



WHITE PAPER

THE IMPROVEMENT OF MANAGEMENT PATHWAYS AND ACCESS TO CARE IN SUB-SAHARAN AFRICA FOR PATIENTS WITH HEPATOCELLULAR CARCINOMA

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EXECUTIVE SUMMARY

During its strategic meeting at the 2022 World Congress in New York, the International Hepato-Pancreato-Biliary Association (IHPBA) launched the concept of a Legacy Initiative associated with future world congresses. The initiative committed to effect, by addressing a particular hepato-pancreato-biliary health care challenge, a long-term, positive and sustainable contribution to the Association, its community and the host region, and a meaningful and long-lasting change in the regions or continents where congresses are hosted, which reflects the vision, mission, and goals of the Association. The focus of the 2024 Legacy Initiative is hepatocellular carcinoma (HCC) in sub-Saharan Africa (SSA).

The primary objective of the 2024 Legacy Initiative is to improve the management pathways and access to care for patients with HCC in SSA. Hepatocellular carcinoma presents a significant global health challenge, with low- and middle-income countries (LMICs) disproportionately affected. Sub-Saharan Africa and South-East Asia bear a considerable burden of the disease. Despite advances in HCC management, significant challenges persist in SSA, hampering efforts to improve patient outcomes. Limited healthcare infrastructure, lack of screening programs, low awareness, and financial constraints and generic systems failure contribute to late-stage diagnosis and suboptimal treatment of HCC in the region.

Effective management of HCC requires a comprehensive, multidisciplinary approach spanning prevention, diagnosis, treatment, palliative and supportive care. Primary prevention strategies through education, vaccination, and lifestyle modifications and secondary prevention through surveillance of high-risk populations are key. Curative treatment options include surgical resection, transplantation, and ablation techniques, while palliative care provides holistic support for patients with advanced disease. Managing HCC in SSA presents unique challenges due to limited healthcare infrastructure, lack of screening programs, low awareness, and financial constraints. The disease often presents at advanced stages, limiting treatment options and compromising prognosis.

Addressing these challenges requires a concerted effort from multiple stakeholders, including healthcare providers, policymakers, advocacy groups, and industry partners. Strategies should focus on expanding healthcare infrastructure, raising awareness, implementing screening and surveillance programs, financing resources, integrating palliative care services, capacity building, supporting research and innovation, and advocacy for policy reform.

In conclusion, the IHPBA 2024 Legacy Initiative represents a concerted effort through a comprehensive, inclusive, and multidisciplinary approach to empower healthcare providers, educate communities, and advocate for policy reforms, driving meaningful change and improving outcomes for HCC patients in SSA and beyond.

1. THE IHPBA 2024 LEGACY INITIATIVE

During the World Congress in New York in 2022, at a strategic meeting the IHPBA resolved to attach a Legacy topic to future World Congresses. Legacy was defined as a positive, long-term contribution that would continue after the congresses for the benefit of the host destination, society at large and the Association and its community. The aim was in line with the Association's vision, mission, and goals to effect meaningful and long-lasting change in the management of surgical Hepato-Pancreato-Biliary (HPB) diseases in the host region or on the continent. Hepatocellular Carcinoma (HCC) was identified as the Legacy project for the 2024 World Congress that will take place in Cape Town, South Africa from the 15th to 18th May 2024, focussing on the improvement of management pathways and access to care for HCC patients in sub-Saharan Africa (SSA).

Translational and multidisciplinary management has become standard practice for all malignant tumour diseases, HCC being a good example. In well-resourced countries, HCC is managed in multidisciplinary team (MDT) settings which include hepatologists, pathologists, radiologists, oncologists, surgeons, and palliative care specialists including rehabilitation specialists in collaboration with allied health care professionals. Focusing on surgical care exclusively in initiatives to improve outcomes for HCC patients across the disease spectrum will be an exercise in futility. Considering the diversity and complexity of variables contributing to the unsatisfactory state of HCC management in SSA, a more broad-based multidisciplinary approach is required, that in addition to the medical disciplines involved, should also address health economic aspects and advocacy.

The IHPBA has therefore partnered with the African Viral Hepatitis Convention (AVHC) and the African Palliative Care Association (APCA) who will have separate dedicated sessions running in parallel to the official IHPBA program. The AVHC will primarily be addressing viral hepatitis in the light of projections that SSA is going to fail to heed the 2016 WHO call for the elimination of viral hepatitis as a public health threat by 2030. However, there will also be focus on other current and emerging aetiologies and risk factors for HCC and the prevention of HCC, in particular primary and secondary prevention. Throughout the whole endeavour, there is partnering with more than 30 regional and international societies and associations covering the whole spectrum of HCC management, as well as patient advocacy and interest groups. The obstacles to and difficulties the industry faces in SSA will be addressed in a dedicated Industry session within the official IHPBA program.

2. BACKGROUND

Hepatocellular carcinoma presents a formidable challenge globally. As the sixth most common malignancy worldwide, HCC accounted for 4.7% of all new cancer diagnoses in 2020. (1) Low- and middle-income countries (LMICs) carry a disproportionate burden of the disease with an estimated 80% of HCCs being diagnosed in patients living in resource-challenged LMICs in SSA and South-East Asia (SEA). (2, 3) Due to a lack of accurate incidence data from SSA, estimates are based on non-population-based sources or approximations, potentially underestimating the true HCC incidence. (4)

3. HEPATOCELLULAR CARCINOMA– A GLOBAL OVERVIEW

3.1 Epidemiology and risk factors

The causes of HCC and contributing risk factors are well described. The two major aetiologies for HCC are chronic infection by the oncogenic hepatitis B virus (HBV), and liver cirrhosis of any cause. The major causes of cirrhosis are chronic hepatitis C virus (HCV) and HBV infection, chronic alcohol over-consumption and metabolic dysfunction-associated steatotic liver disease (MASLD). Several environmental risk factors have also been identified, including exposure to aflatoxins, heavy metals, including arsenic and cadmium, chemical carcinogens such as vinyl chloride, chlorinated hydrocarbons, and polycyclic aromatic hydrocarbons. The number of cirrhosis cases globally has increased by 49% between 1990 to 2019 (1075.12 to 1602.43 million) and affect most countries. (5) With obesity prevalence exceeding 25.65% in North America, Australasia, North Africa, and the Middle East, as well as the rising prevalence of diabetes, MASLD is currently the main driver of the increase in cirrhosis in these regions. In East Asia, Southeast Asia and sub-Saharan Africa, HBV is the main aetiological factor with prevalence exceeding 4.65%. In Western, Central and Eastern Europe, heavy drinking and a relatively high hepatitis C prevalence account for the increase in the prevalence of cirrhosis. (5)

3.2 Clinical presentation

Hepatocellular carcinoma may remain asymptomatic until advanced stages and patients typically present with nonspecific symptoms such as abdominal pain or discomfort, weight loss, fatigue, and jaundice. With advanced disease, abdominal swelling due to ascites or palpable tumours in the upper abdomen may occur. With disease progression, complications such as gastrointestinal bleeding, or symptoms of liver failure may manifest. Notably, some tumours are diagnosed incidentally during imaging for other medical conditions, for example investigation of patients with cirrhosis.

3.3 Diagnosis

The diagnosis of HCC is based on the combination of imaging (ultrasound (US), contrast-enhanced computed tomography (CE-CT), magnetic resonance imaging (MRI)) and tumour markers. Before the advent of screening and surveillance of high-risk individuals, most diagnoses were made by confirming advanced HCC in symptomatic patients. In well-resourced countries with population-based screening and surveillance programs, increasing proportions of patients are diagnosed with asymptomatic early stage tumours. (6, 7)

3.4 Prevention

3.4.1 Primary prevention

Education about the major risk factors for HCC is key to successful primary prevention programs. Populations should be educated on lifestyle modifications that will limit exposure to aetiological and risk factors, including weight control, alcohol consumption, unsafe cultural and injection practices that will reduce the risk for contracting viral hepatitis. Furthermore, the importance of screening for HBV and HCV to allow for early diagnosis and treatment and the importance of HBV vaccination in high-risk populations should be emphasized. This is of particular relevance in pregnant women where the risk for prevention of mother-to-child transmission of HBV can be significantly reduced by treating HBsAg positive women to reduce the viral load and implementing timeous hepatitis B birth-dose vaccination for new-borns at delivery.

3.4.2 Secondary prevention

A randomized controlled trial (RCT) published in 2004, unequivocally showed the value of surveillance of high risk populations. (8) A recently published systematic review and meta-analysis which included four RCTs, showed that HCC screening results in early HCC detection, reduced HCC mortality and prolonged overall survival rates at 1-, 3- and 5-years. (9) Guidelines for screening and surveillance for HCC in high-risk populations based on combinations of ultrasound and alpha-fetoprotein (AFP) are included in all major HCC guidelines. (10, 11)

3.4.3 Tertiary prevention

Tertiary prevention in patients treated with curative intent includes post-intervention screening to detect recurrence at early stages where repeat curative intent treatment would be possible and to prevent recurrence by controlling risk factors such as viral suppression of HBV and curative treatment of HCV which has been shown to prolong recurrence-free survival. (12, 13)

3.5 Treatment

3.5.1 Curative intent treatment

The curative intent treatment options for HCC include liver resection, liver transplantation and local ablation. Improvements in surgical techniques and interventions, better peri-operative care and increasing numbers of patients diagnosed with early stage disease have prompted targets for curative-intent treatment of 40% diagnosed with HCC. (14) In many countries with well-established screening and surveillance programs this target has been achieved. (7, 15)

3.5.2 Palliative treatment

In some countries with well-developed palliative care systems, multidisciplinary palliative care teams are engaged to provide holistic support, including pain management, nutritional and psychosocial support, and end-of-life care, to improve quality of life (QOL) for patients and their families. In patients with sufficiently preserved liver function and performance status, oncologic treatment and tumour-targeting interventions may further improve QOL with better symptom control and potentially prolonged survival. While traditional systemic chemotherapies have limited efficacy in advanced HCC, newer targeted and immunotherapies increasingly used in combination have yielded promising results. Trans-arterial therapies such as trans-arterial chemoembolization (TACE) and radioembolization (TARE) have proven effective in reducing liver tumour volumes.

3.6 Survival

The prognosis of HCC correlates with tumour stage, with 5-year survival rates of 70% being reported in patients with early stage disease, compared to less than 20% in patients with advanced disease. (16) The survival of HCC has improved over the last 10 years. The largest improvements were observed in HICs where all modalities were available and accessible to patients, both in terms of primary prevention, screening and surveillance, and treatment. The improvement was across the disease spectrum, including patients treated palliatively due to the impact of high-end targeted and immunotherapies and increased use of life-prolonging tumour-targeting interventions. Currently, the median survival for patients diagnosed with HCC is >60 months in Taiwan, 60 months in Japan and 24, 31 and 33 months in Europe, South Korea and North America, respectively. (17)

4. THE UNRESOLVED CHALLENGES IN MANAGING HEPATOCELLULAR CARCINOMA IN SSA

4.1 Epidemiology and risk factors

Hepatocellular carcinoma is the second leading cancer in men and the third for women in SSA with an estimated 38 629 incident cases and 36 592 HCC-related deaths in 2020. (4) Chronic HBV infection, highly endemic in many parts of the sub-continent is the predominant risk factor for HCC on the sub-continent with vertical HBV transmission from mother-to-child a major factor. Chronic HCV infection is an emerging aetiology. Dietary exposure to aflatoxin, which synergistically increases the risk of HCC, particularly in combination with HBV infection, is still a significant concern due to inadequate food storage practices, especially in regions with warm and humid climates. Similarly, dietary iron overload due to cooking practices and consumption of traditionally brewed beverages with a high iron content is an important risk cofactor. (18)

4.2 Clinical presentation

Hepatocellular carcinoma in SSA shows a marked male predominance with a male:female ratio of 8:1, compared to 2.5:1 elsewhere. Furthermore, HCC is a disease of the young, with an age of onset ranging from 33–47 years in African patients compared to 60–80 years in non-African populations. Patients more often present with tumour-related symptoms or complications, such as tumour rupture and bleeding. Tumour growth has been reported as more rapid and patients present with larger tumour burdens or metastatic disease. (19) As a result, an estimated 95% of HCC patients in sub-Saharan Africa present at advanced or terminal stages precluding curative-intent treatment, contrasting with high-income countries (HICs) where up to 40% of patients are diagnosed early, allowing for curative intent interventions. (20, 21)

4.3 Diagnosis

There is no data on the proportion of HCC patients in SSA diagnosed within screening and surveillance programs but is likely to be minimal. The diagnosis is often made merely on clinical examinations without confirmation with special investigations. There is no reliable data on the availability of AFP testing, access to imaging techniques or pathology assessment of biopsies.

4.4 Prevention

4.4.1 Primary prevention

Despite efforts, challenges remain in implementing sustainable effective primary prevention programs for HCC in SSA. This is caused by limited healthcare resources, competing health priorities, and socioeconomic disparities. Despite the African region currently accounting for 66% of new HBV infections in the world, only 4.2% of patients will be diagnosed and only 0.2% of people living with chronic HBV infection

will receive viral suppression treatment. (22) Consequently in 99% of pregnancies in HBsAg positive women, the child has a 90% risk of being infected with the virus and developing chronic infection. (23) Only 18 African countries having national viral hepatitis elimination plans and only 14 have introduced a universal HBV birth dose vaccination policy. It is estimated that a mere 18% of babies born in SSA receive HBV birth dose vaccination that would offer 98–100% protection against infection if compliant with WHO recommendations of vaccination within 24 hours after birth, followed by a further 2–3 doses at least four weeks apart.

4.4.2 Secondary prevention

No SSA countries have a national screening and surveillance program for HCC. Due to lack of data, estimating the proportion of HCC cases detected through informal screening and surveillance is not possible, but likely to be negligible.

4.4.3 Tertiary prevention

With very few patients being treated with curative intent, tertiary prevention is irrelevant.

4.5 Treatment

4.5.1 Curative intent treatment

In a recently published systematic review on the management and outcomes of HCC in SSA, curative treatment was offered to only 228 (6%) of 3989 patients. (24) Most of the articles included were from larger referral centres and the proportion of patients who undergo curative intent treatment in SSA is more likely lower than the 0.6% that was reported by Yang et al. (20)

4.5.2 Palliative treatment

With an estimated less than 1% of patients undergoing curative-intent therapy, the proportion of patients with HCC in SSA requiring palliative care either primarily, or secondarily due to failed curative intent treatment, approaches 100%. It is estimated that only 5% of people in need of palliative care on the sub-continent receive it. (25) It is estimated that at least 88% of patients dying of cancer deaths with moderate to severe pain are untreated. (26) There is a paucity of data on the use of trans-arterial therapies, but from the limited data available, it can be deduced that well below 1% of patients will receive this treatment. (20) None of the currently recommended systemic treatments for HCC are available in the public health sector in SSA countries. (27)

5. SURVIVAL

As opposed to the encouraging and improving survival rates for HCC in HICs, the median survival for patients in SSA is a dismal 2.5 months.

6. THE WAY FORWARD

6.1 Factors contributing to the suboptimal treatment of HCC in SSA

- Limited healthcare infrastructure
Sub-Saharan Africa faces challenges with inadequate healthcare infrastructure, including a shortage of medical facilities, equipment, and trained healthcare professionals. This limitation hampers early detection, diagnosis, and treatment of HCC.
- Lack of screening and surveillance programs
All sub-Saharan Africa countries lack comprehensive screening and surveillance programs for HCC, leading to late-stage diagnoses and missed opportunities for early intervention when treatment outcomes are more favourable.
- Low awareness and education
There is often a lack of awareness among both the general population and healthcare professionals about the risk factors for HCC, symptoms, and the importance of early detection and treatment which contributes to delays in seeking medical care and late-stage presentations of HCC.
- Limited access to healthcare services
Access to healthcare services, including laboratory tests, diagnostic imaging, , and cancer treatment facilities, is limited in many parts of SSA. In addition, patients often face financial barriers, long travel distances, and inadequate referral systems, resulting in delayed or no treatment.
- High cost of treatment
Even when healthcare services are available, the cost of HCC treatment, including surgery, chemotherapy, and radiation therapy, is prohibitively expensive for most patients in sub-Saharan Africa, further entrenching poverty in the region.
- Prevalence of advanced disease at diagnosis
Due to the lack of screening programs and limited access to healthcare, a significant proportion of HCC cases in sub-Saharan Africa are diagnosed at advanced stages when treatment options are limited, and prognosis is poor.
- Limited availability of specialized care
Sub-Saharan Africa often lacks specialized healthcare facilities and multidisciplinary expertise in the management of complex cancers like HCC. Patients may not have access to hepatologists, oncologists, or surgical teams with expertise in liver cancer management.

6.2 Interventions to improve HCC management in SSA

- Expansion of healthcare infrastructure
Establishment and upgrading of appropriately equipped healthcare facilities at all levels of care. This should include improved procurement processes to allow better access.
- Implementation of screening and surveillance programs
Establish population-based screening programs targeting high-risk groups, defined by the local prevalence of aetiological and risk factors.
Provide training for healthcare professionals on the use of screening tools and algorithms for HCC detection.
Utilize community health workers and mobile health clinics to reach remote populations for screening and education campaigns.
- Health education and awareness campaigns
Launch public health campaigns to raise awareness about the risk factors for HCC, symptoms, and the importance of early detection and treatment.
Provide education to healthcare providers on HCC management guidelines and best practices.
Engage community leaders, religious institutions, and local media in disseminating health information and promoting preventive measures.
- Financing of resources
Implement government-funded or subsidized healthcare programs to reduce the financial burden of HCC treatment on often indigent patients and their families.
This should include capacity building for treatments, including surgery, interventional treatment and oncologic therapy.
- Integration of palliative care services
Integrate palliative care services into existing healthcare systems to improve symptom management, psychosocial support, and end-of-life care.
Provide training for healthcare providers in palliative care principles and pain management techniques.
- Capacity building and training
Invest in training programs for healthcare professionals, including oncologists, hepatologists, surgeons, nurses, and allied healthcare workers to build expertise in HCC management.
- Research and innovation
Support research initiatives to better understand the epidemiology, risk factors, and treatment outcomes of HCC in sub-Saharan Africa.
Foster collaboration between local researchers, clinicians, and international experts to develop innovative approaches to HCC prevention, diagnosis, and treatment.

- Advocacy and policy reform

Advocate for increased government funding for HCC prevention, screening, and treatment.

Lobby for policy reforms to improve access to all treatment modalities used in the management of HCC.

Engage with policymakers to prioritize cancer care on the national health agenda and allocate resources accordingly.

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