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HEPATO-PANCREATICO-BILIARY SURGERY

Preventing the preventable: Adolescent hepatocellular carcinoma and implications for hepatitis B virus prevention policy in South Africa

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Background: Hepatocellular carcinoma (HCC) is a fatal disease of the young in sub-Saharan Africa (SSA) and chronic hepatitis B virus (HBV) infection remains the predominant aetiology. There is paucity of data regarding HCC in the adolescent population globally.
Methods: Adolescents, defined as individuals aged 10 to 19 years according to the World Health Organization (WHO), with HCC treated at Groote Schuur Hospital (GSH) in South Africa from 1 January 2012 and 31 December 2024 were studied.
Results: Five (0.5%) of the 726 HCC patients managed at GSH during the study period were adolescents. The median age was 18 (13–19) years and three were female. All five had chronic HBV infection and most presented with pain (60%) and/or an abdominal mass (40%). All had advanced disease, with four (80%) having Barcelona Clinic Liver Cancer (BCLC) stage C and one (20%) with BCLC stage D. Two (40%) had extrahepatic metastases and three (60%) had portal vein tumour thrombosis. Treatment included liver resection (1), sorafenib (1), lenvatinib (1), and best supportive care (2). At the time of the study, only one patient was alive. The median survival was 137 (25–425) days.
Conclusions: Despite national HBV vaccination programmes in South Africa, in our experience adolescent HCC was HBV-related in all five patients. Extrahepatic metastases and macrovascular invasion were frequently reported and restricted patient access to curative-intended therapies (ablation, liver resection, transplantation). These findings highlight the urgent need for improved early detection and prevention strategies against perinatal HBV transmission in South Africa, including the rollout of the WHO-recommended universal hepatitis B birth-dose vaccination rather than the current targeted prevention approach.
Keywords: hepatocellular carcinoma, adolescents, hepatitis B virus, sub-Saharan Africa

Introduction

Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related mortality globally.[1-4] In high-income countries (HICs), HCC occurs mainly in older patients with liver cirrhosis caused by metabolic dysfunction-associated steatotic liver disease (MASLD), chronic hepatitis C virus (HCV) infection and alcohol-related liver disease.[1] These patients have access to curative-intended therapies (ablation, liver resection, liver transplantation), resulting in five-year survival rates above 70%.[2] However, the burden of HCC lies in sub-Saharan Africa (SSA) and South-East Asia, where chronic hepatitis B virus (HBV) infection is the main aetiology.

In SSA, HCC affects young adults who frequently present with multifocal disease, extrahepatic metastases and macrovascular invasion (portal vein tumour thrombosis (PVTT) and hepatic vein tumour thrombosis). Only 6% of patients are treated with curative-intended therapies, with almost no survivors at one year.[3,4] In adolescents, HCC is typically diagnosed between the ages of 15 and 19 years and tumours tend to develop in non-cirrhotic livers. Chronic liver diseases such as chronic HBV and HCV infection, glycogen storage diseases and alpha-1 antitrypsin deficiency increase the HCC risk in adolescents.[5-7] In SSA, early acquisition of HBV occurs through mother-to-child-transmission (MTCT) or horizontal transmission through siblings and/or peers. Hepatitis B virus infection acquired in the earlier stages of life leads to HBV DNA integration into the genome at multiple random sites early during the infection and potentially results in HCC development in younger patients.[8]

Despite the endemicity of both HBV and HCC in the SSA setting, there are limited data describing HCC in the adolescent population in SSA. A previous multicentre study from multiple paediatric oncology units in South Africa showed that 35% of hepatic tumours in the paediatric population were HCC and two-thirds of these patients were HBV surface antigen positive.[9] However this study included fibrolamellar tumours and did not assess HCC

alone. There are limited data in describing the demographic characteristics, clinical manifestations, treatment and outcomes of adolescent patients with HCC in South Africa, where HBV is endemic.

The aim of this study was to explore the demographic characteristics, clinical manifestations, treatment and outcomes of adolescent patients diagnosed with HCC at Groote Schuur Hospital (GSH) in South Africa.

Methods

The institutional review board of the Faculty of Health Sciences at the University of Cape Town granted ethical approval (IRB00001938, HREC:1006/2024) for this study. Adolescent patients (World Health Organization definition: persons aged 10 to 19 years) who underwent treatment for HCC at Groote Schuur Hospital, Cape Town, South Africa from 1 January 2012 to 31 December 2024 were studied in this single centre descriptive case series of five patients. The following patient data were extracted: demographics, Eastern Cooperative Oncology Group (ECOG) Performance Status (PS), symptoms and duration thereof, clinical examination findings, comorbidities, lifestyle factors (alcohol consumption, smoking) and whether the HCC diagnosis was made through surveillance. In addition, routine laboratory investigations (full blood count, international normalised ratio (INR), renal and liver function tests (LFTs), baseline serum alpha-fetoprotein (AFP), HBV and human immunodeficiency virus serology were analysed. Abdominal imaging (ultrasound, computed tomography and magnetic resonance imaging) were reviewed and relevant findings recorded. The Child-Turcotte-Pugh (CTP) Score, Model for End Stage Liver Disease-Sodium (MELD-Na) score and Barcelona Clinic Liver Cancer (BCLC) stage were recorded. Treatment modalities were categorised as curative-intended (ablation, liver resection, liver transplantation), life-prolonging treatments (transarterial chemoembolisation, sorafenib) and best supportive care (BSC). Treatment outcomes were recorded and analysed across various patient categories.

Descriptive statistics were presented as median and interquartile range and categorical statistics were presented as frequencies and percentages.

Results

Five (0.5%) of the 726 HCC patients managed at GSH over the study period were adolescents (Figure 1). The median age was 18 (13–19) years and three were females. Chronic HBV infection was the aetiology of HCC in all five patients. Four out of the five patients had data available on HIV status, for which all four patients were HIV negative. The most common presenting complaint was abdominal pain in three out of the five patients (60%), and 40% had hepatomegaly and a palpable abdominal mass on initial clinical examination. The median AFP was 191679 (78.1-1704590) µg/L (Table I).

Three patients (60%) presented with CTP grade A and two (40%) presented with CTP grade B disease. The median MELD-Na score for the five patients was 10 (IQR:10–12). All five patients presented with advanced disease, with four patients (80%) having BCLC stage C disease and one patient (20%) with BCLC stage D disease. At the time of diagnosis, two patients (40%) had extrahepatic metastases, with lung and bone being the most common, and three patients (60%) had PVTT (Table I).

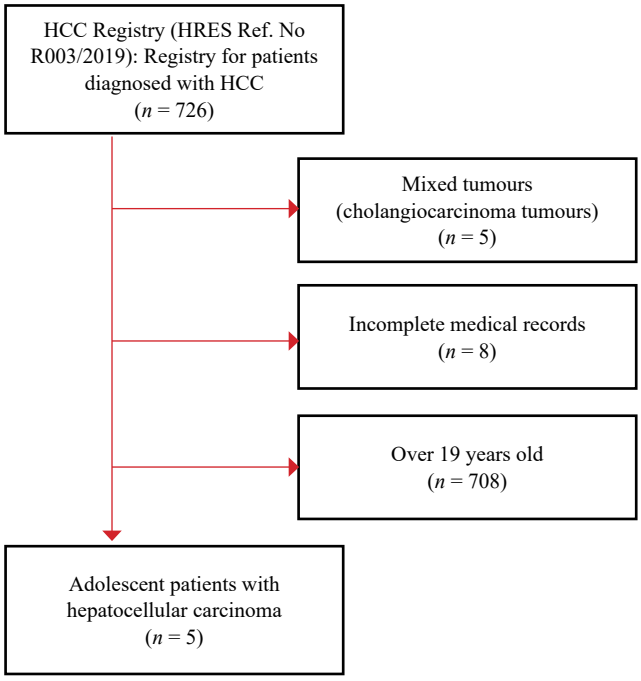

Figure 1: Flowchart showing the hepatocellular carcinoma patient numbers treated at Groote Schuur Hospital

Only one patient received curative-intended therapy and underwent liver resection and survived for 249 days. Two patients received life-prolonging treatment with systematic therapies: Sorafenib (1) and Lenvatinib (1). The remaining two patients received BSC only. At the time of analysis, only one patient was alive. The median overall survival was 137 (25–425) days.

Discussion

To our knowledge, this is the first comprehensive report describing adolescent HCC in sub-Saharan Africa (SSA). In this case series, all five patients (100%) developed HCC in the setting of chronic HBV infection as a result of early-life acquisition of the virus. Disease presentation was uniformly advanced, with a high prevalence of extrahepatic metastases and PVTT. Only one patient was eligible for surgical resection, and long-term survival was uniformly poor. These findings mirror reports from south-east Asia, where early HBV acquisition similarly drives aggressive HCC phenotypes in adolescents.[10]

This study highlights the persistent public health burden posed by HBV endemicity across SSA, particularly due to vertical and early horizontal transmission. Despite the introduction of a national HBV immunisation programme in 1995, targeted HBV birth dose vaccination for neonates born to HBV surface antigen (HBsAg) positive pregnant women was only introduced in 2023. In 2017, the overall prevalence of HBsAg positive disease in pregnant women was 11.2%.[11] The current prevalence of HBsAg positivity in children under the age of five years remains high, at 4.8%.[12]

Our findings suggest that existing prevention strategies, particularly for MTCT, remain inadequate and contribute to the development of early-onset, aggressive HCC. Since 2023, South Africa has implemented the following measures to prevent MTCT of HBV: HBsAg screening for all pregnant

Table I: Characteristics, clinical presentation, treatment and outcomes of five adolescent patients with hepatocellular carcinoma. Data reported as *n* (%) and or median (range)

Patient characteristics	Patients (*n* = 5)
Age (years)	
13	1 (20%)
17	1 (20%)
18	1 (20%)
19	2 (40%)
Gender	
Female	3 (60%)
Male	2 (40%)
ECOG PS	
0	1 (20%)
1	3 (60%)
2	0 (0%)
3	1 (20%)
4	0 (0%)
Symptoms	
Pain	3 (60%)
Weight loss	1 (20%)
Anorexia	1 (20%)
Nausea	1 (20%)
Vomiting	1 (20%)
Abdominal mass	2 (40%)
Signs	
Jaundice	1 (20%)
Ascites	0 (0%)
Palpable mass	2 (40%)
Hepatomegaly	2 (40%)
Encephalopathy	0 (0%)
Fever	0 (0%)
Child Turcotte Pugh Grade	
A	3 (60%)
B	2 (40%)
C	1 (20%)
MELD-Na score	10 (7–15)
Serum alpha-fetoprotein (µg/L)	191679 (78.1–1704590)
Background liver	
Cirrhotic	2 (40%)
Non-cirrhotic	2 (40%)
Unknown	1 (20%)
Number of lesions	
1	3 (60%)
≥ 2	1 (20%)
Unknown	1 (20%)
Extra-hepatic metastases	2 (40%)
Lung	2 (40%)
Bone	1 (20%)
Lymph nodes	1 (20%)
BCLC stage	
C	4 (80%)
D	1 (20%)
Treatment	
Resection	1 (20%)
Sorafenib	1 (20%)
Lenvatinib	1 (20%)
Best supportive care	2 (40%)
Overall survival	137 days (25–425)

ECOG – Eastern Cooperative Oncology Group, PS – Performance status, HBV – Hepatitis B virus, HIV – Human immunodeficiency virus, MELD-Na – Model for end-stage liver disease, BCLC – Barcelona clinic liver cancer, PVTT – Portal vein tumour thrombosis

women, tenofovir prophylaxis provided to all HBsAg positive pregnant women and targeted HBV birth dose vaccination for neonates born to HBsAg positive pregnant women. There has been variable uptake of these recommended preventative strategies across the provinces. In addition to the suboptimal uptake of these preventive strategies, South Africa has yet to implement the WHO-recommended universal hepatitis B birth dose vaccine (HepB-BD), which when administered within 24 hours of birth reduced the MTCT rate by 95%.[13-15] Targeted prevention alone cannot protect those missed by screening, such as mothers who do not receive HBsAg testing during antenatal care, leading to undetected MTCT of HBV. Universal HepB-BD vaccination as part of routine immunisation is essential for broad protection in endemic regions like South Africa. Yet, only 11 out of 54 (20.3%) of sub-Saharan African countries have introduced the universal HepB-BD vaccination strategies.[13]

The successful implementation of the universal HepB-BD vaccine requires collaboration among multiple stakeholders, including national government authorities, policy makers, and local community members, particularly those in rural settings. However, insufficient data on HBV seroprevalence amongst children and MTCT rates, due to limited surveillance and centralised data collection, hampers effective advocacy efforts with these stakeholders.[13] Limited stakeholder involvement results in inadequate political commitment, insufficient financial allocation, and a subsequent lack of essential resources such as the vaccines themselves, infrastructure (including cold chain facilities), and support for community health care worker participation.[13]

In summary, early-life HBV infection is strongly associated with the development of chronic HBV and significantly increases the lifetime risk of cirrhosis and HCC.[8] Our study highlights the devastating consequences of failing to implement effective HBV transmission prevention strategies. Chronic HBV infection, a vaccine-preventable condition, continues to drive the emergence of aggressive HCC phenotypes in adolescents and represents a critical public health concern in SSA. It highlights the need for the universal HepB-BD vaccination in SSA.

Limitations

We acknowledge that this retrospective study was conducted from a single centre with a limited number of five patients. Data on the maternal HBV status, HBV screening or treatment received during the antenatal period, and childhood vaccination records were not available and thus not included in the analysis.

Conclusions

Despite the implementation of a national HBV vaccination programme in South Africa, all five adolescents had HBV-related HCC. In keeping with international reports, most present with an aggressive clinical phenotype characterised by frequent multifocal tumours, extrahepatic metastases and PVTT. This study re-iterates the significance of gaps in HBV transmission prevention strategies in South Africa and emphasises the imperative for reevaluation and expansion of screening programmes antenatally and during early childhood. Finally, our study re-emphasises the necessity of implementing the universal HepB-BD as outlined by the WHO elimination strategies.

Conflict of interest

All authors declare no conflict of interest.

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Ethical approval

The institutional review board of the Faculty of Health Sciences at the University of Cape Town granted ethical approval (IRB00001938, HREC:1006/2024) for this study.

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