COLLEGE OF MEDICINE AND HEALTH SCIENCES

DEPARTMENT OF SURGERY

DIVISION OF GI AND ENDOCRINE SURGERY

HPB SURGERY UNIT

EPIDEMIOLOGY AND CLINICAL FEATURES OF PATIENTS WITH HEPATOCELLULAR CARCINOMA IN TIKUR ANBESSA SPECIALIZED HOSPITAL

PRINCIPAL INVESTIGATOR: YOSEPH SOLOMON (M.D., GENERAL SURGEON, HPB SURGERY FELLOW)

EMAIL: josephsol87@gmail.com PHONE NO: +251911335136

ADVISOR: Dr. Zeki Abdurahman

A RESEARCH THESIS SUBMITTED TO DEPARTMENT OF SURGERY COLLEGE OF MEDICINE AND HEALTH SCIENCES, ADDIS ABABA UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE SUB-SPECIALITY CIRTIFICATE IN HEPATOPANCREATICOBILIARY SURGERY.

July 2023

ADDIS ABABA, Ethiopia

Name of Investigator	Yoseph Solomon (General Surgeon and HPB Fellow) Phone Number: +251911335136 Email address: josephsol87@gmail.com
Name of Adviser	Zeki Abdurahman (Consultant General and HPB Surgeon, Associate Professor of Surgery Phone Number: +251918350100 Email Address: zaksurgery@gmail.com
The full title of the research project	EPIDEMIOLOGY AND CLINICAL FEATURES OF PATIENTS WITH HEPATOCELLULAR CARCINOMA IN TIKUR ANBESSA SPECIALIZED HOSPITAL
Study Period	From January 2018 to December, 2022
Study Area	Tikur Anbessa Specialized Hospital
Budget	31,800

DECLARATION

This is to certify that the research thesis entitled "Epidemiology and clinical features of patients with hepatocellular carcinoma in Tikur Anbessa Specialized Hospital"; submitted as partial fulfillment of sub-specialty certificate in Hepatopancreaticobiliary Surgery, Addis Ababa University, is a record of my original work and has not been submitted to any other institution for any purpose. The references used for this thesis are properly cited and the assistance I received has been duly acknowledged.

Yoseph Solomon Bezabih _____

Name of the candidate

_____

Date

APPROVAL OF THESIS FOR DEFENSE

I hereby certify that I have supervised, read, and evaluated this research thesis titled "Epidemiology and clinical features of patients with hepatocellular carcinoma in Tikur Anbessa Specialized Hospital" by Yoseph Solomon under my guidance. I recommended the thesis for oral defense.

Advisor's name	Signature	Date
1. Dr. Zeki Abdurahman	_____	_____

ACKNOWLEDGMENTS

I would like to acknowledge Addis Ababa University College of Health science, department of surgery for providing me this opportunity to conduct this research project. I would like to thank my advisor Dr. Zeki Abdurahman for his guidance and advice in preparation of this research thesis.

Table of Contents

List of tables Page No.

Acronyms and Abbreviations:

AAU	Addis Ababa University
AFP	Alfa-Feto Protein
BCLC	Barcelona-Clinic Liver Cancer
CHS	College of health Science
CT	Computed Tomography
DM	Diabetes Mellitus
EMR	Electronic Medical Record
HBV	Hepatitis B Virus
HBsAg	Hepatitis B surface Antigen
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C Virus
HCVAb	Hepatitis C Virus Antibody
HMIS	Health Management Information System
NASH	Non-alcoholic steatohepatitis
TASH	Tikur Anbessa Specialized Hospital
T2DM	Type 2 Diabetes Mellitus

Abstract

Introduction: Hepatocellular carcinoma (HCC) is a primary malignant neoplasm derived from hepatocytes, accounting for about 80% of all liver cancers. HCC ranks as the 5th most prevalent malignancy and the 2nd-leading cause of cancer-related death worldwide. The incidence of HCC varies widely according to geographic location. The distribution of HCC also differs among racial and ethnic groups within the same country.

Methods: Descriptive cross – sectional study design was used. The study was conducted at Tikur Ambessa Specialized Hospital from April 2018 to March 2023. Data was gathered from HMIS, patient charts, and EMR by trained residents and interns.

Results: From a cohort of 145 participants, 106 were male and 39 were female. The mean and the median age of the study participants were 52.8 years and 55 years respectively. we found that 16.55% had one or more co-morbid conditions. In our cohort, 32.41% of HCC cases were attributed to HBV infection, while 19.31% tested positive for HCV. Patients with HBV-associated HCC had a median age of 43 years and a mean age of 44.85 years. We identified 36 patients with a history of alcohol use. Among our study participants, 19 individuals (22.62%) were diagnosed with decompensated cirrhosis.

Conclusion: HCC presenting to TASH affects more males than females. Hepatitis B virus infection is the leading etiological risk factor associated with HCC. Health facilities should implement policies that: Prevent HBV/HCV transmission and implement surveillance for high-risk groups. There is an urgent need to improve education of the population on hepatitis and its dreaded complication HCC. Health care providers should also be provided with HCC surveillance education and should establish programmes to implement surveillance.

Key Words: Clinical feature, Epidemiology, Hepatocellular carcinoma.

1. Introduction

1.1. Background of the study

Liver cancer is one of the world common malignant tumours. It accounts as the sixth most common cancer, and the second global cancer related death [1]. Hepatocellular carcinoma (HCC) is a primary malignant neoplasm derived from hepatocytes, accounting for about 80% of all liver cancers. Other types of liver cancers, including intrahepatic cholangiocarcinoma, hepatoblastoma and angiosarcoma, are relatively rare compared to HCC. Therefore, the morbidity of liver cancer can be regarded to be a broadly accurate reflection of HCC incidence [1, 2]. In 2012,HCC had an estimated global incidence of 782,000 cases, representing the fifth most common cancer in male individuals and ninth most common cancer in female individuals [3]. More importantly, HCC is a lethal cancer as it is the second leading cause of cancer deaths globally and accounted for 746,000 deaths worldwide in 2012 [3]. The number of deaths per year in HCC is virtually identical to the incidence throughout the world, underscoring the high case fatality rate of this aggressive disease [4]. HCC has unique geographic, sex, and age distributions that are likely determined by specific etiologic factors.

The incidence of HCC varies widely according to geographic location [4]. The distribution of HCC also differs among racial and ethnic groups within the same country, and between regions within the same country [5]. The highest incidence countries (>10 per 100 000/year) are observed in China, Southeast Asia, sub-Saharan western and eastern Africa [3].

The global age distribution of HCC varies by region, gender, and aetiology [6]. In all parts of the world, men are more likely than women to develop HCC. The disparity is more pronounced in high-incidence regions, where men are affected 2.1 to 5.7 times more frequently than women (mean 3.7:1) [4]. It usually appears after the age of 40 years and reaches a peak around 70 years of age [7].The majority of HCCs occur in patients with chronic liver disease or cirrhosis. Thus, older patients with longstanding liver disease are more likely to develop HCC. In most high-risk Asia-Pacific populations (e.g., Hong Kong), the highest age specific rates are people aged beyond 75, which is like that in the most low-risk Western countries. On the other hand, the age-specific rates of men in high-risk African populations (e.g., Gambia and Mali) tend to peak in the 60 to 65 age group, while that of

women peak between 65 and 70 years old. These variations of age-specific patterns are likely related to the differences in the dominant hepatitis virus in the population, the age at viral infection as well as the existence of other risk factors [1] [8].

Based on available epidemiological data, HCC is a complex disease entity with multiple possible aetiologies, and associated with many risk factors and cofactors [9, 10]. Approximately 70% to 90% of patients with HCC have an available case history of chronic liver disease and liver cirrhosis, with major risk factors including chronic infection with hepatitis B virus (HBV), hepatitis C virus (HCV), alcoholic liver disease, and non-alcoholic steatohepatitis (NASH) [11, 12].

The incidence of hepatocellular carcinoma (8.9 cases per 100 000 person-years) is higher in Africa than in most of the rest of the world because of high prevalences of chronic infections with hepatitis B and C [3, 8, 13, 14]. Hepatocellular carcinoma is a leading cause of cancer-related death in many African countries because of the combination of high incidence and high cancer-specific mortality [3]. The disease burden of hepatocellular carcinoma in Africa appears to be higher than has been reported in the scientific literature; this underestimation might be partly due to a shortage of resources and incomplete data collection [15]. In addition to its high incidence, hepatocellular carcinoma is diagnosed at an earlier age and at more advanced stages in Africa than in the rest of the world. Findings from previous study showed that hepatocellular carcinoma occurs at a young age in Africa, at a median of 45 years (IQR 35–57) [16]. Results from another cohort study from The Gambia also showed that most patients in this country with hepatocellular carcinoma present at an advanced stage of disease [17].

1.2. Statement of the problem

The disease burden of HCC in Africa appears to be higher than has been reported in the scientific literature; this underestimation might be partly due to a shortage of resources [13]. In addition to its high incidence, HCC is diagnosed at an earlier age and at more advanced stages in Africa than in the rest of the world. Findings from previous study showed that HCC occurs at a young age in Africa, at a median of 45 years (IQR 35–57) [14]. Results from another cohort study from Gambia also showed that most patients in this country with HCC present at an advanced stage of disease [15]. As Ethiopia is a country where HBV infection is prevalent, the incidence of HCC is expected to be high.

1.3. Significance of the study

Hepatocellular carcinoma is a leading cause of cancer-related death in Africa, but there is still no comprehensive description of the status of its epidemiology in Africa including Ethiopia. There are scarce studies done in Ethiopia regarding liver cancer, particularly HCC. As Ethiopia is a country where HBV infection is prevalent, the incidence of HCC is expected to be high. We therefore initiated this study aiming to establish a database of cases to describe the clinical features of patients with this disease in our population. Here, we will try to describe the demographic characteristics, risk factors, clinical presentation, and characteristics of the tumour in of patients with hepatocellular carcinoma. We hope this study can be a baseline data for future population based nationwide studies and it may highlight the burden of the illness so that policy makers give attention to this fatal cancer.

2. Literature Review

In a study done in a USA, they identified a national cohort of 518 veterans diagnosed with HCC from 2004 through 2011, with follow-up ending in 2014, who received no palliative or curative treatment. The mean age at HCC diagnosis was 65.7 years; with 177 (33.4%), 139(26.9%), 138(26.6%) and 68 (13.1%) in the age group of >70, 61-70, 56-60 and <55 years respectively. All but 2 participants were male (99.6%). Most patients had HCV (314; 60.6%) or alcohol abuse (411; 79.3%), whereas non-alcoholic fatty liver disease (48; 9.3%), HBV (27; 5.2%), and other causes (18; 3.5%) of liver disease were less common. Most patients had cirrhosis (426; 82.2%) and were Child-Pugh Class B (227; 43.8%) at time of HCC diagnosis. A total of 14 (2.7%) patients had BCLC stage 0/A, 76 (14.7%) had stage B, 227 (43.8%) had stage C, and 166 (32.0%) had stage D disease at the time of diagnosis. Serum AFP levels were <10 in 99, 10-100 in 95, 100-1000 in 103 and >1000 in 168 of patients. 274 patients had ascites and in 244 patients' ascites was not detected. Regarding the tumour, 186 patients had unilocular tumours and 331 had multilocular lesion, whereas the largest lesion measured <5cm, 5-10 cm and > 10cm in 193, 154 and 152 patients. Portal vein invasion or thrombosis was reported in 176 cases, while 86 patients had metastatic lesion. Almost all patients (99%) died within the observation period; the median overall survival time was 3.6 months and survival times were 13.4, 9.5, 3.4, and 1.6 months for patients with Barcelona Clinic Liver Cancer stages 0/A, B, C, and D, respectively [16].

In one study done between 2008 and 2014 at King Abdulaziz University Hospital, Jeddah, Saudi Arabia, 128 adult patients with a diagnosis of HCC were included. Men comprised 77.3 % (99) of the cases. Abdominal pain was the chief complaint in 18.8% of the patients. In 68.0% (87) of the cases, patients presented with multiple complaints. Disease duration ranged from ≤3 months to >5 years, with 29.7% of the patients having a duration of ≤3 months. Abdominal mass, Hepatomegaly, Ascites, Jaundice and Multiple signs were present in 1 (0.8%), 14 (10.9%), 8 (6.3%), 4 (3.1%) & 92 (71.9%) of cases respectively. AFP levels were normal in 25.0% of the sample, whereas 40.6% had AFP levels ≥1000 ng/mL. Cirrhosis was diagnosed in 60.2% of the patients, and approximately two-fifths (39.8%, N=51) had Child's Class B disease; a smaller proportion had Child's Class A (22.7%) or Class C cirrhosis (35.2%). Palliation was offered to 68.0% of the patients while 14.1% underwent multiple therapies. Less than 2% of the patients survived to 5 years. The most common risk factors included HBV and HCV infections, documented in 24.2% and 33.6% of the patients, respectively. More than half of the patients (60.2%) had multiple liver tumours, and approximately 50.8% of the cases had tumours >5 cm in diameter. Patients with unilobular lesions comprised about two-fifths (34.9%) of the sample. Metastatic disease was documented in 44.6% of the patients; 28.1% and 27.3% had localized and locoregional disease, respectively. Patients with tumours >5 cm were more likely to have Child's Class C disease, whereas those with tumours ≤2 cm were more likely to have Child's Class A [$P < 0.001$]. Similarly, patients with bilobular or metastatic tumours were more likely to have Child's Class C disease ($P = 0.001$ and 0.002, respectively). No difference in Child-Pugh score was found between patients with single or multiple tumours ($P = 0.480$). Furthermore, patients who were both hepatitis B and C positive were more likely to have Child's Class C disease ($P = 0.018$). Likewise, those who had abnormal AFP and ALP levels ≥1000 ng/mL were more likely to have Child-Pugh's Class C liver disease ($P = 0.021$ in both cases) [17].

In a study carried out on patients admitted to Al-Thawra Teaching Hospital, Sana'a, Yemen; with confirmed hepatocellular carcinoma from January 2001–December 2008; 251 patients were included. Most of the patients 75.3% (189) were males giving a male to female ratio of 3.05:1. Age range was 26–75 years, with mean 53.5 (SD 13.9) years. Almost half the patients, 49% (123), were aged 41–60 years. The majority of patients 98% (246) presented with frequent abdominal pain, followed by hepatomegaly 94% (236) and

abdominal mass 61.0% (153). Most of the patients, 109 (43.4%) had right lobe involvement and 154 (61.3%) presented with multiple lesions. The size of the single focal lesion was > 10 cm in 61 (62.9%) patients, 5–10 cm in 23 (23.7%) and only 13 (13.5%) had a lesion < 5 cm. Chronic hepatitis B virus infection (48.2 %) and hepatitis C virus infection (38.2%) were the most frequently identified risk factors. Double infection (HBsAg and HCV Ab) was found in only 6 patients. Virus markers were negative in only 13.5% of the patients and this was more obvious in non-cirrhotic cases. 74.0% (187) of patients had cirrhotic liver associated with hepatocellular carcinoma. Serum α-fetoprotein level was greater than 200 ng/mL in 44.6% of patients. Overall mortality rate within 6 months of admission to hospital was 24.3% [18].

In a multicentre, retrospective observational cohort study, done in various African countries information was obtained for 2566 patients at 21 tertiary referral centres (two in Egypt, nine in Nigeria, four in Ghana, and one each in the Ivory Coast, Cameroon, Sudan, Ethiopia, Tanzania, and Uganda). 1251 patients were from Egypt and 1315 were from the other African countries (491 from Ghana, 363 from Nigeria, 277 from Ivory Coast, 59 from Cameroon, 51 from Sudan, 33 from Ethiopia, 21 from Tanzania, and 20 from Uganda). The overall median age of patients was 54 years (IQR 44–61) and almost three-quarters were male (73.2%, N=1877). HCV was the leading cause of hepatocellular carcinoma in Egypt whereas HBV was the leading cause in other African countries. Overall, 64 (3%) of 2333 patients had evidence of HBV–HCV co-infection. The proportion of patients with unknown or other causes was higher in other African countries than in Egypt. The age at onset of HCV-induced hepatocellular carcinoma was significantly different between African countries (p=0•02). The median ages of HCV-associated hepatocellular carcinoma were 62 years (IQR 52–75) in Cameroon, 67 years (55–72) in Ivory Coast, 59 years (44–69) in Ethiopia, 65 years (54–75) in Ghana, 55 years (47–67) in Nigeria, 58 years (53–63) in Egypt, and 80 years in Sudan (only one patient; appendix). The median age of HBV-associated hepatocellular carcinoma also varied by country (appendix; p<0•0001). Although the median age of HBV-associated hepatocellular carcinoma was younger than 45 years in most other African countries (Cameroon 41 years [IQR 29–48]; Ivory Coast 44 years [36–54]; Ethiopia 39 years [31–50]; Ghana 41 years [34–50]; Nigeria 38 years [31–49]; Tanzania 43 years [34–48]; and Uganda 32 years [27–43]), the median age was older in Sudan (57 years [IQR 45–65]) and Egypt (52 years [50–62]). Thus, the median age at onset of HBV-associated hepatocellular carcinoma was younger than the median age at

onset of HCV-associated hepatocellular carcinoma in all African countries (42 years [IQR 34–51] vs58 years [53–63]; p<0•0001). The median ages of patients with hepatocellular carcinoma associated with HBV–HCV co-infection were older in Egypt (59 years [IQR 54–62]), Cameroon (52 years [52–52]), and Ivory Coast (60 years [50–63]) than in Uganda (45 years [33–56]), Ghana (43 years [37–51]), and Nigeria (47 years [38–58]; p=0•003; appendix).For HCV-associated hepatocellular carcinoma, the peak age ranges were 57•5–62•5 years in Egypt and 47•5–52•5 years in other African countries. The most frequent age range at diagnosis for HBV-associated hepatocellular carcinoma was 47•5–52•5 years in Egypt and 37•5–42•5 years in other African countries; for hepatocellular carcinoma associated with HBV–HCV co-infection, the peak age ranges were 57•5–62•5 years in both Egypt and other African countries. The BCLC stage at presentations for patients from Egypt were stages A–B 342/1103 (31%), C 672/1103 (62%) and D 73/1103 (7%) in proportion, whereas in other African countries they presented with Stage A-B, C and D in 27/288 (5%), 125/288 (23%) and 393/288 (72%) of cases respectively. Consistent with the high prevalence of HBV in other African countries and the known tendency of HBV-associated hepatocellular carcinoma to develop in the absence of cirrhosis, the proportion of patients with non-cirrhotic hepatocellular carcinoma and mean platelet counts were higher in other African countries than in Egypt. The severity of underlying liver dysfunction, tumour extent, serum α-fetoprotein concentrations, patient performance status, and the Barcelona-Clinic Liver Cancer (BCLC) stage were all worse in other African countries than in Egypt, most probably reflecting the absence of surveillance and the consequent diagnosis of hepatocellular carcinoma at advanced symptomatic stages in other African countries [19].

3. Objective

3.1. General Objective

To assess the epidemiologic and clinical characteristics of patients with HCC at TASH, Department of surgery.

3.2. Specific Objectives

- To describe risk factors associated with HCC.
- To describe the clinical characteristics of patients with HCC.

4. Material and Methods

4.1. Study area and study period.

✓ The study was conducted at Tikur Ambessa Specialized Hospital from April 2018 to March 2023.

4.2. Population

4.2.1. Source population.

✓ All adult patients in the study area who were diagnosed with HCC.

4.2.2. Study population.

✓ All adult patients who were diagnosed with HCC in the study period.

4.3. Eligibility criteria

4.3.1. Inclusion criteria

- All adults with HCC who are above 18 years.

4.3.2. Exclusion criteria

- Patients with incomplete data

4.4. Study design,

Descriptive cross – sectional study design was used.

4.5. Sample size determination and sampling procedure.

Single population proportion formula was used with the following assumption.

$$n = \frac{(Z_a/2)^2 pq}{d^2} = \frac{(1.96)^2 * 0.5 * 0.5}{0.05^2}$$

✓ P = 0.5

✓ q = 0.5

- ✓ d = 0.05
- ✓ Z = 1.96

- The sample size become 384. By adding 10% for incomplete data the total sample size will be 422. A simple random sampling technique was used.

4.6. Data collection method

A semi-structured questionnaire written in English was used to collect the data. Data was gathered from HMIS, patient charts, and EMR by trained residents and interns. The PI rechecked the data collection forms to ensure their completeness and accuracy.

4.7. Statistical analysis

For normally distributed data mean (SD) and for non-normally distributed data median with IQR was reported. Frequency distribution and graphs was used. Data distributed was checked by using Shapiro–Wilk test or graphically using histogram.

4.8. Data quality

Various precautions and appropriate data quality control mechanism will be mainstreamed in all data management processes to assure quality of data. These include pretesting data collection tool, intensive training of data collector, close supervision of data collection process, verification of completeness. A pre-test of the questioner will be carried out at TASH, 5% of the sample population will be used for the pre-test.

4.9. Ethical consideration

Letter of permission to carry out the study will be obtained from AAU, CHS, IRB (Institutional Review Board). Then a cooperation letter was sent to TASH to obtain consent to perform data collection. Confidentiality of patient information was maintained by taking the data anonymously. The data extracted from secondary sources was used only for the study and every data was kept confidential.

5. Results and discussion

In our study, we examined a cohort of 145 participants with a diagnosis of HCC. Among them, 106 were male and 39 were female, resulting in a male-to-female ratio of 3:1. The age distribution was diverse, spanning from 18 to 91 years. The median age of the study participants was 55 years, with an interquartile range (IQR) of 40 to 63 years. The mean age of the study participants was 52.8 years. Regarding marital status, a substantial 90% of the study participants were married. Additionally, we observed that 51.72% of the participants were from Addis, emphasizing the local representation in our study population. In one study done in sub-Saharan Africa, annually, approximately 46,000 new cases are diagnosed in this region, with high incidence rates of up to 41.2 cases per 100,000 persons per year. Notably, Mozambique reports the highest occurrence of HCC. Demographically, it predominantly affects rural-dwelling Black Africans, with a gender disparity favouring men, especially among younger patients [20].

In our study cohort of HCC patients, we found that 16.55% had one or more co-morbid conditions. Among these, hypertension was prevalent in 13.79%, while diabetes affected 11.03% of the participants. Notably, eight patients presented with both diabetes (DM) and hypertension concurrently. In two large, prospective cohorts of individuals in the United States, followed for a duration exceeding 26 years, the researchers identified a statistically significant correlation between the diagnosis of type 2 diabetes (T2D) and an elevated risk of developing hepatocellular carcinoma (HCC) [21]. By considering associated health conditions, we can enhance the prevention and management of liver cancer [22].

In our cohort, among the symptomatic patients, abdominal pain was reported by 90.23%, weight loss by 69.17%, and abdominal swelling by 59.40%. These symptoms serve as crucial indicators for diagnosis and management, emphasizing the need for timely intervention and improved patient care. A significant proportion of our participants, specifically 72.41%, exhibited a palpable abdominal mass. Understanding these co-morbidities is crucial for comprehensive patient management and personalized treatment approaches. In developed nations with robust surveillance systems, such as Japan, the majority of hepatocellular carcinoma (HCC) cases manifest without overt symptoms and are incidentally detected [23].

In our study, we investigated the underlying causes and contributing factors in hepatocellular carcinoma (HCC) cases. Here are the key findings: 32.41% of HCC cases were attributed to HBV (Hepatitis B Virus) infection, while 19.31% tested positive for HCV (Hepatitis C Virus). Hepatitis B virus (HBV) stands out as the primary risk factor for hepatocellular carcinoma (HCC) on a global scale, contributing to nearly 50% of all HCC cases [24]. Notably, three patients exhibited co-infection with both HBV and HCV. Additionally, 50.34% of cases lacked a clear etiological link. Alcohol use was reported in 34.48% of HCC patients, and 11.03% had a history of diabetes mellitus (DM). Several factors have been well-documented as risk factors for HCC, including exposure to aflatoxins, cigarette smoking, excessive alcohol consumption, inadequate vegetable intake, inorganic arsenic exposure, exposure to radioactive thorium dioxide, iron overload, and the use of oral contraceptives and anabolic steroids [25]. Unfortunately, we did not elicit information regarding family history of HCC. These findings underscore the multifactorial nature of HCC and emphasize the importance of tailored prevention strategies and vigilant surveillance.

Among our study participants, 19 individuals (22.62%) were diagnosed with decompensated cirrhosis. Decompensated cirrhosis signifies advanced liver disease, where the liver's functional capacity is compromised, leading to complications such as ascites, hepatic encephalopathy, and variceal bleeding [26]. Patients with HBV-associated HCC had a median age of 43 years and a mean age of 44.85 years. In a Chinese study, cancer patients who tested positive for serum HBsAg were found to have significantly younger median ages at diagnosis, all-cause death, and cancer-specific death compared to those who tested negative for serum HBsAg. While the exact mechanism remains to be investigated, there is speculation that the DNA virus hepatitis B (HBV) may lead to hepatocellular carcinoma (HCC) before cirrhosis develops [27-29]. HBV remains a significant risk factor for HCC development, and early detection is crucial for timely intervention [29, 30]. In contrast, patients with HCV-associated HCC had a median age of 56 years and a mean age of 56.28 years. HCV infection also contributes to liver cancer, emphasizing the need for targeted screening and management [31, 32].

We identified 36 patients with a history of alcohol use. These individuals did not exhibit other identified risk factors for HCC. In extensive European patient cohorts with alcoholic cirrhosis, a substantial annual incidence of hepatocellular carcinoma (HCC) has been documented, reaching 2.9%**.** This risk is influenced by various host factors, including age, gender, liver failure, and genetic polymorphisms affecting oncogenic pathways . Chronic alcohol consumption is a well-established risk factor for liver diseases, including cirrhosis and HCC [33, 34]. Among the alcoholic patients, 19 individuals (52.78%) were reported to have cirrhosis. Cirrhosis is a progressive condition characterized by liver scarring, impaired function, and increased susceptibility to HCC. Vigilant surveillance and lifestyle modifications are essential for this subgroup [35, 36].

Among the HCC patients, 31 exhibited splenomegaly on CT scans, with 26 of these cases **(**83.87%**)** occurring in patients with cirrhosis. Additionally, CT imaging was used to characterize liver nodules (table 1). Patients with hepatocellular carcinoma (HCC) who exhibit splenomegaly, as measured by CT scan, tend to have a diminished liver functional reserve compared to those with a normal splenic volume. Additionally, splenomegaly serves as an independent prognostic factor for overall survival in these patients [37, 38]. Serum alpha-fetoprotein (AFP) levels were determined for 115 patients (table 2). Notably, 16 participants **(**11.03%**)** had a platelet count below 100,000**,** indicating potential thrombocytopenia. Furthermore, 28 HCC patients (19.31%) had a total bilirubin level exceeding 2 mg/dL, while 65 patients (44.83%) exhibited low serum albumin levels (< 3.5 g/dL).

CCx of Liver nodules	**Freq.**	**Percent**	**Cum.**
Single nodule>2cm	83	57.64	57.64
3 nodules largest<3cm	12	8.33	65.97
Multiple nodule	49	34.03	100.00
Total	144	100.00	

Table 1: characteristics of liver nodules based on CT scan (n=144)

AFP value	Freq.	Percent	Cum.
<20	38	33.04	33.04
20-400	21	18.26	51.30
>400	56	48.70	100.00
Total	115	100.00	

Table 2: Pattern of AFP elevation in patients with HCC (n=115)

	AFP			
Cirrhosis	<20	20-400	>400	Total
No	19	8	22	49
	38.78	16.33	44.90	100.00
Yes	19	13	34	66
	28.79	19.70	51.52	100.00
Total	38	21	56	115
	33.04	18.26	48.70	100.00

Table 3: Association between cirrhosis and AFP levels.

6. Limitations

This was a retrospective review of medical records and therefore some aspects of the data collected were incomplete. This had the potential to create bias in the analysis and interpretation. Additionally, vital information like HBeAg status and HBV DNA levels were unavailable for all the patients. Also, TASH is a referral centre, and so data from here may not be representative of the HCC burden and characteristics in other facilities across the country.

7. Conclusion

HCC presenting to TASH affects more males than females. Hepatitis B virus infection is the leading etiological risk factor associated with HCC. Most HCC patients presenting to TASH were not identified through surveillance; Majority of HCC patients do not qualify for both surgical and non-surgical therapies. Presentations with the major symptoms of weight loss and abdominal pain qualifies most patients for only supportive rather than curative HCC treatment at TASH. Health facilities should implement policies that: Prevent HBV/HCV transmission and Implement surveillance for high-risk groups. There is an urgent need to improve education of the population on hepatitis and its dreaded complication HCC. Health care providers should also be provided with HCC surveillance education and should establish programmes to implement same. Finally, policy makers should invest resources to improve diagnosis and treatment. If these are done, only then can we hope to identify.

References

1. Boyle, P. and B. Levin, *World cancer report 2008*. 2008: IARC Press, International Agency for Research on Cancer.
2. Ahmed, F., et al., *Peer reviewed: national trends and disparities in the incidence of hepatocellular carcinoma, 1998–2003.* Preventing chronic disease, 2008. **5**(3).
3. Plummer, M., et al., *Global burden of cancers attributable to infections in 2012: a synthetic analysis.* The Lancet Global Health, 2016. **4**(9): p. e609-e616.
4. Teo, E. and K. Fock, *Hepatocellular carcinoma: an Asian perspective.* Digestive Diseases, 2001. **19**(4): p. 263-268.
5. Jemal, A., et al., *Global cancer statistics.* CA: a cancer journal for clinicians, 2011. **61**(2): p. 69-90.
6. El-Serag, H.B., *Current concepts.* N Engl J Med, 2011. **365**: p. 1118-27.
7. Yang, J.D. and L.R. Roberts, *Hepatocellular carcinoma: a global view.* Nature reviews Gastroenterology & hepatology, 2010. **7**(8): p. 448-458.
8. Di Bisceglie, A.M., *Epidemiology and clinical presentation of hepatocellular carcinoma.* Journal of vascular and interventional radiology, 2002. **13**(9): p. S169-S171.
9. El–Serag, H.B. and K.L. Rudolph, *Hepatocellular carcinoma: epidemiology and molecular carcinogenesis.* Gastroenterology, 2007. **132**(7): p. 2557-2576.
10. Poon, D., et al., *Management of hepatocellular carcinoma in Asia: consensus statement from the Asian Oncology Summit 2009.* The lancet oncology, 2009. **10**(11): p. 1111-1118.
11. De Martel, C., et al., *Global burden of cancers attributable to infections in 2008: a review and synthetic analysis.* The lancet oncology, 2012. **13**(6): p. 607-615.
12. Stanaway, J.D., et al., *The global burden of viral hepatitis from 1990 to 2013: findings from the Global Burden of Disease Study 2013.* The Lancet, 2016. **388**(10049): p. 1081-1088.
13. Sartorius, K., et al., *Global and country underestimation of hepatocellular carcinoma (HCC) in 2012 and its implications.* Cancer epidemiology, 2015. **39**(3): p. 284-290.
14. Yang, J.D., et al., *Hepatocellular carcinoma occurs at an earlier age in Africans, particularly in association with chronic hepatitis B.* Official journal of the American College of Gastroenterology| ACG, 2015. **110**(11): p. 1629-1631.
15. Umoh, N.J., et al., *Aetiological differences in demographical, clinical and pathological characteristics of hepatocellular carcinoma in The Gambia.* Liver International, 2011. **31**(2): p. 215-221.
16. Khalaf, N., et al., *Natural history of untreated hepatocellular carcinoma in a US cohort and the role of cancer surveillance.* Clinical Gastroenterology and Hepatology, 2017. **15**(2): p. 273-281. e1.
17. Qari, Y. and M. Mosli, *Epidemiology and clinical features of patients with hepatocellular carcinoma at a tertiary hospital in Jeddah.* Nigerian Journal of Clinical Practice, 2017. **20**(1): p. 43-47.
18. Salem, A., et al., *Hepatocellular carcinoma in Yemeni patients: a single centre experience over an 8-year period.* EMHJ-Eastern Mediterranean Health Journal, 18 (7), 693-699, 2012, 2012.
19. Yang, J.D., et al., *Characteristics, management, and outcomes of patients with hepatocellular carcinoma in Africa: a multicountry observational study from the Africa Liver Cancer Consortium.* The lancet Gastroenterology & hepatology, 2017. **2**(2): p. 103-111.
20. Kew, M.C., *Epidemiology of hepatocellular carcinoma in sub-Saharan Africa.* Annals of hepatology, 2015. **12**(2): p. 173-182.
21. Simon, T.G., et al., *Diabetes, metabolic comorbidities, and risk of hepatocellular carcinoma: results from two prospective cohort studies.* Hepatology, 2018. **67**(5): p. 1797-1806.

22. Mu, X.-M., et al., *Patterns of comorbidity in hepatocellular carcinoma: a network perspective.* International Journal of Environmental Research and Public Health, 2020. **17**(9): p. 3108.
23. Yamashita, T. and S. Kaneko, *Liver cancer.* Rinsho byori. The Japanese journal of clinical pathology, 2016. **64**(7): p. 787-796.
24. Mittal, S. and H.B. El-Serag, *Epidemiology of HCC: consider the population.* Journal of clinical gastroenterology, 2013. **47**: p. S2.
25. CHEN, C.J., M.W. YU, and Y.F. LIAW, *Epidemiological characteristics and risk factors of hepatocellular carcinoma.* Journal of gastroenterology and hepatology, 1997. **12**(9-10): p. S294-S308.
26. Premkumar, M. and A.C. Anand, *Overview of complications in cirrhosis.* Journal of Clinical and Experimental Hepatology, 2022. **12**(4): p. 1150-1174.
27. Wei, X.l., et al., *Hepatitis B virus infection is associated with younger median age at diagnosis and death in cancers.* International journal of cancer, 2017. **141**(1): p. 152-159.
28. Li, Y., et al., *Risk factors for naturally-occurring early-onset hepatocellular carcinoma in patients with HBV-associated liver cirrhosis in China.* International journal of clinical and experimental medicine, 2015. **8**(1): p. 1205.
29. Zhang, X., et al., *Risk factors and prevention of viral hepatitis-related hepatocellular carcinoma.* Frontiers in oncology, 2021. **11**: p. 686962.
30. Guan, M.-C., et al., *Early diagnosis and therapeutic strategies for hepatocellular carcinoma: From bench to bedside.* World Journal of Gastrointestinal Oncology, 2021. **13**(4): p. 197.
31. McMahon, B., et al., *Hepatitis-associated liver cancer: gaps and opportunities to improve care.* Journal of the National Cancer Institute, 2016. **108**(4): p. djv359.
32. Pradat, P., V. Virlogeux, and E. Trépo, *Epidemiology and elimination of HCV-related liver disease.* Viruses, 2018. **10**(10): p. 545.
33. Ganne-Carrié, N. and P. Nahon, *Hepatocellular carcinoma in the setting of alcohol-related liver disease.* Journal of hepatology, 2019. **70**(2): p. 284-293.
34. Moon, A.M., A.G. Singal, and E.B. Tapper, *Contemporary epidemiology of chronic liver disease and cirrhosis.* Clinical Gastroenterology and Hepatology, 2020. **18**(12): p. 2650-2666.
35. De Raffele, E., *Liver Cancer.* Liver Diseases: A Multidisciplinary Textbook, 2020: p. 341-368.
36. Zhang, H., et al., *Liver Cancer: Interdisciplinary Approach.* Hepatobiliary Cancers: An Interdisciplinary Approach, 2022: p. 41-83.
37. Wu, W.-C., et al., *Prognostic significance of computed tomography scan-derived splenic volume in hepatocellular carcinoma treated with radiofrequency ablation.* Journal of clinical gastroenterology, 2012. **46**(9): p. 789-795.
38. Bae, J.S., et al., *Association between spleen volume and the post-hepatectomy liver failure and overall survival of patients with hepatocellular carcinoma after resection.* European Radiology, 2021. **31**: p. 2461-2471.