

## Mandatory multidisciplinary management of hepatocellular carcinoma: Need of the hour in a country with high prevalence of hepatitis C virus infection

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### Abstract

Hepatocellular carcinoma is the sixth common cancer diagnosed and fourth leading cause of cancer-related deaths worldwide. Its incidence is on rise due to increasing prevalence of chronic hepatitis C virus infection. Pakistan is ranked second in countries burdened by hepatitis C virus in the world. Management of hepatocellular carcinoma is complex as it develops on the back of liver cirrhosis, and the risk of mortality is an accumulation of both tumour-related factors as well as liver decompensation. A multidisciplinary tumour board is an ideal approach to improve the outcomes of hepatocellular carcinoma since this ensures assimilation of input from a diverse group of care-providers, including hepatobiliary and transplant surgeons, gastroenterologists, interventional radiologists, oncologists and palliative care specialists. A multidisciplinary tumour board provides tailored approach to individual cases in a timely fashion to avoid treatment delays and communication gaps to improve the overall outcomes.

**Keywords:** Hepatocellular carcinoma, Multidisciplinary approach, MDT.

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### Introduction

Hepatocellular carcinoma (HCC) is the sixth common cancer diagnosed and fourth leading cause of cancer-related deaths worldwide.<sup>1</sup> The incidence of HCC is on the rise due to increasing prevalence of chronic hepatitis C virus (HCV) infection.<sup>2</sup> Pakistan is ranked second in HCV-burdened countries in the world,<sup>3</sup> with transmission being driven by both healthcare practices, involving injections, transfusions and dental procedures, and community spread through barbers and intravenous (IV) drug abusers.<sup>4</sup> According to a survey, seven million individuals in Pakistan were chronically infected in the year 2013, contributing one-tenth to the global HCV burden.<sup>5</sup> HCV remains the most common aetiology of HCC, contributing to 60-70% of all cases.<sup>6</sup> However, these figures come from single-centre

experiences and the actual percentages are still unknown due to lack of a national cancer registry.

Unlike other gastrointestinal (GI) malignancies, the management of HCC is more complex. Optimal care dictates the involvement of multiple care providers because of the presence of tumour as well as the underlying cirrhosis of liver with competing mortality risk. No single specialty offers complete continuum of care demanding dedicated care from different specialties with a team approach.

### Multidisciplinary tumour board for HCC:

The multidisciplinary tumour (MDT) board approach is defined as an alliance of all medical and healthcare professionals related to a specific tumour disease whose approach to cancer care is guided by their willingness to agree on evidence-based clinical decision and to coordinate the delivery of care.<sup>7</sup> A liver MDT should comprise healthcare providers from each relevant specialty, including hepatobiliary and transplant surgeons, gastroenterologists, interventional radiologists, oncologists, and palliative care specialists who are intricately involved in the management of HCC patients. It is imperative for MDT conference to be regular, preferably weekly for high-volume centres and every 2-4 weeks for low-volume centres. This coordination allows the exchange of technical information, and improves communication between all the experts involved in the decision-making process. MDTs are becoming standard of care for the management of various cancers and are endorsed by many cancer societies.<sup>8</sup>

HCC management is complex as it develops on the back of liver cirrhosis, and the risk of mortality is the accumulation of both tumour-related factors and liver decompensation. The management plan for such patients includes the identification of high-risk patients with underlying cirrhosis who are likely to develop HCC, treatment of tumour depending upon the stage, and regular surveillance of patients. This dictates the commitment of multiple specialists to provide tailored treatment strategies according to recent recommendations within the confines of local resources. This minimises communication failures and efficiently utilise resources to provide appropriate therapeutic regimens to get best possible outcomes.<sup>9</sup>

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## Pakistan's outlook

The incidence of HCC is on the rise because of increasing burden of HCV infection. Local factors involved in the transmission of HCV include transfusion of unscreened blood products, IV drug abuse, use of unsterilised instruments for dental and minor surgical procedures by quacks, use of unsterilised blades for shaving by barbers, unprotected sexual practices and lack of awareness in the general community.<sup>10,11</sup> Furthermore, 66% of infected patients are from rural areas with limited educational background.<sup>6</sup> Due to lack of awareness about the natural course of disease and resource restrictions, most infected patients do not undergo screening and usually present late when HCC has already advanced. According to literature, only 10% patients are diagnosed with HCC on routine screening, 44.3% patients have tumours >5cm and 52-62% patients have more than one tumour nodule. Advanced liver disease, Child-Pugh B and C, is present in 86% patients and <15% patients are candidates amenable to any form of definitive treatment.<sup>12</sup>

Surgical resection is considered the most effective treatment for HCC in patients with preserved liver functions. Unfortunately, most patients in this part of the world have advanced disease at the time of diagnosis because of extensive tumour involvement of the liver, vascular invasion and extra-hepatic spread. Therefore, most patients are eligible for palliative therapies only. Due to limited resources, data regarding the outcome of HCC patients is scant and true presentation of the burden of disease and outcome is largely unknown. Yusuf et al.<sup>13</sup> studied 584 HCC, and only 79 of them were found eligible for definitive treatment and the rest were managed with supportive care. Of the 79 patients, only 17.7% received curative surgical resection, while 60.7% had transarterial chemoembolisation (TACE) and 21.5% had percutaneous ethanol injection (PEI). Another study involving 645 HCC patients revealed that TACE was the most performed therapeutic modality (38.2%) and all these patients had Barcelona clinic liver cancer (BCLC) stage B. Only 2.8% patients had BCLC 0 or A.<sup>11</sup> This data exemplifies the advanced nature of disease in the local context with limited possibilities for curative therapies.

## Need for multidisciplinary approach in Pakistan

Only a few centres in Pakistan provide integrated multimodal hepatobiliary services, including surgery, interventional therapies and targeted molecular therapy. The number of liver transplant centres is quite low. Technical expertise for surgical resection, TACE, radiofrequency ablation and PEI is confined to a few centres. Access to these facilities by patients is often difficult as one-third cases of chronic HCV infection belong to rural areas.

Even if diagnosed on screening or incidentally, there is delay in the initiation of definite treatment due to lack of proper referral system to specialised centres. Therefore, MDT is mandatory for every patient with HCC to improve the survival of these patients. Involvement of multiple specialists provides individualised treatment strategies, and collaborates on how to provide best management within the confines of local resources. One of the reasons for treatment delay even after timely diagnosis of HCC here is failure to seek the appropriate level of care at the right time. Not all tertiary care hospitals are equipped with facilities of interventional radiology, hepatobiliary surgery or liver transplantation, and controversies in the management of HCC mandate coordination of healthcare professionals in these centres with specialised teams in dedicated hepatobiliary and transplant centres to decide the optimum care for patients. This could be done by organising online MDT meetings with specialised centres by rural and district level hospitals managing HCC patients and timely referring them to specialised centres to avoid delays that can result in the progression of disease. Coordination between the teams may minimise the risk of miscommunication which can otherwise result in treatment delays. Patient history and radiological investigations can be shared in online meetings with the expert panel for a joint decision.

In the context of Pakistan, this approach can help identify patients who need to be referred to specialised centres for definitive management, including liver transplant, surgical resection and ablative therapy, and those who need supportive/palliative care at their own healthcare facility to avoid unnecessary consumption of resources in already resource-restricted settings. This can also improve the outcomes of patients with early disease, and increase the chances of survival. Benefits of timely MDT decisions are not limited to initial patients. For example, a patient who initially undergoes resection or transplantation and develops local recurrence on surveillance may be eligible for locoregional or systemic therapy. Discussing every patient's case in MDT and keeping a regular log of patients can help develop a national cancer registry of HCC patients in Pakistan to give correct estimate of healthcare burden. On the bases of this registry, national plans can be devised; starting from community screening programmes to pick early tumours eligible for curative treatment to improve overall survival of patients, to surveillance of the treated patients to provide timely care in case of recurrence or liver decompensation. In addition, this data can be used for further research and to develop national guidelines for the management of HCC.

## Support from literature

Several studies suggest that MDT approach for HCC management is associated with improved survival

outcomes. Agarwal et al.<sup>14</sup> reported that patients managed through MDT were more likely to present at an earlier tumour stage and with lower serum alpha fetoprotein. Overall survival was significantly higher in these patients (19.1±2.5 vs 7.6±0.9 months,  $p<0.0001$ ). Yopp et al.<sup>15</sup> compared the outcomes of HCC patients managed through MDT with those managed before MDT formation and found that the MDT group had fewer symptoms and earlier stage of presentation. The median time to treatment after diagnosis in the MDT group was significantly shorter (2.3 vs 5.3 months) and median survival was longer (13.2 vs 4.8 months) than the other group. Multivariate analysis revealed that being seen in HCC MDT was independently associated with better overall survival. Charriere et al.<sup>16</sup> in a study comprising 387 patients found that negative prognostic factor for overall survival was not following the MDT decision, while Serper et al.<sup>17</sup> reported that MDT management was associated with reduced mortality in a study of 3,988 patients involving 128 centres in the United States. Another retrospective cohort study by Sinn et al.<sup>18</sup> compared the overall survival of patients who were and were not managed via MDT, and found that the 5-year survival rate was significantly higher in patients who were managed via MDT compared to those who were not (71.2% vs. 49.4%,  $p=0.001$ ).

## Conclusion

The diagnosis and management of HCC is challenging due to the rising incidence, presence of underlying chronic liver disease, lack of screening programmes and shortage of dedicated hepatobiliary and liver transplant centres in Pakistan. A multidisciplinary liver tumour board seems an ideal approach by assimilating the diverse components of care together to improve the outcomes of patients with HCC. MDT provides tailored approach to individual cases in a timely fashion to avoid treatment delays and communication gaps between different specialties. In view of evidence from literature, MDT should be the standard of care for the management of HCC patients.

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