Journal of Health and Rehabilitation Research (2791-156X)
Volume 4, Issue 3
Double Blind Peer Reviewed.
https://jhrlmc.com/
DOI: https://doi.org/10.61919/jhrr.v4i3.1650
www.lmi.education/

Multidisciplinary Approach Towards Managing Hepatocellular Carcinoma - Experience of a Single Hepatobiliary Center

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Keywords
Hepatocellular carcinoma, multidisciplinary team, liver cancer, hepatitis C, transarterial chemoembolization, survival, Pakistan, BCLC staging, portal vein thrombosis

Disclaimers

Authors' Contributions	All authors contributed to the study design, data collection, analysis, and manuscript preparation
Conflict of Interest	None declared
Data/supplements	Available on request.
Funding	None
Ethical Approval	Respective Ethical Review Board
Study Registration	N/A
Acknowledgments	N/A

ABSTRACT

Background: Hepatocellular carcinoma (HCC) is a leading cause of cancer-related mortality worldwide. A multidisciplinary approach is crucial for optimal management. This study aimed to evaluate the outcomes of HCC patients managed by a multidisciplinary team at a single hepatobiliary center.

Objective: To assess the demographics, clinical characteristics, treatment modalities, and survival outcomes of HCC patients managed with a multidisciplinary approach.

Methods: A retrospective observational study was conducted on 212 HCC patients diagnosed and managed at a tertiary care hospital in Pakistan. Data on demographics, etiology, tumor characteristics, treatment received, and survival were collected and analyzed.

Results: The majority of patients were male (80.7%) with a mean age of 55.96 years. Hepatitis C (66.5%) was the most common risk factor. Most patients presented with intermediate to advanced stage disease (BCLC B: 45%; BCLC C: 24.5%). Transarterial chemoembolization (TACE) was the most frequently used treatment (46.2%). The presence of portal vein thrombosis was significantly associated with mortality ($p<0.001$).

Conclusion: A multidisciplinary approach is essential for the management of HCC. Early detection and timely intervention are crucial for improved survival.

INTRODUCTION

Hepatocellular carcinoma (HCC) is the most prevalent primary liver malignancy, accounting for approximately 90% of primary liver cancers (1). It is a significant global health concern, ranking as the 5th most common cancer in men and the 7th in women worldwide (2). The incidence of HCC is increasing in both developed and underdeveloped countries, driven by risk factors such as cirrhosis, chronic liver disease, and viral infections like hepatitis B and C (3, 4). While vaccination programs have reduced HBV-related HCC in some regions, South Asian countries are experiencing a rise in HCC cases secondary to viral infections (3, 4).

Early detection of HCC is crucial for improved outcomes. In resource-rich countries, routine screening with alpha-fetoprotein measurements and abdominal ultrasound facilitates early diagnosis in high-risk individuals. However, the operator-dependent nature of ultrasound sometimes necessitates further imaging with computed tomography (CT) or magnetic resonance imaging (MRI) to identify small tumors (up to 10mm) (12). Unfortunately, in resource-poor countries like Pakistan, HCC is often diagnosed at a symptomatic stage, leading to delayed intervention and poorer prognosis.

The management of HCC has evolved significantly, with the emergence of new treatment options. However, a multidisciplinary approach remains paramount due to the heterogeneous nature of the disease (5). Treatment decisions cannot be based solely on algorithms but must be individualized considering tumor characteristics (size, number, vascular invasion), liver function (Child-Pugh score), and performance status (5). The Barcelona Clinic Liver Cancer (BCLC) staging system provides a framework for incorporating these factors into treatment planning (5).

The multidisciplinary team (MDT) plays a vital role in tailoring treatment strategies to each patient's unique circumstances. This collaborative approach, involving specialists from various disciplines (hepatology, surgery, radiology, oncology, pathology), ensures comprehensive evaluation and personalized care. Studies have demonstrated that patients treated by an MDT experience reduced diagnostic delays, improved access to therapy, and enhanced overall survival (5-7).

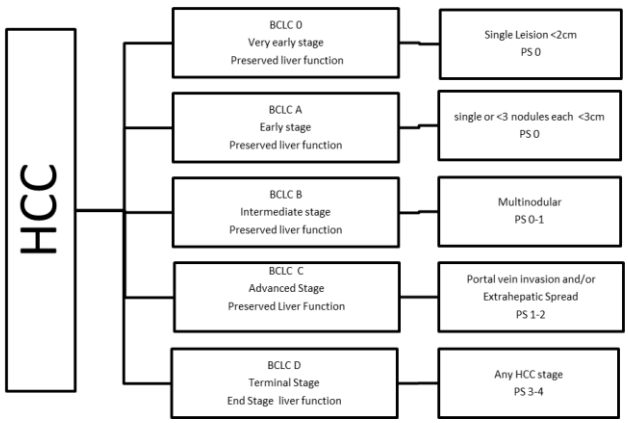

Figure 1 BCLC HCC Staging. BCLC, Barcelona clinic liver cancer staging system; HCC, Hepatocellular carcinoma; PS, Performance status score

Manuscript Submitted under JHRR ID 1650: August 14/2024 | Accepted: September 18/2024

The MDT approach is essential for navigating the complex treatment landscape of HCC, which ranges from potentially curative options like surgery, liver transplantation, and local ablation for early-stage disease (BCLC 0 and A) to palliative treatments such as trans-arterial chemoembolization (TACE) and systemic therapy for advanced stages (BCLC B and C) (8-11).

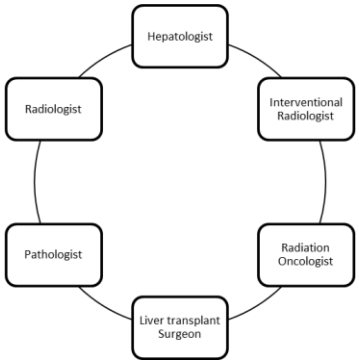

Figure 2 Multidisciplinary team in HCC care

MATERIAL AND METHODS

This study was conducted in the Liver Transplant Unit of PEMH Rawalpindi from April 2023 to April 2024. All patients diagnosed with HCC during this period were considered for inclusion. The diagnosis of HCC was confirmed by contrast-enhanced computed tomography (CECT), utilizing characteristic radiological features such as arterial phase hyper-enhancement, washout appearance, and capsule appearance (12). Patients with multiple malignancies, recurrent HCC, or a history of previous surgery for any other malignancy were excluded.

Ethical approval was obtained from the hospital's ethical committee, and all participants provided written informed consent before enrolment in the study. A convenience sampling technique was employed, and an observational study design was utilized. Data were collected on patient demographics (age, gender), performance status, Child-Pugh score, BCLC stage, alpha-fetoprotein (AFP) levels, liver function tests (serum alanine aminotransferase [ALT], serum alkaline phosphatase [ALP]), hepatitis B and C status, presence of portal vein thrombosis, serum bilirubin and hemoglobin levels, tumor size, and number of tumors (based on CECT findings).

Each patient's case was discussed in a weekly multidisciplinary tumor board meeting, which included a hepatobiliary surgeon, interventional radiologist, radiologist, oncologist, pathologist, and gastroenterologist. The MDT reviewed the patient's clinical and radiological data and formulated an individualized treatment plan. All patients were followed up for 6 months, with a repeat contrast-enhanced CT scan performed at the end of this period to assess treatment response.

Statistical analysis was performed using SPSS version 25. Descriptive statistics were used to summarize patient characteristics and biochemical parameters. The Chi-square ($\chi 2$) test was used to evaluate the correlation between tumor size and the effect of TACE treatment, as well as the association between portal vein thrombosis and mortality. A p-value of less than 0.05 was considered statistically significant.

RESULTS

This study examined the demographic and clinical characteristics of 212 patients with hepatocellular carcinoma (HCC) managed at a single hepatobiliary center. As detailed in Table 1, the patient population was predominantly male (80.7%), with a mean age of 55.96 years.

Table 1: Patient Demographics and Baseline Characteristics

Parameter	Value
Total Patients (n)	212
Age (years)	55.96 ± 12.2 (Range: 26-80)
Gender	Male: 80.7%, Female: 19.3%
Smoking Status	Smokers: 3.3%, Non-Smokers: 96.7%
Portal Vein Thrombosis	Present: 22.6%, Absent: 77.4%
Hepatitis B (HBsAg)	Positive: 14.2%
Hepatitis C (Anti-HCV)	Positive: 66.5%
HBsAg and Anti-HCV	Positive: 3.3%
Hemoglobin (g/dL)	11.55 ± 2.2
Serum Albumin	33.58 ± 6.4
Tumor Size (cm)	6.25 ± 3.88
Serum Bilirubin	26.58 ± 30.7
ALT (U/L)	50.06 ± 42.2
ALP (U/L)	235.07 ± 176.19
Alpha-fetoprotein	3515 ± 19499

A significant proportion of patients had underlying hepatitis C infection (66.5%), highlighting the contribution of this viral infection to HCC burden in the study population.

The distribution of patients across BCLC stages (Table 2) revealed a concerning trend: the majority presented with intermediate or advanced-stage disease (BCLC B and C), indicating a lack of early detection. This underscores the need for robust screening programs to identify HCC at earlier stages when curative treatment options are more likely to be successful. Notably, no patients were diagnosed at BCLC Stage 0.

Transarterial chemoembolization (TACE) was a frequently recommended treatment modality, particularly for patients with BCLC Stage B tumors. Analysis of treatment outcomes revealed a significant effect of TACE in reducing tumor size (mean decrease of 2 cm, $p < 0.001$). This finding supports the use of TACE as an effective treatment strategy for intermediate-stage HCC, aligning with current BCLC guidelines.

Table 2: BCLC Stage Distribution and Treatment Outcomes

BCLC Stage	Number of Patients	MDT Recommended Treatment (examples)	6-Month Follow-up Observations (examples)
A	47	Surgical resection, Liver transplantation, Local ablation	Disease-free survival, Awaiting transplantation, Tumor recurrence
B	96	TACE, Bridging therapy to transplantation	Tumor response to TACE, Successful downstaging, Progression to BCLC C
C	52	TACE, Systemic therapy	Stable disease, Partial response, Disease progression
D	17	Best supportive care	Palliative care, Death

Unfortunately, 15 deaths occurred during the 6-month follow-up period. Mortality was significantly associated with the presence of portal vein thrombosis ($p < 0.001$), a known poor prognostic factor in HCC.

Table 3: MDT Decision Outcomes by BCLC Stage

BCLC Stage	MDT Decision	Tumor Regression (%)	Tumor Size Increase (%)	Disease Relapse(%)	Stable Disease (%)	Death (%)	Tumor Free (%)
A	PEI	83.33	16.67	0.00	16.67	100.00	100.00
	TACE	100.00	0.00	0.00	0.00	100.00	100.00
	PEI + LT	0.00	100.00	0.00	0.00	100.00	100.00
	LT	0.00	100.00	0.00	0.00	100.00	100.00
	TACE + LT	0.00	100.00	0.00	0.00	100.00	100.00
B	PEI	0.00	0.00	0.00	0.00	0.00	0.00
	TACE	90.63	16.67	4.17	8.33	100.00	91.67
	Sorafenib	18.18	54.55	27.27	27.27	100.00	0.00
	Best Supportive Care	0.00	50.00	50.00	50.00	100.00	0.00
	LT	0.00	0.00	0.00	0.00	100.00	0.00
	TACE + LT	0.00	0.00	0.00	0.00	100.00	0.00
C	TACE	37.50	37.50	0.00	12.50	100.00	12.50
	Sorafenib	2.63	60.53	2.63	34.21	100.00	0.00
	Best Supportive Care	0.00	33.33	0.00	33.33	100.00	0.00
D	Best Supportive Care	29.41	5.88	5.88	64.71	100.00	5.88

Table 3 summarizes the outcomes of MDT decisions across different BCLC stages, highlighting the effectiveness of various treatments. In stage A, PEI and TACE demonstrated high tumor regression rates (83.33% and 100%, respectively), while PEI + LT, LT, and TACE + LT were associated with 100% tumor size increase but also tumor-free outcomes. For stage B, TACE showed the highest tumor regression (90.63%), while Sorafenib and Best Supportive Care had higher tumor size increases (54.55% and 50%, respectively) and relapse rates. Stage C revealed moderate regression with TACE (37.50%) and low with Sorafenib (2.63%), with Best Supportive Care showing no regression. Stage D, primarily managed with Best Supportive Care, had modest tumor regression (29.41%) but high stable disease rates (64.71%). These findings illustrate varying treatment efficacy based on stage and intervention.

Patients with advanced-stage disease (BCLC D) experienced the lowest survival rates, with most succumbing to the disease within 6 months. This observation emphasizes the urgent need for novel therapies to improve outcomes for patients with advanced HCC.

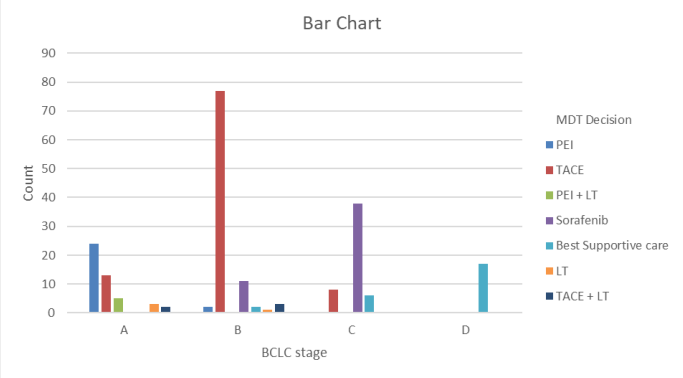

Figure 3 BCLC Stage & MDT recommended treatment

Finally, a direct correlation was observed between alpha-fetoprotein (AFP) levels and tumor size. This finding reinforces the clinical utility of AFP as a biomarker for HCC, with higher levels suggesting more advanced disease.

In conclusion, this study provides valuable insights into the characteristics and management outcomes of HCC patients at a single center. The findings highlight the importance of a multidisciplinary approach, the need for

improved early detection strategies, and the ongoing challenge of managing advanced-stage disease.

DISCUSSION

This study investigated the multidisciplinary approach to managing hepatocellular carcinoma (HCC) at a single hepatobiliary center in Pakistan. The findings highlight several important aspects of HCC management in this setting, including patient characteristics, treatment modalities, and outcomes.

The study found that the mean age of patients with HCC was 55.96 years, which is consistent with previous research indicating that HCC typically affects individuals in their sixth decade of life (14). However, the male-to-female ratio of 4:1 observed in this study is higher than the global average, suggesting potential gender-specific risk factors or healthcare access disparities in the Pakistani population (14).

The high prevalence of hepatitis C infection (66.5%) among the study participants is concerning but aligns with previous reports from Pakistan, where hepatitis C is a major public health issue (4). This emphasizes the urgent need for expanded screening and antiviral treatment programs to reduce the burden of hepatitis C-related HCC in this region (16). In contrast, the prevalence of hepatitis B infection (14.2%) was lower than that reported in Western populations (17), highlighting the regional variations in HCC etiology.

The majority of patients in this study presented with intermediate or advanced-stage HCC (BCLC B and C), reflecting a common challenge in many healthcare settings, particularly in resource-constrained environments where access to early screening and diagnosis may be limited. This late presentation underscores the need for improved public health initiatives to promote early detection and timely referral for HCC management.

The study demonstrated the effectiveness of TACE in reducing tumor size, particularly in patients with BCLC Stage B tumors. This finding supports the established role of TACE as a valuable treatment option for intermediate-stage HCC (18). The multidisciplinary team approach employed in this study facilitated individualized treatment selection, ensuring that patients received the most appropriate therapy based on their specific clinical and tumor characteristics.

The significant association between portal vein thrombosis and mortality observed in this study is consistent with previous research, confirming that portal vein thrombosis is a strong predictor of poor prognosis in HCC (16). The high mortality rate among patients with advanced-stage disease (BCLC D) emphasizes the need for continued research into novel therapies for this challenging patient population.

The study's findings are strengthened by the use of a multidisciplinary team approach, which is widely recognized as best practice in HCC management (10, 13). However, the study has limitations, including its single-center design and relatively short follow-up period. Further research involving larger, multicenter studies with longer follow-up is needed to validate these findings and provide a more comprehensive understanding of HCC management in Pakistan.

Despite these limitations, this study provides valuable insights into the multidisciplinary management of HCC in a Pakistani population. The findings underscore the need for increased awareness, early detection strategies, and improved access to care for this challenging disease.

CONCLUSION

This study reinforces the critical importance of a multidisciplinary approach in managing hepatocellular carcinoma (HCC), particularly in regions with a high prevalence of hepatitis C infection. The findings underscore the urgent need for comprehensive public health programs focused on vaccination, antiviral therapy, and early detection strategies to improve outcomes and reduce the burden of HCC. By integrating these efforts, healthcare systems can strive towards earlier diagnosis, timely intervention, and ultimately, better quality of life for individuals affected by this challenging disease.

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