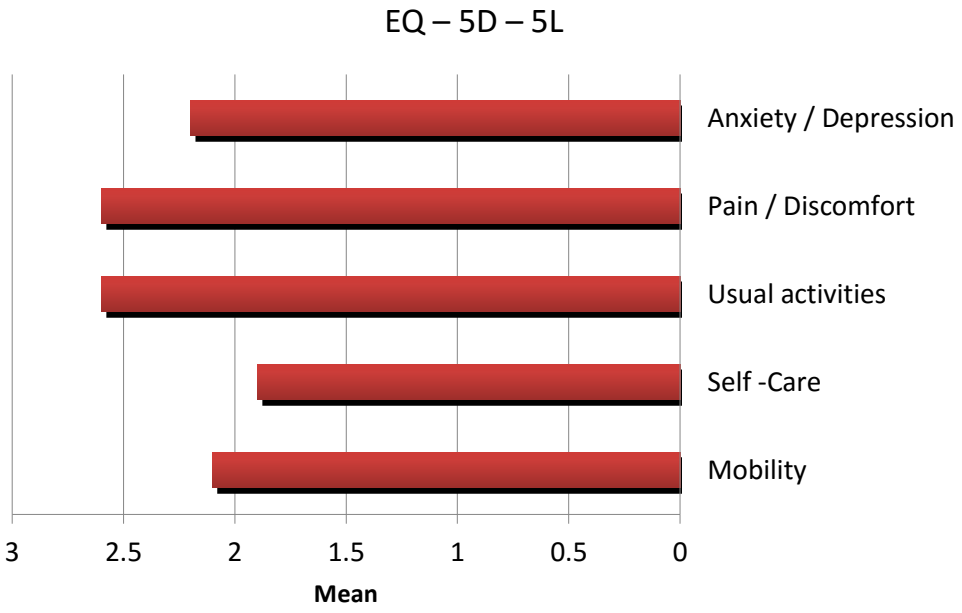

Figure 2: Mean and SD of the EQ-5D-5L dimensions.

4.5.2 Original Liver Disease Symptom Index:

Table 4٩ : Distribution of the sample according to the Liver Disease Symptom Index LDSI.

N	Rank	Items	Mean	Std. Deviation	%	Verbal Result
Symptoms items:						
OLDS1	22	itching	1.75	1.049	35.0%	Very low
OLDS2	24	Itching hindrance in daily activities	1.55	.877	31.0%	Very low
OLDS3	23	Itching hindrance in sleep	1.60	.973	32.0%	Very low
OLDS4	12	Joint pain	2.10	.992	42.0%	Low
OLDS5	20	joint pain hindrance in daily activities	1.90	.962	38.0%	Low
OLDS6	3	pain in the right upper abdomen	2.36	1.117	47.2%	Low
OLDS7	14	pain in the right upper abdomen hindrance in daily activities	2.08	.988	41.6%	Low
OLDS8	7	Feel sleepy during the day?	2.23	1.040	44.6%	Low
OLDS9	16	Sleepiness hindrance in daily activities	2.05	1.120	41.0%	Low
OLDS10	11	worries about the home/family situation	2.13	1.188	42.6%	Low
OLDS11	19	worries about the home/family situation hindrance in daily activities	1.99	1.102	39.8%	Low
OLDS12	2	Decreased appetite	2.48	1.147	49.6%	Low
OLDS13	8	decrease appetite hindrance	2.22	1.187	44.4%	Low
OLDS14	15	depression due to your disease?	2.06	1.097	41.2%	Low
OLDS15	18	Depression hindrance in daily activities	2.00	1.168	40.0%	Low
OLDS16	17	Fear of complications	2.03	1.114	40.6%	Low
OLDS17	5	Jaundice	2.31	1.169	46.2%	Low
OLDS18	5	Jaundice hindrance in daily activities and/or social contacts	2.31	1.169	46.2%	Low
Extra items NLV:						
OLDS18	21	Memory difficulties	1.77	.953	35.4%	Very low
OLDS19	9	Personality has changed	2.18	1.079	43.6%	Low
OLDS20	4	Financial hindrance	2.35	1.106	47.0%	Low
OLDS21	1	Time management	2.74	1.622	54.8%	Middle
OLDS22	10	Sexual interest	2.17	1.142	43.4%	Low
OLDS23	13	Sexual activity	2.09	1.430	41.8%	Low
Original Liver Disease Symptom Index			**2.08**	**.614**	**41.6%**	**Low**

The above table reveals the index of liver disease symptoms. The overall liver disease symptom index mean is low with mean ± SD 2.08 ± 0.614. The most hindrance that faced by the patients is jaundice hindrance with mean ± SD 2.31 ± 1.169 followed by decrease appetite hindrance with mean ± SD 2.22 ± 1.187. The most hindrance that faced by the patients regarding the extra items (NLV) time management with mean ± SD 2.74 ± 1.622 followed by finance hindrance with mean ± SD 2.35 ± 1.106.

Table 4- 10: Mean and SD of the overall and EQ-5D-5L dimensions.

EQ – 5D – 5L	Mean ± SD	Verbal Results
Mobility	2.1 ± 0.88	**Slight problems**
Self -Care	1.9 ± 1.13	**Moderate problems**
Usual activities	2.6 ± 1.03	**Moderate problems**
Pain / Discomfort	2.6 ± 1.03	**Moderate problems**
Anxiety / Depression	2.2 ± 1.15	**Moderate problems**
Overall Mean ± SD	**2.28 ± 0.87**	**Moderate problems**

The table (4.11) and figure (4.2) show the mean and standard deviation of the overall and EQ-5D-5L dimensions. The patients have slight problem with mobility while they have moderate problem in the other dimensions and the overall mean score.

Table 4- 11: Distribution of the sample according to the visual analog scale of EQ (VAS-EQ) about today health status.

Health is TODAY	N	%
1	1	0.6%
2	10	5.7%
3	9	5.2%
4	16	9.2%
5	33	19.0%
6	27	15.5%
7	37	21.3%
8	22	12.6%
9	17	9.8%
10	2	1.1%
Total	**174**	**100.0%**
Mean ± SD	**6.01 ± 1.97**	

The above table reports the patients' perception of their health status today which (1) indicates the worst health and (10) indicates the best health. 21.3% of the patients indicate that their health is 7 out of 10 followed by 19% of them indicate 5 out of 10. The overall mean and standard deviation of today health status of the patients are 6.01± 1.97.

4.6 Differences among patients regarding the demographic characteristics:

Liver Disease Symptom Index LDSI

Table 4١٢□: Differences among patients' demographic data regarding the liver disease symptom index.

Demographic Data		Liver Disease Symptom Index			
		N	Mean	SD	P - value
Gender	Male	132	2.06	0.59	0.708
	Female	42	2.17	0.63	
Age	Less than 25 years	23	2.12	0.74	0.663

Demographic Data		Liver Disease Symptom Index			
		N	Mean	SD	P - value
	25-35 years	41	2.10	0.61	
	36-45 years	26	1.95	0.52	
	46-55 years	30	2.03	0.59	
	More than 55 years	54	2.16	0.59	
Residency	Urban	97	2.05	0.57	0.349
	Rural	77	2.14	0.64	
Education level	Illiterate	44	2.13	0.56	0.060
	can read & write	36	2.12	0.59	
	Secondary	19	2.42	0.68	
	High level	52	1.95	0.58	
	Postgraduate	23	2.02	0.61	
Occupation	Officer	24	2.19	0.67	0.286
	No job	21	2.31	0.68	
	Businessman	6	1.93	0.54	
	Free worker	79	2.01	0.54	
	Student	18	1.99	0.67	
	Housewife	26	2.16	0.63	
Monthly income level	Less than 30,000 YER	28	2.35	0.55	0.017*
	30,000-50,000 YER	59	2.14	0.52	
	50,000- 100,000YER	54	1.89	0.55	
	100,000- 150,000YER	20	2.02	0.75	
	More than 150,000 YER	13	2.20	0.83	
Yearly income	Enough	26	2.11	0.67	0.829
	Not enough	148	2.08	0.59	

The above table shows the differences between the patients' liver disease symptom index regarding their demographic characteristics. It is clear that there are statistically significant differences among patient liver disease symptom index regarding the monthly income with P value = 0.017.

While, there are not statistically significant differences in other demographic characteristics.

EQ-5D-5L:

Table 4١٣□: Differences among patients' demographic data regarding the EQ -5D – 5L.

Demographic Data		EQ – 5D – 5L			
		N	Mean	SD	P - value
Gender	Male	132	2.21	0.839	0.063
	Female	42	2.50	0.941	
Age	Less than 25 years	23	2.00	0.880	0.029*
	25-35 years	41	2.13	0.828	
	36-45 years	26	2.15	0.962	
	46-55 years	30	2.26	0.660	
	More than 55 years	54	2.58	0.900	
Residency	Urban	97	2.28	0.862	0.996
	Rural	77	2.28	0.888	
Education level	Illiterate	44	2.70	0.982	0.000*
	can read & write	36	2.32	0.737	
	Secondary	19	2.47	0.772	
	High level	52	1.98	0.807	
	Postgraduate	23	1.96	0.680	
Occupation	Officer	24	2.15	0.752	0.006*
	No job	21	2.81	0.922	
	Businessman	6	2.20	0.726	
	Free worker	79	2.14	0.808	
	Student	18	2.00	0.870	
	Housewife	26	2.60	0.954	
Monthly income level	Less than 30,000 YER	28	2.59	0.652	0.004*
	30,000-50,000 YER	59	2.46	0.856	
	50,000- 100,000YER	54	1.93	0.757	
	100,000- 150,000YER	20	2.25	1.153	
	More than 150,000 YER	13	2.29	0.929	
Yearly income	Enough	26	1.97	0.591	0.012*
	Not enough	148	2.33	0.902	

The table (4.14) reveals the differences between the patients' EQ-5D-5L score regarding their demographic characteristics. It is noticed that there are statistically significant differences among patients' EQ-5D-5L score regarding the age, the level of education, the occupation, the monthly income and the yearly income with P value = 0.029, 0.000,0.006, 0.004 and0.012, respectively.

4.7 Differences among patients regarding the admission status:

Quality of life:

Table 4١٤□: Differences among patients' quality of life scale regarding the admission status.

Quality of Life	Admission Status	N	Mean	SD	P - value
LDSI	In-patient	156	2.08	0.57	0.861
	Out-patient	18	2.11	0.90	
EQ – 5D – 5L	In-patient	156	2.30	0.83	0.268
	Out-patient	18	2.06	1.27	

The above table the illustrates that there are no statistics significant differences among patients' quality of life scales regarding the admission status.

Disease severity

Table 4١٥: Differences among patients' severity of liver disease regarding the admission status.

Severity of disease	Admission Status	N	Mean	SD	P - value
Child-Pugh	In-patient	156	15.55	11.04	0.003
	Out-patient	17	24.11	10.70	
MELD	In-patient	148	8.87	1.81	0.000
	Out-patient	15	11.60	2.13	

The table (4.16) reports that there are high statistics significant differences among patients' quality of life scales regarding the admission status with P-value = 0.003 for Child-Pugh scale and 0.000 for MELD.

4.8 Differences among patients regarding the Severity of the Liver Disease:

Table 4١٦: Differences among patients quality of life scales regarding the Child- Pugh score.

Quality of Life	Child-Pugh Score	N	Mean	SD	P - value
LDSI	Class A	16	1.90	0.48	0.009
	Class B	84	1.98	0.54	
	Class C	74	2.25	0.66	
EQ – 5D – 5L	Class A	16	2.10	1.01	0.240
	Class B	84	2.20	0.77	
	Class C	74	2.40	0.93	

The above table shows that there are statistically significant differences among patients' Child-Pugh score regarding the liver disease

symptom index with P-vale = 0.009. while there are no statistically significant differences among patients' Child-Pugh score regarding the EQ-5D-5L score.

4.9 Correlation between the quality of life and disease severity

Quality of life and Child-Pugh Score

Table 4- 17: Correlation between quality of life and Child- Pugh score.

Correlations		Child-Pugh Score
LDSI	Pearson Correlation	0.315
	Sig. (2-tailed)	0.000*
	N	١٧٤
EQ – 5D – 5L	Pearson Correlation	0.142
	Sig. (2-tailed)	0.072
	N	١٧٤

The table (4.18) reveals the correlation between the quality of life and the Child-Pugh Score. It is clear that there is statistically significant and weak positive relationship between the LDSI and the Child-Pugh score with P-value= 0.000. While there is no statistically significant relationship between the EQ-5D-5L and the Child-Pugh score.

Quality of life and MELD

Table 4- 18: Correlation between quality of life and MELD

Correlations		MELD
LDSI	Pearson Correlation	0.131
	Sig. (2-tailed)	0.087
	N	١٧٤
EQ – 5D – 5L	Pearson Correlation	0.112
	Sig. (2-tailed)	0.141
	N	١٧٤

The table (4.19) illustrates the correlation between the quality of life and the MELD. It is noticed that there is no statistically significant relationship between the MELD and neither the LDSI nor the EQ-5D-5L with P-value= 0.087 and 0.141.

Table 4- 19: Correlation between EQ-5D-5L Dimensions and MELD.

Correlations		**MELD**
EQ – 5D – 5L		
Mobility	Pearson Correlation	0.096
	Sig. (2-tailed)	0.210
	N	174
Self-care	Pearson Correlation	0.065
	Sig. (2-tailed)	0.397
	N	174
Usual activity	Pearson Correlation	0.108
	Sig. (2-tailed)	0.156
	N	174
Pain	Pearson Correlation	0.036
	Sig. (2-tailed)	0.634
	N	174
Anxiety	Pearson Correlation	0.157
	Sig. (2-tailed)	0.039*
	N	174

The above table shows the correlation between the dimension of the EQ-5D-5L and the MELD. It is clear that there is no statistically significant relationship between the MELD and all of the EQ-5D-5L dimensions except the anxiety has a weak positive relationship with MELD with P-value= 0.039.

CHAPTER FIVE

DISCUSSION

6.1 Introduction

This study is an attempt to assess the quality of life among patients with liver disease and to determine the differences of the quality of life between various patients' groups at public hospital in Sana'a city. In this chapter the major findings of the study will be discussed in relation to the previous studies conducted by other researchers; this helped the researchers to prove those findings.

The findings will be discussed in four parts: the sociodemographic characteristics, the clinical data, the severity of the disease, and quality of life.

6.2 Socio-demographic data:

In the present study, the demographic characteristics of the patients shows that 75.9% of them are male and 31.0% are above 55 years old followed by 23.6% between 25 – 35 years old. While approximately the same percentage of the patient live in urban and rural areas with 55.7% and 44.3%, respectively. Regarding the level of education, the illiterate, read and write, and the high level have high percentage with 25.3%, 20.7%, 29.9%, respectively. Nearly the half of patients 45.4% are free workers and 33.9% of them, their monthly income between 30000, 50000 YER followed by 31% between 50000, 100000. 85% of them indicate that their yearly incomes are not enough.

In contrast, a study carried in Northern India, shows that the majority of patients were above 50 years of age (41.7%), male (72.2%), married (85.2%),regarding the education participants the majority of the population were in the middle-secondary (32.6%), and the unemployed (38.3%) specially in the urban (37.8%). (Mathai et al., 2022)

In Franciosi, (2021) they found, regarding the education level, most of the participants' (34.3%) had High school degree, (33.5%) had Secondary degree and (19.7%) had primary degree. (Gazineo et al., 2021)

majority of participants had monthly income with (31%), While another study in the United States (2021), reported that the majority of the participants' (70%) residence in urban area and (30%) rural area. were between (5000-9.999) and (20%) of participants month income with less than (1.999$). (Akel, Masters, Shih, Lu, & Wagner, 2021)

Another study in Nepal, found that the mean age of the patients was 52.5 ±9.8 years. Among the 60 patients, 60% of them were males, 70% of them were Hindus, 75% were unemployed, 55% were from the Hilly region of Nepal, 60% belonged to the Janjati caste (based on the traditional caste system), 40% were illiterate, and 91.7% were married. A majority of the patients (70%) had an annual family income of less than 500,000 Nepalese rupees (NPR) ($1 is equivalent to around 123 NPR). (Pradhan & Sigdel, 2020)

Bagny, A.et al, (2015) reported that the average age of the patients was 46 ± 12 years old with a male predominance (sex-ratio: 2.9). Of the sample group, married people represented the majority with 85.1%. The distribution of patients according to their education level showed that

21.1% were not in school; 55.3% had a high school; and 15.8% had a university level.

According to a study done in 2015, the findings were was as follows: most of the participants (40%) were between 51-60 years old, (33%) of participants were between 41-50 years and (31%) of participants' age more ther 60 years. The females were (33,8%) less than the males, males were (66,2%). (de Araujo Silva, Ruela, de Oliveira Mamede, & de Paula Pereira, 2023)

6.3 Clinical Data:

In the current study 91.4% of participants complain of fatigue followed by Rt. hypochondrium pain and anorexia with 73% for both. Nausea takes 69.5% between the patients. And approximately half of the patients with 49.4% suffer from itching and vomiting. Finally, 40.8% of them had encephalopathy. Compared to a study done by (Gazineo et al., 2021), it was found that most of frequent symptoms were muscle cramps (31.15) followed by pruritus (23.6%), while fatigue, jaundice and anorexia represent (18.5%), (2.8%) and (1.6%), respectively. Another study in the USA showed that the percentage of patient who have abdominal pain was 38.1% followed by 36.8% with fatigue. (Mendez-Sanchez et al., 2021)

In the present study the most frequent signs that patients suffered from ascites is about 73.6% followed by jaundice 64.4%. In contrast, the ascites was present with 86.7% of the patients, in a study that carried in Nepal.(Pradhan & Sigdel, 2020) whereas only 24.4% of the patients suffering from ascites as reported by (Gazineo et al., 2021)

The current study reports that most frequent causes of CLD that affect the patients is the positive antibody by 41.4% and 20.7% Hepatitis B. Compared to other study in Nepal, they found that the most frequent cause was alcohol with 75% (Pradhan et al, 2020). Another study found that Hepatitis C represented 21.2% and Hepatitis B with9.6%. (Sepanlou et al., 2020). In Togo, an African country, the etiologies of those chronic liver diseases were alcoholic (57%), hepatitis B virus (66.7%) and hepatitis C virus (12.3%). (Bouglouga, Lawson-Ananissoh, Bagny, Kaaga, & Amegbor, 2015)

In the current study, regarding on the U/S or CT scan reports, it showed that 77% of patients had ascites, 60.9% splenomegaly and about 31.6% hepatic focal lesion, (Gazineo et al., 2021) 18.1% of patients had Splenomegaly.

6.4 Severity of disease:

In the current study Approximately half of the patients were in class B followed by class C with 42.5%. This result is similar to the result reported by (Pradhan & Sigdel, 2020) which was 50% of the patients in class C followed by class B with 43.3%. In contrast, (Gibbs et al., 2015) stated that most of the patients were in class A (74%) followed by 20% in class B.

In the current study the maximum score is 123 with mean (SD) 16.3 (11.27). Compared with other studies in (Franciosi). the maximum score is 178 with mean (SD) 62.28 (Gazineo et al., 2021) (11.58). Regarding

MELD, 124 (93.2%) individuals were at low risk (≤15), seven (5.3%) were at moderate risk, and two (1.5%) were at high risk for mortality (>25). (De Souza et al., 2015)

6.5 Quality of life

regarding the quality of life of the patients according to the European Quality of life–5 Dimensions–5 levels, in the mobility dimension present study reveals that 41.4% of the patients have slight problems, 51.1% with no problems in self-care dimension, Less than half of the patients (43.7%) have slight problems with the usual activities dimension, Pain and discomfort represent slight problems with about 31.6% of the patients and approximately one third (34.5%)of the patients had no problem with anxiety or depression. Mean EQ-5D descriptive score was 82.28 ± 0.87 and EQ-Vas score was 6.01 ± 1.97. Compared to study done in (Italy 2020), they reported that the patients had no problems regarding the mobility, 76.6% and about the self-care 91.4%. Also, 79.1 % had no problems with usual activities, 53.9% with Pain and discomfort and (57.8%) of the patients no had problem with anxiety or depression. (Smith et al., 2020)

In Malaysia, they found that the HRQoL scores among the study population, mean: EQ-5D descriptive score was 0.37 ± 0.3 and EQ-Vas score was 57.21 ± 10.8. A total of 41 different EQ-5D health states were described by the patients. Sixty-three (16.1 %) reported some problem in the first, third, fourth and fifth domains, whereas no problem in the second domain. There was not a single patient without a stated problem in all five domains. (Haq et al., 2014)

Stern et al., (2022) reported that the mean EQ- 5D score for forty chronic hepatitis patients was 0.639 ± 0.062 and 0.562 ± 0.048 for the forty patients with compensated cirrhosis. Among the 150 patients admitted to ICU/HDU, mean EQ- 5D score of 0.295 ± 0.031 was reported at the time of admission. At the time of discharge, this score improved significantly to 0.445 ± 0.055.

The present study reveals that the index of liver disease symptoms index mean is low (2.08 ± 0.614). The most hindrance that faced by the patients is jaundice hindrance with mean ± SD 2.31 ± 1.169 followed by decrease appetite hindrance with mean ± SD 2.22 ± 1.187. The most hindrance faced by the patients regarding the extra items is the time management with mean ± SD 2.74 ± 1.622 followed by financeat hindrance with mean ± SD 2.35 ± 1.106. Contradictory to these results, in Netherlands, it was found that the most hindrance faced by patients was fatigue followed by worries about families. After that, the depression and the joint pain which hinder the patients with daily activities and social life. Regarding the extra items and the time management came first in the hindrance of the patients. (Gutteling et al., 2006)

A study carried out in Brazil; they measured the specific quality of life by the chronic liver disease questionnaire CLDQ scores. They found that the mean, and standard deviation of the CLDQ scores were as follows: Higher mean CLDQ scores were found for emotional function (39.70 ± 12.98) while lower mean CLDQ scores were obtained for abdominal symptoms (16.00 ± 6.25). Fifty-two patients (39.1%) obtained low (<5) overall CLDQ scores. (De Souza et al., 2015)

The same scale (CLDQ) was used with Janani et al, (2018) and they found that the higher mean CLDQ score was for emotional function followed by systemic symptoms. The lowest score was for the activities.

The current study shows that there are statistically significant differences between the patients' liver disease symptom index regarding their demographic characteristics and the monthly income with P value = 0.017. While, there are not statistically significant differences in other demographic characteristics. These results similar to that found by Li et al., (2018) in which the significant difference was only in age the the physical dimension.

It is noticed in the present study that there are statistically significant differences among patients' EQ-5D-5L score regarding the age, the level of education, the occupation, the monthly income and the yearly income with P value = 0.029, 0.000,0.006, 0.004 and0.012, respectively.

In Brazil, the CLDQ was evaluated according to age, gender, family income and school level. Family income was correlated to CLDQ with P= 0.031. (De Souza et al., 2015)

In addition, another study reported that depression, pain in the right upper abdomen, fatigue and decreased appetite were also strongly related to HRQoL. Daily time management, memory problems, change of personality, age and gender showed a weak relationship , but nevertheless statistically significant relationship with HRQoL in the overall group of liver patients. In the group of patients with HCV, disease severity ($P < 0.001$) and depression,they were strongly related to HRQoL ($P < 0.001$). Use of interferon, fatigue, joint pain and hindrance in financial affairs were also

statistically significantly related to HRQoL in HCV patients, but less strongly than disease severity and depression. (Gutteling et al., 2006)

The current study shows a high statistically significant difference among patients' severity of disease scores regarding the admission status with P-value = 0.003 for Child-Pugh scale and 0.000 for MELD. Also, there are statistically significant differences among patients' Child-Pugh score regarding the liver disease symptom index with P-vale = 0.009. while there are no statistically significant differences among patients' Child-Pugh score regarding the EQ-5D-5L score.

An analysis of the data based on the Child-Pugh classification there were lower scores in stage B and stage C patients in 8 of the tested areas (physical force, physical role, general health, vitality, social functioning, emotional role, physical component summary and mental component summary). These differences were statistically significant for Physical force (-19.2 points; p = 0.05), RP (-27.6 points; p = 0.002) and emotional role (-22.7 points; p = 0.017). Similarly, a direct relationship between other estimates of the severity of cirrhosis and quality of life in these patients was also observed. This ratio reached statistical significance in the physical role scale (p = 0.014). Also, as MELD scores increased, six scales decreased. Nevertheless, this association was statistically significant only for the RP subscale, (Gibbs et al., 2015)Another study found that MELD indices were correlated to age (r = 0.185; p = 0.033 (De Souza et al., 2015)

The present study reveals that there is statistically significant and weak positive relationship between the LDSI and the Child-Pugh score with P-value= 0.000. While there is no statistically significant relationship between the EQ-5D-5L and the Child-Pugh score. The correlation between the

dimension of the EQ-5D-5L and the Child-Pugh Score is not statistically significant in all of the EQ-5D-5L dimensions except the pain and the anxiety has a weak positive relationship with Child-Pugh Score with P-value= 0.014 and 0.013, respectively. It is noticed that there is no statistically significant relationship between the MELD and neither the LDSI nor the EQ-5D-5L with P-value= 0.087 and 0.141. And there is no statistically significant relationship between the MELD and all of the EQ-5D-5L dimensions except the anxiety has a weak positive relationship with MELD with P-value= 0.039.

The previous study found that patients with Child-Pugh stage C had lower scores in all domains of HRQOL, and their scores in domains social functioning SF (22), E/F (22.08), and pain (26.90) were significantly lower compared with patients in stages A and B. The domains physical functioning PF, energy/fatigue E/F, pain, and general health GH scores were significantly lower in patients with ascites in all domains of HRQOL. Also, a significant negative correlation was observed between MELD scores and all domains of HRQOL except the domain of role limitations due to physical health; RLEP. Age and duration of diagnosis of CLD did not show any significant correlation with the domains of HRQOL. (Pradhan & Sigdel, 2020)

CHAPTER Six

CONCLUSIONS AND RECOMMENDATION

7.1 Conclusion

This study was conducted in chronic liver disease patients in three public hospitals in Sana a city. The aim is to evaluate the health-related quality of life patient with chronic liver disease and investigate the factors affecting HRQoL among CLD patients. Data were collected by the liver disease symptom index LDSI and the EQ-5D-5L questionnaires that were translated from English and tested before collecting the data. The following are the main conclusion;

- The sample included 174 patients. The mean age of the patients was more than 55 years, two third of them are males, approximately half of them are free workers, and most of them indicate that the yearly income is not enough.
- Approximately all of the patients complain of fatigue, and two third have right hypochondrium pain and ascites, approximately half of them presented with encephalopathy, jaundice and pallor.
- Half of the patients are in class B followed by class C according to the Child-Pugh Score and the mean ± SD Score of the MELD score is16.3 ± 11.27 for the disease severity.
- Regarding the quality of life, the EQ-5D-5L, approximately half of patients have slight problems in mobility and in usual activity, half of them have problems in self-care, and approximately one third of them have slight problems in pain and discomfort while one third have no problems with anxiety or depression

- The overall LDSI is low in the hindrance of the patient daily activities and social life. The majority of patients suffer from the jaundice and loss of appetite hindrance.
- There are statistically significant differences among patients' EQ-5D-5L scores regarding the age, the level of education, the occupation, the monthly income and the yearly income.
- There are high statistically significant differences among patients' severity of disease scores regarding the admission status.
- There are statistically significant differences among patients' Child-Pugh score regarding the liver disease symptom index LDSI, while there are no statistically significant differences among patients' Child-Pugh score regarding the EQ-5D-5L scores.
- There is a weak positive relationship between the LDSI and the Child-Pugh score with. while there is no statistically significant relationship between the EQ-5D-5L and the Child-Pugh score.
- There is a weak positive relationship between Child-Pugh scores and the dimensions of pain and anxiety of EQ-5D-5L. There is lso, a weak positive relationship between MELD and the dimension of anxiety of EQ-5D-5L.

7.2 Recommendations

- ost The current findings show that autoimmune hepatitis was the m common cause among chronic liver diseases in Sana'a city, Yemen; In the light of the findings public awareness about ، health education hepatitis virus screening tests and schistosomiasis screening and treatment are the be considered. primary preventive strategy to Health education and public awareness about hazard of Hepatitis A, B and c virus (HBV) and increase the vaccination coverage to reduce alcoholic fatty liver disease -the morbidity and mortality . Non herefore, more studies NAFLD) is likely to increase in Yemen. T) need to be done to identify risk factors. Liver disease and the consequent cirrhosis of the liver are considered a public health problem in Yemen because it is a major cause of mortality and ying the risk factorsmorbidity. Other studies needed to identif that
- We recommend that Ministry of Health has to build centers for liver diseases.
- We recommend creating awareness leaflets about liver diseases and - ways to prevent them .
- making courses and field trips to educ We recommendate people about chronic liver diseases.
- We should supporting people who are looking for chronic liver - diseases.
- We recommend making educational and educational programs on - television and radio.
- We recommend that tions Ministry of Health to make the organiza support and fund the centers and provide the material for conducting examinations related to liver diseases.
- We recommend Holding conferences and seminars for health - system workers and training them to spread awareness about chronic sliver disease.
- We recommend that the patients with liver must their psychological state and anxiety.
- At psychologists.

- We recommend the Ministry of Health has to build centers for liver diseases.

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APPENDIX

9.1 Appendix 1: Questionnaire

Symptoms of chronic liver disease

Symptom	Yes	No
1. Jaundice		
2. Rt. hypochondrium pain		
3. Itching		
4. Fatigue		
5. Nausea		
6. Vomiting		
7. Anorexia		
8. Diarrhea		
9. Ascites		
10.Encephalopathy		

Signs of chronic liver disease

Signs	Yes	No
1. Ascites		
2. Clubbing		
3. Leukonychia		
4. Palmar erythema		
5. Dupuytren contracture		
6. Spider neavi		
7. Skin pigmentation		
8. Jaundice		
9. Anemia pallor		
10. Central cyanosis		
11. Fetor hepaticus		
12. Ankle edema		
13. Gynecomastia		
14. Scratch marker.		

Cause of chronic liver disease

Cause	Yes	No
1- viral -Hepatitis B		
-Hepatitis C		
-Hepatitis B+D		

CAUSE	YES	NO
2- Hemochromatosis		
3- Wilson's disease		
4- Alpha 1-antirypsine deficiency		
5- Alcoholic		
6- primary biliary cholangitis		
7-primary sclerosing cholangitis		
8- toxicity (Drug)		
9- unkown -autoantibody positive (Autoimmune)		
_ autoantibody negative		

Lab tests

Lab tests	Value
Total--Bilirubin	mg/dL
Albumin (g/dL)	g/dL
INR	%
PT	
RBC	mg/dL
S-creatinine	mg/dL
ALT	
AST	

Depend to U/S or CT Scan check of the following:

	Yes	No
Ascites		
Hepatic focal lesion		
Splenomegaly		

Clinical and lab criteria	Points*		
	1	2	3
Encephalopathy			
Total-Bilirubin (mg/dL)			
Albumin (g/dL)			
International normalized ratio			
Ascites			
Result			

Modal of end stage liver disease (MELD) Score

LABORATORY TESTS	VALUE LABS
Bilirubin	(mg/dL)
Creatinine	(mg/dL)
INR	%
3.8[Ln serum bilirubin (mg/dL)]+11.2[Ln INR] +9.6 [Ln serum creatinine (Mg\dl0]+6.4	Result

تقييم جودة الحياة لمرضى الكبد المزمن

استبيان صحي :

الجنس : □ ذكر □ انثى

العمر بالسنة :

مكان الإقامة : □ حضر □ ريف

المؤهل العلمي:

□ أمي □ يقرأ ويكتب □ أساسي □ ثانوي □ بكالوريوس □ دراسات عليا

المهنة: □ موظف □ غير موظف □ رجل اعمال □ عمل حر □ طالب □ ربة بيت

الدخل العائلي : □ اقل من ٣٠٠٠٠ ريال يمني □ ٣٠٠٠٠-٥٠٠٠٠ ريال يمني □ ٥٠٠٠٠-١٠٠٠٠٠ريال يمني

□ ١٠٠٠٠٠-١٥٠٠٠٠ ريال يمني □ اكثر من ١٥٠٠٠٠ ريال يمني

الدخل السنوي: □ كافي □ غير كافي

موشر أعراض مرض الكبد 2. 0

استبيان

هذا الاستبيان يستفسر عن شدة الأعراض التي تشعر بها و تعاني منها و الى اى مدى هذه الاعراض تاثر على عملك او انشطتك اليومية او الاجتماعية. سوف تقوم بتحديد الإجابة التي تنطبق عليك جميع الأسئلة متصلة بالأسبوع الماضي.

على سبيل المثال :

البند 1 : إلى أي مدى في الاسبوع الماضي: شعرت بالم؟

0 لم يحدث على الإطلاق	1	2	3	4 إلى حد كبير

البند 2 : إلى أي مدى في الاسبوع الماضي: أعاقك الالم في عملك أو في أنشطتك اليومية ؟

0 لم يحدث على الإطلاق	1	2	3	4 إلى حد كبير

موشر أعراض مرض الكبد .0 .2	لم يحدث على الإطلاق 0 — 4 إلى حد كبير
(1أ) إلى أي مدى في الأسبوع الماضي: عانيت من حكة / هرش بجسمك؟	لم يحدث على الإطلاق □□□□□ إلى حد كبير
(1ب) الى أي مدى في الأسبوع الماضي: اعاقتك الحكة /الهرش بجسمك في عملك أو أنشطتك اليومية؟	لم يحدث على الإطلاق □□□□□ إلى حد كبير
(1ج) إلى أي مدى في الأسبوع الماضي: اعقتك الحكة /الهرش بجسمك اثناء النوم؟	لم يحدث على الاطلاق □□□□□ إلى حد كبير
(2أ) إلى أي مدى في الأسبوع الماضي: عانيت من ألم في المفاصل؟	لم يحدث على الإطلاق □□□□□ إلى حد كبير
(2ب) إلى أي مدى في الأسبوع الماضي: اعاقك ألم المفاصل في عملك أو في أنشطتك اليومية؟	لم يحدث على الإطلاق □□□□□ إلى حد كبير
(3أ) إلى أي مدى في الأسبوع الماضي: عانيت من ألم في الجانب العلوي الأيمن من البطن؟	لم يحدث على الاطلاق □□□□□ إلى حد كبير
(3ب) إلى أي مدى في الأسبوع الماضي: اعاقك ألالم في الجانب العلوي الأيمن من البطن في عملك أوفي انشطتك اليومية؟	لم يحدث على الإطلاق □□□□□ إلى حد كبير
(4أ) إلى أي مدى في الأسبوع الماضي: كان النوم يغلبك أثناء النهار؟	لم يحدث على الإطلاق □□□□□ إلى حد كبير
(4ب) إلى أي مدى في الأسبوع الماضي: اعاقك النوم أثناء النهار في عملك أوفي أنشطتك اليومية؟	لم يحدث على الإطلاق □□□□□ إلى حد كبير
(5أ) إلى أي مدى في الأسبوع الماضي: كنت قلقاً بشأن تأثير مرض الكبد الذي تعاني منه على الوضع العائلي/ اسرتك؟	لم يحدث على الإطلاق □□□□□ إلى حد كبير
(5ب) إلى أي مدى في الأسبوع الماضي: أعاقك القلق (القلق من تاثير مرض الكبد على حياتك العائلية) في عملك أو في أنشطتك اليومية؟	لم يحدث على الإطلاق □□□□□ إلى حد كبير
(6أ) إلى أي مدى في الأسبوع الماضي: كان لديك ضعف في الشهية؟	لم يحدث على الإطلاق □□□□□ إلى حد كبير
(6ب) إلى أي مدى في الأسبوع الماضي: أعاقك ضعف الشهية الذي تعاني منه؟	لم يحدث على الإطلاق □□□□□ إلى حد كبير
(7أ) إلى أي مدى في الأسبوع الماضي: شعرت بالاكتئاب (الحزن الشديد) بسبب مرضك؟	لم يحدث على الإطلاق □□□□□ إلى حد كبير
(7ب) إلى أي مدى في الأسبوع الماضي: أعاقك الاكتئاب بسبب مرضك في عملك، أنشطتك اليومية و/أو علاقاتك الاجتماعية؟	لم يحدث على الإطلاق □□□□□ إلى حد كبير

١

- **الحركه**

١. ليس لدي أي مشاكل اثناء المشي
٢. امتلك مشاكل خفيفة اثناء المشي
٣. امتلك مشاكل متوسطة اثناء المشي
٤. انا غير قادر على المشي

الرعاية الذاتية

١. ليس لدي أي مشاكل في تنظيف نفسي او ارتداء الملابس
٢. لدي مشاكل خفيفة في تنظيف نفسي او ارتداء الملابس
٣. لدي مشاكل متوسطة في تنظيف او ارتداء الملابس
٤. لدي مشاكل شديدة في تنظيف او ارتداء الملابس
٥. انا غير قادر على تنظيف او ارتداء الملابس

الأنشطة المعتادة) مثل العمل او الدراسة او الاعمال المنزلية او الأنشطة العائلية او الترفيهية

١. انا لا اشعر باي مشاكل اثناء عملي او نشاطاتي اليومية
٢. انا اشعر بمشاكل خفيفة او ضئيلة اثناء عملي ونشاطاتي اليومية (أي قد لا انتبه لها اطلاقا ولا تمنعني عن عملي ونشاطاتي اليومية اطلاقا)
٣. انا اشعر بمشاكل متوسطة اثناء عملي ونشاطاتي اليومية (أي قد لا تمنعني عن عملي ولكن تتعبني بعض الوقت اثناء عملي ونشاطاتي اليومية)
٤. انا اشعر بمشاكل شديدة اثناء عملي ونشاطاتي اليومية (أي قد تتعبني كل الوقت تعب شديد اثناء عملي ونشاطاتي اليومية)
٥. انا اشعر بمشاكل شديده جدا اثناء عملي ونشاطاتي اليومية (ولا أستطيع ان اعمل اطلاقا)

عدم الارتياح

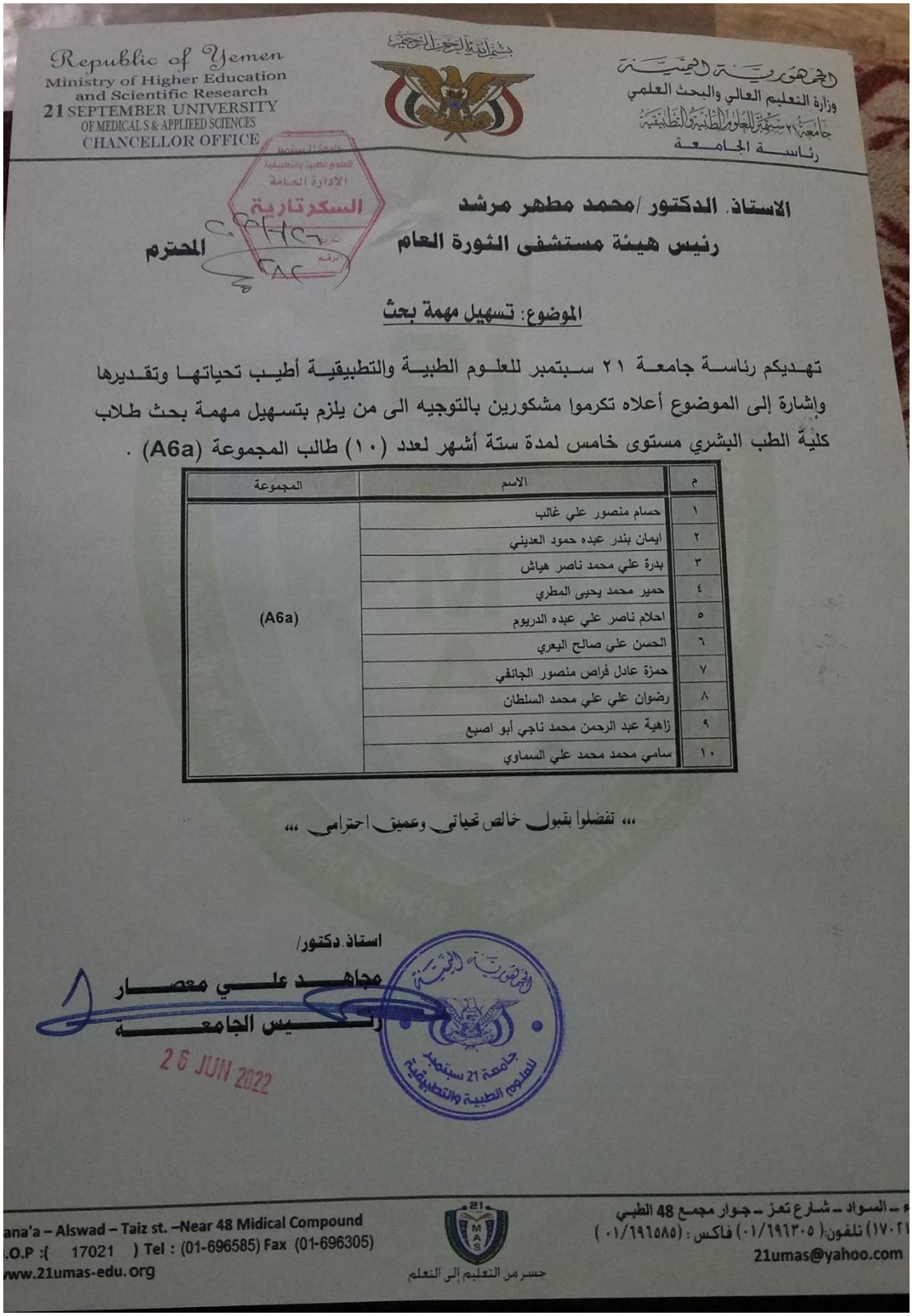
١. انا لا اشعر ب الم ولا مضايقة
٢. انا اشعر ب الم ومضايقة خفيفة (يعني لا اتنتبه للألم وليؤثر على نشاطك وعملك اليومي)
٣. انا اشعر ب الم متوسط ومضايقة (يعني تشعر ب الألم ومن الممكن يمنعك من عملك لكن تأخذ ادوية وتتحسن)
٤. انا اشعر ب الم ومضايقة شديدة (يعني بحيث هذا الألم يمنعك من القيام بنشاطك اليومي واخذت ادويه وما تحسنت)
٥. انا اشعر ب الم ومضايقة شديدة جدا (بحيث مثلا فقدت وعيك وتم اسعافك الى المستشفى)

القلق/ الاكتئاب

١. لست قلق او مكتئب
٢. انا قلق او مكتئب قليلا (لا يؤثر على حياتي اليومية)
٣. أعاني من قلق او اكتئاب متوسط (يؤثر على نشاطاتي وحياتي اليومية)
٤. اشعر بقلق او اكتئاب شديد (لدرجة لا أقدر على أداء نشاطاتي وحياتي اليومية بشكل جيد)
٥. أشعر بقلق او اكتئاب لأقصى حد (لدرجة أنى اظل طول اليوم في البيت)

- نحن نريد ان نعرف ما مدى صحتك لهذ اليوم
- هذا المقياس من رقم 1الى رقم ١٠
- رقم 10يمثل أحسن مستوى لصحتك ممكن تتخيلها
- رقم 0 يمثل أسوأ مستوى لصحتك ممكن تتخيله
  - 1
  - 2
  - 3
  - 4
  - 5
  - 6
  - 7
  - 8
  - 9
  - 10
- اعمل إشارة على المقياس الذي اخترته الذي يمثل صحتك لهذا اليوم
- الان اكتب الرقم الذي تم الإشارة علية في المقياس في المربع اسفل
- صحتك لهذا اليوم ☐

9.2 Appendix 2



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بسم الله الرحمن الرحيم

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رئاسة الجامعة

السكرتارية

الاستاذ. الدكتور /محمد مطهر مرشد
رئيس هيئة مستشفى الثورة العام

المحترم

الموضوع: تسهيل مهمة بحث

تهديكم رئاسة جامعة ٢١ سبتمبر للعلوم الطبية والتطبيقية أطيب تحياتها وتقديرها وإشارة إلى الموضوع أعلاه تكرموا مشكورين بالتوجيه الى من يلزم بتسهيل مهمة بحث طلاب كلية الطب البشري مستوى خامس لمدة ستة أشهر لعدد (١٠) طالب المجموعة (A6a) .

م	الاسم	المجموعة
١	حسام منصور علي غالب	(A6a)
٢	ايمان بندر عبده حمود العديني	
٣	بدرة علي محمد ناصر هياش	
٤	حمير محمد يحيى المطري	
٥	احلام ناصر علي عبده الدريوم	
٦	الحسن علي صالح البعري	
٧	حمزة عادل فراص منصور الجائفي	
٨	رضوان علي علي محمد السلطان	
٩	زاهية عبد الرحمن محمد ناجي أبو اصبع	
١٠	سامي محمد محمد علي السماوي	

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استاذ.دكتور/
مجاهد علي معصار
رئيس الجامعة

26 JUN 2022

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ء – السواد – شارع تعز – جوار مجمع 48 الطبي
١٧٠٢١) تلفون: (٠١/٦٩٦٣٠٥) فاكس : (٠١/٦٩٦٥٨٥)
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الدكتور/أمين الجنيد

مدير عام مستشفى الكويت التعليمي

المحترم

السكرتارية

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رئاسة الجامعة

الإدارة العامة
السكرتارية
الرقم: ٢٨١

الاستاذ الدكتور/ محمد جحاف

رئيس هيئة المستشفى الجمهوري

المحترم

الموضوع: تسهيل مهمة بحث

تهديكم رئاسة جامعة ٢١ سبتمبر للعلوم الطبية والتطبيقية أطيب تحياتها وتقديرها وإشارة إلى الموضوع أعلاه تكرموا مشكورين بالتوجيه الى من يلزم بتسهيل مهمة بحث طلاب كلية الطب البشري مستوى خامس لمدة ستة أشهر لعدد (١٠) طالب المجموعة (A6a) .

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المحترم
الإدارة العامة للشؤون السكرتارية
الوارد
الرقم ٢٠١٢

الاخ/ مدير عام مكتب الصحة – امانة العاصمة

الموضوع: تسهيل مهمة بحث

تهديكم رئاسة جامعة ٢١ سبتمبر للعلوم الطبية والتطبيقية أطيب تحياتها وتقديرها وإشارة إلى الموضوع أعلاه تكرموا مشكورين بالتوجيه الى من يلزم بتسهيل مهمة بحث طلاب كلية الطب للدفعة الاولى مستوى خامس قسم الباطنة لعدد(١٠) طلاب المجموعة (A6a) تحت اشراف الدكتور/ احمد البحيري، والدكتور/ فواز ابو الغيث، بحسب عنوان البحث الموضح قرين اسمائهم:-

م	الاسم	عنوان البحث
١	حسام منصور علي غالب	Health Related Quality of life among Chronic Liver Diseases patients at Public Hospitals in Sana'a City2022.
٢	ايمان بندر عبده حمود العديني	
٣	بدرة علي محمد ناصرهياش	
٤	حمير محمد يحيى المطري	
٥	احلام ناصر علي عبده الدريوم	
٦	الحسن علي صالح اليعري	
٧	حمزة عادل فراص الجانفي	
٨	رضوان علي علي محمد السلطان	
٩	زاهية عبدالرحمن محمد ابو اصبع	
١٠	سامي محمد محمد علي السماوي	
	//////////	

،،، تفضلوا بقبول خالص تحياتي وعميق احترامي ،،،

استاذ.دكتور/
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جسر من التعليم إلى التعلم

صنعاء – السواد – شارع تعز – جوار مجمع 48 الطبي
ص.ب(١٧٠٢١) تلفون:(٠١/٦٩٦٣٠٥) فاكس : (٠١/٦٩٦٥٨٥)
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الملخص

الخلفية: مرض الكبد المزمن هو سبب رئيسي للوفيات والمراضة في جميع أنحاء العالم. إنه السبب الحادي عشر للوفاة والسبب الرئيسي الخامس عشر للمراضة، وهو مسؤول عن ٢.٢٪ من الوفيات و١.٥٪ من سنوات العمر المعدلة حسب الإعاقة في جميع أنحاء العالم. نوعية الحياة المتعلقة بالصحة (HRQL) هي بناء متعدد الأبعاد يشمل الجوانب النفسية والاجتماعية والوظيفية للمرض بالإضافة إلى جوانبه الجسدية. عادةً ما يتم تقييم HRQL بمساعدة التدابير المبلغ عنها ذاتيًا، والتي تعكس تقييم المريض لمرضه أو مرضها والعيوب المصاحبة له.

الهدف من الدراسة: كان الهدف العام من الدراسة هو تقييم نوعية الحياة المتعلقة بالصحة HRQOLبين مرضى أمراض الكبد المزمنة في المستشفيات العامة في مدينة صنعاء.

المنهجية: تم استخدام دراسة مقطعية وصفية قائمة على المستشفى. كان حجم العينة ١٩٧ مريضا. تم الاتصال بالعينة في المستشفيات العامة في الأجنحة الطبية وأقسام العيادات الخارجية للمرضى. تتكون أدوات جمع البيانات من جزأين: استبيانات جودة الحياة المتعلقة بالصحة وصحيفة البيانات السريرية. استغرقت تعبئة الاستبيان من (١٥ - ٣٠) دقيقة. قدم الباحثون شرحًا موجزًا لموضوع الدراسة وأهدافها. تم توضيح أي استفسارات حول أسئلة المرضى من قبل الباحثين. تم جمع البيانات السريرية من خلال مراجعة سجلات المرضى والفحص البدني المباشر. تم تحليل البيانات بواسطة برنامج.SPSS

النتائج: كان متوسط عمر المرضى أكثر من ٥٥ سنة ٧٥.٩٪ منهم ذكور و٤٥.٤٪ عامل حر. ٩١.٤٪ من المرضى يشكون من التعب و٧٣.٠٪ يعانون من ألم المراق الأيمن والاستسقاء. يمثل الجسم المضاد الإيجابي ٤١.٣٪ من أسباب .CLD حوالي ٤٨.٣ ٪ من المرضى في الفئة B متبوعًا بالفئة C وفقًا لدرجة Child-Pugh ومتوسط SD ± من درجة MELD هو ١٦.٣ ± ١١.٢٧ لشدة المرض. يعاني ٤١.٤٪ من المرضى من مشكلة طفيفة في الحركة و٤٣.٧٪ في النشاط المعتاد، ونصفهم يعانون من مشكلة في الرعاية الذاتية، وحوالي ثلثهم يعانون من مشاكل

طفيفة في الألم وعدم الراحة بينما لا يعاني ثلثهم من القلق أو الاكتئاب. يعاني غالبية المرضى من اليرقان وانخفاض الشهية.

الخلاصة: إن LDSI الكلي منخفض في إعاقة أنشطة المريض اليومية والحياة الاجتماعية. توجد فروق ذات دلالة إحصائية بين درجة EQ-5D-5L للمرضى فيما يتعلق بالعمر ومستوى التعليم والمهنة والدخل الشهري والدخل السنوي. تم العثور على فروق ذات دلالة إحصائية بين درجة Child-Pugh للمرضى فيما يتعلق بمؤشر أعراض أمراض الكبد LDSI، بينما لا توجد فروق ذات دلالة إحصائية بين درجة Child-Pugh للمرضى فيما يتعلق بنتيجة EQ-5D-5L.

الجمهورية اليمنية

وزارة التعليم العالي والبحث العلمي

جامعة ٢١ سبتمبر للعلوم الطبية والتطبيقية

كلية الطب البشري

Republic of Yemen
Minister of Higher Education and Scientific Education
21 September University for Medical and Applied Science
Faculty of Medicine

جودة الحياة المرتبطة بالصحة بين مرضى الكبد المزمن في المستشفيات العامة في مدينة صنعاء-٢٠٢٢

إعـــــــداد /

احـلام ناصر الـدريـوم

أيـمان بنـدر العـديني

حسـام منصـور علـي

حميـر محمـد المطـري

زاهيـه عبد الرحمـن أبـو اصبـع

الحـسن علي اليعـري

بـدره علـي هياش

حمـزه عـادل الجـائـفي

رضـوان علي السلطـان

سامـي محمـد السمـاوي

المـشرف الرئيسي /
د. احمـد البحيـري

مشرف طب المجتمع /
د. فـوز أبـو الـغيث

مشروع بحث تخرج إكمال متطلبات درجة البكالوريوس في تخصص الطب البشري

٢٠٢٢م \ ١٤٤٣هـ

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