Section: Oncology

Original Research Article

TREATMENT AND OUTCOMES OF DIFFERENT PROGNOSTIC FACTORS AND CORRELATION OF AFP AND MTD IN HEPATOCELLULAR CARCINOMA IN A RESOURCE LIMITED SETTING- A TERTIARY CARE CENTRE EXPERIENCE

Anand Praveen Kumar A[1], Chandralekha K[2], P.N.Sathiyamoorthy[3], Naveen Ravel[4]

[1]Resident, Department of Medical Oncology, Stanley Medical College, Chennai, India
[2]Assistant Professor, Department of Medical Oncology, Stanley Medical College, Chennai, India
[3]Associate Professor, Department of Medical Oncology, Stanley Medical College, Chennai, India
[4]Professor & HOD, Department of Medical Oncology, Stanley Medical College, Chennai, India

Received : 18/11/2023
Received in revised form : 27/01/2024
Accepted : 15/02/2024

Keywords:
HCC, Alpha feto protein, MTD, Survival.

Corresponding Author:
Dr. Chandralekha.K,
Email:
drchandralekhamedonco@gmail.com

DOI: 10.47009/jamp.2024.6.1.375

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (1); 1895-1899

Abstract

Background: To assess the treatment outcomes with respect to different prognostic factors in hepatocellular carcinoma and compare the characteristics of Normal or low AFP vs elevated AFP. **Materials and Methods:** Retrospective study. From Jan 2018 to Dec 2022, all the Hepatocellular carcinoma patients registered, evaluated and treated in Tertiary care institute were studied. **Result:** Total 220 cases registered of which 87% are Males, mean age 57 years. Alcohol and cirrhosis present in about 56% cases, 33% had viral aetiology. 48% were multifocal tumours and 40% patients have portal vein thrombosis.16% of patients present with metastasis of which more common is lung. Most common stage BCLC C 62%, Child Pugh B 68%. Most of the patients started with Sorafenib 78%, Resection 12%, and TACE 7%. There is no significant correlation between the Sr. AFP levels with Maximum Tumour diameter (MTD) (p=0.480), Multifocality (p=0.384), PVT (p=0.077) and Cirrhosis (p=0.548). Of 220 cases 25 cases lost to follow up. So survival analysis done for only 195 cases. Median overall survival was 6 months. With respect to AFP, patients with low AFP had better survival than elevated AFP which is statistically significant (p<0.01). In Cox Regression analysis, Portal vein thrombus (p<0.001), Alcoholism (p=0.001), Cirrhosis (p=0.009), BCLC stage (p<0.001) and Child pugh Score (p<0.001) shows statistically significant difference in survival. Others factors like Tumour diameter (p=0.081), Nodal status (p=0.409), Multifocality (p=0.084), Viral etiology (p=0.303) shows no significant statistical difference in survival. **Conclusion:** Regarding Sr. AFP there is no correlation between the tumour characteristics. Patients with Low AFP also presents with advanced disease and vice versa. So for patients with low AFP other markers like PIVKA, EpCAM, Glypican 3 can be used. But these markers need to be evaluated in detail. In our study Sr. AFP, PVT, Cirrhosis, BCLC Stage and Child pugh score were determined to be the important prognostic factors predicting survival mainly in a resource limited setting. This will help in treating the HCC with poor prognostic features aggressively.

INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver with an annual incidence of 40000 cases per year and it is in 11th place and 8th place in mortality.[1] It stands as a formidable global health challenge, reflecting its rising incidence and complex clinical manifestations. As we confront the nuances of this malignancy, the imperative to discern prognostic factors governing treatment outcomes becomes increasingly evident. This study navigates the intricacies of HCC prognosis, in our institute—a setting emblematic of resource limitations and diverse patient demographics. The burgeoning prevalence of HCC places an onus on the scientific community to unravel the intricacies that underscore its heterogeneity. In this pursuit, an exploration of

ISSN (O): 2687-5365; ISSN (P): 2753-6556

various prognostic factors—ranging from demographic characteristics to tumor attributes—emerges as imperative. Traditional markers, such as Alpha-fetoprotein (AFP), have long-guided diagnostic and therapeutic decisions.[2] However, the evolving landscape of HCC research prompts a critical reevaluation of AFP's role as an isolated prognostic determinant, necessitating a comprehensive investigation into its correlation with treatment outcomes.[3] Tumor size and number of lesions also play an important role in prognostication along with AFP.[4] The treatment armamentarium for HCC spans a spectrum of modalities, each bearing unique considerations and implications. From Sorafenib as a systemic therapeutic option to surgical resection and transarterial chemoembolization (TACE) as locoregional strategies, the multifaceted nature of HCC management unfolds.[5,6] Amidst this diversity, risk factors such as alcoholism, cirrhosis, and viral etiology intricately weave into the clinical tapestry, warranting a comprehensive analysis of their influence on patient survival.[7] This retrospective journey, spanning from January 2018 to December 2022, is poised to contribute not merely empirical data but profound insights into the intricate interplay of factors shaping HCC prognosis.

MATERIALS AND METHODS

We analyzed the data from our institute who are all underwent treatment for Hepatocellular carcinoma from January 2018 to December 2022. The total number of cases analyzed was 220. Patient characteristics, Baseline blood parameters, Serum AFP, and CT scan reports are all collected. Of these 220 cases, we found 25 cases lost to follow-up. So for survival analysis, only 195 cases were analyzed.

Statistical Method

For patient characteristics, Numerical variables are expressed in Median, and Categorical variables are expressed in percentage. Overall survival is calculated using the Kaplan-Meier curve. Correlations between Sr.AFP and MTD are done using Spearman's rho test. All other prognostic features were analyzed using Cox Regression analysis. Data collection was done in MS Excel 2016. All these statistical computations were made using SPSS v25.

RESULTS

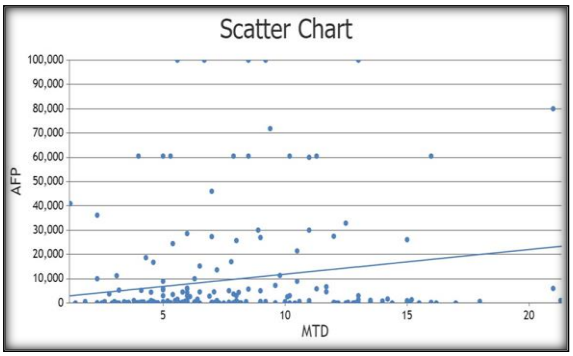

Figure 1: Scatter chart

A total of 220 cases were registered, with 86.8% of them being male. The predominant age group was over 40 years, and the median age was 60 years. Risk factors such as alcohol and cirrhosis were present in approximately 56% of cases, while about one-third of patients had a viral etiology. Idiopathic causes were identified in around 15% of cases. Tumor characteristics revealed that 40% of tumors were multifocal. Additionally, 47.7% of patients exhibited portal vein thrombosis, which may have implications for inoperability. Metastasis was observed in 7.3% of cases, with the lung being the more common site [Table 1] In terms of disease staging, the most common stage was BCLC C (62%), and Child-Pugh B was prevalent in 68.2% of cases.

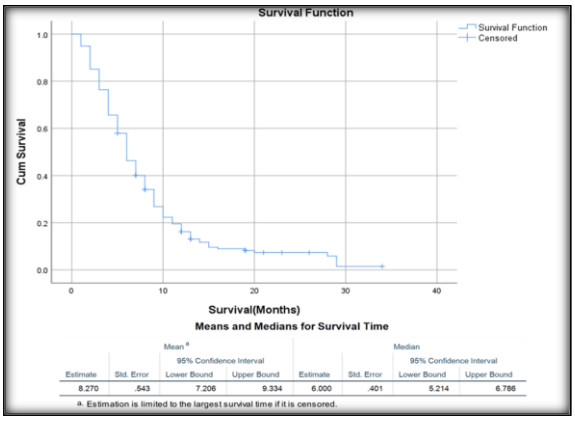

Figure 2: Overall survival

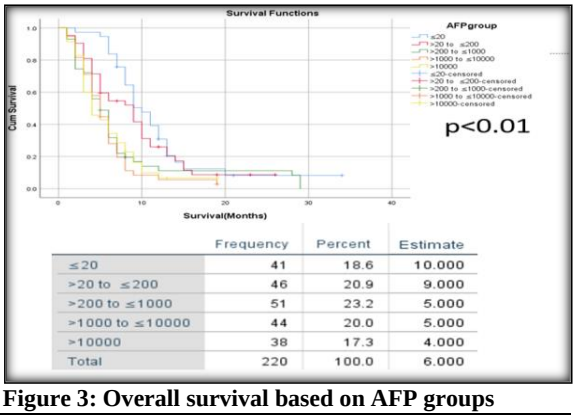

Figure 3: Overall survival based on AFP groups

ISSN (O): 2687-5365; ISSN (P): 2753-6556

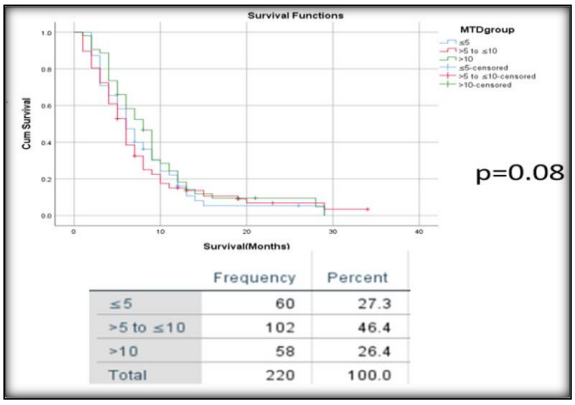

Figure 4: Overall Survival based on MTD groups

Treatment modalities varied, with 78% of patients receiving Sorafenib, 12% underwent resection and 7% for TACE. Correlation analysis indicated no significant correlation between Serum AFP and Maximum Tumor Diameter (MTD) [Figure 1] [Table 2]. Survival analysis for 195 patients showed a median survival of 6 months [Figure 2]. Categorizing AFP into five parameters revealed significant differences in survival among groups [Figure 3]. However, MTD (Maximum Tumour Diameter) did not show significance in survival which is based on size [Figure 4). Cox regression analysis identified specific factors, including portal vein thrombosis, alcoholism; cirrhosis, BCLC stage, and Child-Pugh score, demonstrating a significant difference in survival. Other factors were deemed insignificant. In multivariate analysis, AFP was also shown as an independent prognostic factor in survival [Table 3].

Table 1: Patient Characteristics

S.no	Patient characteristics		220 (100%)
1.	Sex	Male	191 (86.8)
		Female	29 (13.2)
2.	Age	Median	60 yrs
3.	Performance status	1	81 (36.8)
		2	128 (58.2)
		3	10 (4.5)
		4	1 (0.5)
3.	Alcoholism	Yes	122 (55.5)
		No	98 (44.5)
4.	Cirrhosis	Yes	125 (56.8)
		No	95 (43.2)
5.	HBV/HCV	Yes	73 (33.2)
		No	147 (66.8)
6.	Multifocality	Yes	88 (40)
		No	132 (60)
7.	Portal vein thrombus	Yes	105 (47.7)
		No	115 (52.3)
8.	Metastasis	Yes	36 (16.4)
		No	184 (83.6)
9.	BCLC stage	A	23 (10.5)
		B	44 (20)
		C	137 (62.3)
		D	16 (7.3)
10.	Child pugh	A	55 (25)
		B	150 (68.2)
		C	15 (6.8)
11.	Treatment	Hepatectomy	25 (11.4)
		TACE	16 (7.3)
		Sorafenib	172 (78.2)
		Palliation	7 (3.2)

Table 2: Correlation between AFP and MTD

Correlations		AFP
MTD	Correlation coefficient	0.113
	Sig (2 tailed)	0.096

Table 3: Regression Analysis of each factor

Parameter		P value	Exp (B) (95% CI)
Multifocality		0.096	0.77(0.57-1.05)
Portal vein thrombus*		<0.001	0.56(0.41-0.75)
Alcoholism*		0.001	0.61(0.45-0.82)
Cirrhosis*		0.009	0.67(0.49-0.90)
Nodal status +ve		0.409	0.84(0.55-1.27)
HBV/HCV		0.303	0.85(0.62-1.16)
BCLC Stage	A	Ref	Ref
	B	<0.001	0.12(0.06-0.25)
	C	<0.001	0.28(0.15-0.52)

ISSN (O): 2687-5365; ISSN (P): 2753-6556

	D	<0.107	0.64(0.38-1.1)
Child Pugh	A	Ref	Ref
	B	<0.001	0.14(0.07-0.28)
	C	0.062	0.60(0.34-1.02)

DISCUSSION

Our analysis delved into the intricate relationship between tumor characteristics and serum biomarkers in Hepatocellular Carcinoma (HCC). Notably, a striking observation emerged as tumor size (MTD) displayed no significant correlation with Serum AFP levels. This intriguing finding challenges the conventional notion, revealing that even small lesions can produce elevated AFP, while larger lesions may exhibit normal or low AFP. This incongruence suggests a complex interplay involving cell growth and inflammatory cytokines, providing a nuanced understanding of AFP dynamics in HCC.[8] Consequently, relying solely on AFP may not suffice to predict the disease burden accurately. This is in contrast to the study by Daniel Rusie et al, where tumor size and tumor burden had a positive correlation with the alpha-fetoprotein.[9] Despite this disconnection between tumor size and AFP, the latter proved to be a pivotal predictor of survival. The data unequivocally demonstrated that lower or normal AFP levels were associated with markedly better survival outcomes compared to elevated AFP levels which correlates with the previous studies.[10] This underscores the clinical significance of AFP as an essential prognostic marker in Hepatocellular Carcinoma, providing clinicians with valuable insights into patient outcomes.[11] Interestingly, when considering tumor size alone, there was no significant difference in survival, emphasizing the paramount role of AFP in prognostication. This observation challenges the traditional emphasis on tumor size alone and suggests that AFP levels should be a central consideration in assessing disease severity and predicting patient outcomes. Beyond tumor characteristics, our study identified BCLC Staging and Child-Pugh scores as crucial factors influencing survival. Higher disease stage and advanced Child-Pugh scores consistently correlated with lower survival rates, establishing these metrics as robust indicators of prognosis. In contrast, other tumor characteristics like multifocal disease, node positivity, and viral etiology exhibited limited influence on survival, highlighting the distinct predictive power of these factors in the context of HCC. Notably, patients with specific risk factors, such as portal vein thrombosis, a history of chronic alcoholism, and cirrhosis, displayed poorer survival outcomes. This underscores the importance of considering these factors in tailoring treatment plans and predicting prognosis in HCC patients. The prevalence of alcohol and cirrhosis highlights the importance of addressing these risk factors in liver cancer prevention and management. The presence of portal vein thrombosis and multifocal tumors suggests advanced disease stages, influencing prognosis. The lack of correlation between Sr.AFP and MTD underscores the independent roles of these parameters in disease progression. Treatment patterns reflect the predominant use of Sorafenib, indicating its relevance in this patient population. Identified significant factors in survival analysis can guide prognostic assessments and personalized treatment approaches. Despite resource constraints leading to the predominant use of Sorafenib in advanced-stage patients, our study revealed a median overall survival of 6 months which is less than the standard trials.[12] This highlights the harsh reality faced by patients in advanced stages of HCC and underscores the urgent need for more accessible and diverse treatment options. Looking ahead, our findings also suggest avenues for further research. While AFP remains a standard test for prognosis, alternative markers such as PIVKA, Glypican-3, alpha 1 glycoprotein, CRP, and hepatic miRs show promise.[13] Ongoing studies aim to elucidate their potential role in enhancing prognostic accuracy, paving the way for a more comprehensive understanding of HCC biology, and refining clinical decision-making.

CONCLUSION

Regarding Sr.AFP there is no correlation between the tumour characteristics. Patients with Low AFP also present with advanced disease and vice versa. So for patients with low AFP other markers like PIVKA, EpCAM, and Glypican3 can be used. However, these markers need to be evaluated in detail. In our study Sr.AFP, PVT, Cirrhosis, BCLC Stage and Child Pugh score were determined to be the important prognostic factors predicting survival mainly in a resource-limited setting. This will help in treating the HCC with poor prognostic features aggressively.

REFERENCES

1. Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2024). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.who.int/today.
2. Adigun OO, Yarrarapu SNS, Zubair M, Khetarpal S. Alpha Fetoprotein. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Feb 1]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK430750/
3. Brar G, Greten TF, Graubard BI, Mc Nell T, Petrick J, McGlynn K et al. Hepatocellular carcinoma survival by etiology: a SEER-Medicare Database analysis. Commun. 2020 Aug 9;4(10):1541–51. doi:10.1002/hep4.1564
4. Wang X, Wang Z, Wu L. Combined measurements of tumor number and size helps estimate the outcome of resection of Barcelona clinic liver cancer stage B hepatocellular carcinoma. BMC Surg. 2016;16:22.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

5. Suresh, D., Srinivas, A.N., Prashant, A. et al. Therapeutic options in hepatocellular carcinoma: a comprehensive review. Clin Exp Med 23, 1901–1916 (2023). https://doi.org/10.1007/s10238-023-01014-3
6. Current Management of Hepatocellular Carcinoma - PMC [Internet]. [cited 2024 Feb 1]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4014047/
7. Calderon-Martinez E, Landazuri-Navas S, Vilchez E, Cantu-Hernandez R, Mosquera-Moscoso J, Encalada S, Al Lami Z, Zevallos-Delgado C, Cinicola J. Prognostic Scores and Survival Rates by Etiology of Hepatocellular Carcinoma: A Review. J Clin Med Res. 2023 Apr;15(4):200-207. doi: 10.14740/jocmr4902. Epub 2023 Apr 28. PMID: 37187717; PMCID: PMC10181349.
8. Galle PR, Foerster F, Kudo M, Chan SL, Llovet JM, Qin S, et al. Biology and significance of alpha-fetoprotein in hepatocellular carcinoma. Liver Int. 2019;39(12):2214–29.
9. Rusie D, Stanciu AM, Toma L, Iliescu EL, Rusie DI, Stanciu AM, et al. Correlation Between Serum Alpha-Fetoprotein and Tumour Size in Patients With Hepatocellular Carcinoma Treated With Direct-Acting Antivirals. Cureus [Internet]. 2022 Apr 26 [cited 2024 Feb 6];14(4). Available from: https://www.cureus.com/articles/94258-correlation-between-serum-alpha-fetoprotein-and-tumour-size-in-patients-with-hepatocellular-carcinoma-treated-with-direct-acting-antivirals
10. Carr BI, Guerra V. Low Alpha-Fetoprotein Levels Are Associated with Improved Survival in Hepatocellular Carcinoma Patients with Portal Vein Thrombosis. Dig. Dis. Sci. 2016; 61:937–947. [PubMed: 26576554]
11. Nomura F, Ohnishi K, Tanabe Y. Clinical features and prognosis of hepatocellular carcinoma with reference to serum alpha-fetoprotein levels. Analysis of 606 patients. Cancer. 1989; 64:1700–1707. [PubMed: 2477133]
12. Llovet J, et al. Sorafenib improves survival in advanced Hepatocellular Carcinoma (HCC): Results of a Phase III randomized placebo-controlled trial (SHARP trial); Proceedings from the American Society of Clinical Oncology Conference; Chicago, IL: 2007.
13. Choi JY, Jung SW, Kim HY, et al. Diagnostic value of AFP-L3 and PIVKA-II in hepatocellular carcinoma according to total-AFP. World J. Gastroenterol. 2013; 19:339–346. [PubMed: 23372355]

ISSN (O): 2687-5365; ISSN (P): 2753-6556