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Correlation of Serum AFP with Different Stages of Hepato cellular Carcinoma

Dr. Pusuluri Leela Sameer., Dr. EVS Maben
Junior resident, Department of General Medicine, A.J.Institute of Medical Sciences, Mangalore, Professor - Department of General Medicine, A.J.Institute of Medical Sciences, Mangalore.

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ABSTRACT :
AFP is a serum glycoprotein that was first recognised as a marker for HCC more than 40 years ago and has since been described to detect preclinical HCC. The fetal yolk sac and fetal liver generate high levels of AFP, which decline to<10 ng/dl within 300 days of birth [37]. Serum elevations thereafter suggest underlying pathology which may be malignant. Any tumor arising from organs derived from the same endodermal lining as the hepatic diverticulum can be associated with elevations in serum AFP levels, including cancers of the stomach, pancreas, and biliary tree. Pregnancy and non seminomatous germ-cell tumors must also be considered. Chronic hepatitis or cirrhosis raise AFP in 20% and 40% of patients, respectively, and tend to fluctuate in parallel with underlying inflammatory activity.
OBJECTIVE : This study was aimed to systematically estimate the performance of AFP in different stages of HCC.
METHOD : This is a Prospective Study, involved 42 patients diagnosed with hepatocellular carcinoma satisfying inclusion criteria, admitted in A.J. Institute of Medical Sciences, Mangalore over a period of 2 years i.e., between Dec 2021 to Dec 2022.
RESULTS: In the present study, 41.86 % of the patients shows elevated serum alpha feto-protein. We also observed no statistical association between various stages of the disease and alpha fetoprotein.
CONCLUSION: Our study suggests that serum AFP has no significant correlation with various stages of HCC. AFP level may serve as a useful marker for detection of Hepatocellular carcinoma and to differentiate between early and advance stage. But with values of that magnitude, the specificity of AFP is noted to be high, but at a cost to the sensitivity which decreases.
KEY WORDS: AFP (alpha feto-protein) , hepatocellular carcinoma.

I. INTRODUCTION:

HCC screening includes both radiographic and serological marker assessments. AFP is one serum marker which helps in diagnosis of HCC. (6) Alpha feto-protein (AFP)'s main function is the regulation of fatty acids in both fetal and proliferating adult liver cells. 32.85% of the HCC patients had AFP of > 400 ng/ml. (16)

HCC can produce a range of AFP values from normal to>100000 ng/ml. Normal AFP

levels are present in as many as 30% of patients at time of diagnosis and usually remain low, even with advanced HCC . AFP >400–500 ng/ml is considered diagnostic for HCC, although fewer than half of patients may generate levels that high.

AFP has been shown to correlate with tumor size and volume at time of diagnosis. A study from Thailand found that HCC patients with AFP >400 ng/ml tend to have greater size, bi-lobar involvement, portal vein thrombosis, and decreased survival. When left untreated, AFP-producing tumors continue to increase over time, coinciding with progression of disease. Poorly differentiated tumors with more aggressive features can be seen more often in patients with high levels of AFP. Prognosis has been shown to be reduced when AFP levels are>1000 ng/ml, but exceptions do exist. Inconsistencies in tumor AFP levels reflect variables associated with its synthesis in HCC and pose a challenge in making systematic assumptions on tumor characteristics based on AFP level alone.

II. MATERIALS AND METHODS:

Data collection:

Based on the study conducted by Paul S.B. on clinical profile, etiology and therapeutic outcome in 324 patients of Hepatocellular carcinoma in tertiary care centre in Manglore assuming P = 12 % with 95% CONFIDENCE INTERVAL (CI) and 10% absolute allowable error (l) sample size estimated for the study of 39. Further, assuming 10% lost to follow-up, the final sample size estimated for the study of 42.

$$n = \frac{Z^2\ 1-\alpha/2\ P(1-P)}{L^2}$$

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From the patients satisfying inclusion criteria and willing to participate in study
This study will be conducted as a prospective study, where in written informed consent will take prior to the investigation. After detailed information given to the participants/ patient party regarding the study.

INCLUSION CRITERIA
1. All patients admitted and newly diagnosed with Hepatocellular carcinoma.
2. All patients already diagnosed with Hepatocellular carcinoma and came for follow up
3. Patients of age group more than 18yrs will be included in the study.
4. Informed written consent to participate in the study.

EXCLUSION CRITERIA:
1. Patients below age of 18yrs for the study
2. Patients not consenting for participating for the study.

III. RESULTS:

In present study, 42.9% of the patients shows elevated serum AFP. We also observed no statistical association between various stages of the disease and alpha fetoprotein. A study by musunuri B et al, showed high AFP levels (>400 ng/mL) were seen in 48.9% of patients.(28) A study by Colli A found that using AFP, with 20 ng/mL as a cut-off, about 40% of HCC occurrences would be missed. But the combination of AFP and abdominal USG showed the highest sensitivity and less than 5% of HCC occurrences would be missed. 57.1% of the population did not have elevated AFP in our study.

In our study conducted in AJIMS among 42 patients 18 patients having significant increase in serum AFP levels . Among them 0 patients in stage A having significant increase in serum AFP levels ,9 (39.1%) patients in stage B and 9 (60%) in stage C have significant increase in serum AFP levels. But there's no certain correlation between the AFP levels and the stage of the disease. Increase in AFP levels do not necessarily explain the stage of hepatocellular carcinoma.

Table no 5: Diagnostic marker

42.9% were positive for alpha feto protein and 57.1% were negative for the same.

SERUM ALPHA FETO PROTEIN (&>400 ng/mL)	Frequency	Percent
YES	18	42.9
NO	24	57.1
	42	100.0

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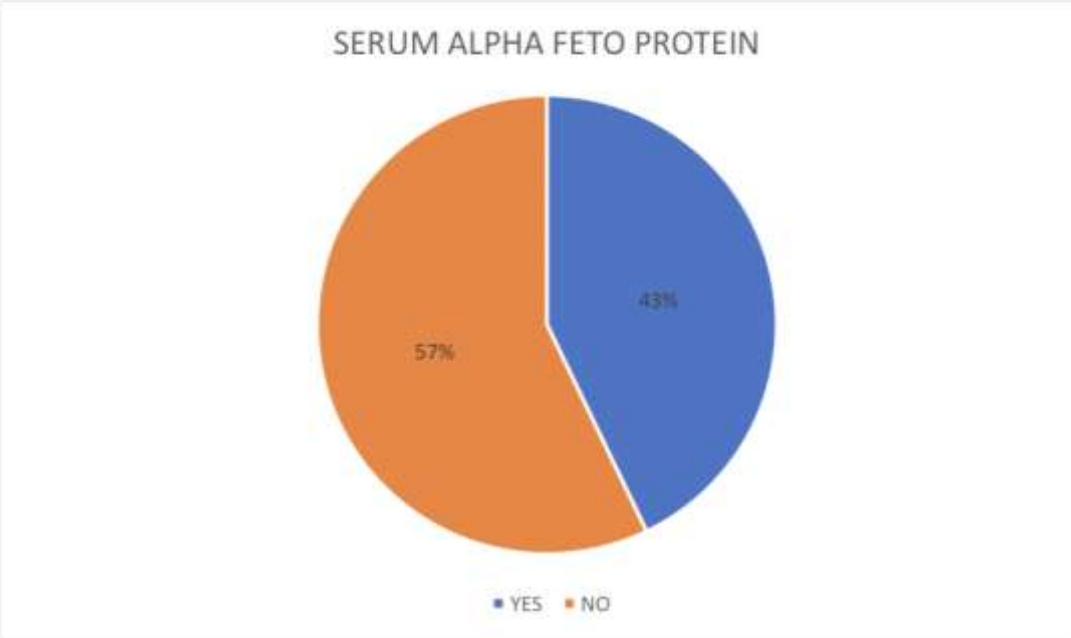
Figure no 12: Diagnostic marker-alpha fetoprotein.



STAGES OF THE DISEASE

9.5% of the patients were in stage A of the disease, 54.8% were in stage B of the disease and 35.7% were in stage C of the disease.

Table no 6a: STAGE A of Disease

9.5% of the study population were in stage A of the disease.

STAGE A	Frequency	Percent
YES	4	9.5
NO	38	90.5
	42	100.0

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Table no 8: Associations of alpha fetoprotein with stage A

Sensitivity=0, Specificity=52.6%, False positivity=47.4% and False Negative100% observed in stage A patient's association with serum alpha fetoprotein. There was no statistical significance observed between the various stage A of the disease and positive serum alpha fetoprotein.

SERUM APLHA FETO PROTEIN	STAGE A		Total	P value
	YES	NO		0.095
YES	0 (0.0%)	18(47.4%)	18(42.9%)	
NO	4(100%)	20(52.6%)	24(57.1%)	

Table no 9: associations of alpha fetoprotein with stage B

Sensitivity=39.1%, Specificity=52.6%, False positivity=47.4% and False Negative 60.9%

SERUM APLHA FETO PROTEIN	STAGE B		Total	P value
	YES	NO		0.411
YES	9(39.1%)	9(47.4%)	18(42.9%)	
NO	14(60.9%)	10(52.6%)	24(57.1%)	

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Table no 10: associations of alpha fetoprotein with stage C

Sensitivity=60.9%, Specificity=66.7%, False positivity=33.3% and False Negative 40%

SERUM APLHA FETO PROTEIN	STAGE C		Total	P value
	YES	NO		0.089
YES	9(60%)	9(33.33%)	18(42.9%)	
NO	6(40%)	18(66.7%)	24(57.1%)	

IV. DISCUSSION :

HCC is now the fifth-most common cancer in the world and the third cause of cancer-related mortality as estimated by the World Health Organization. Pre-existing cirrhosis is found in more than 80% of individuals diagnosed with HCC. Several etiologic factors including hepatitis viruses, alcohol and smoking have been implicated in the pathogenesis of hepatocellular carcinoma (HCC). However, limited evidence was observed in Indian sub-continent.

This is a Prospective Study, involved 42 patients diagnosed with hepatocellular carcinoma satisfying inclusion criteria. In our study conducted in AJIMS among 43 patients 18 patients having significant increase in serum AFP levels . Among them 0 patients in stage A having significant increase in serum AFP levels ,9 (39.1%) patients in stage B and 9 (60%) in stage C have significant increase in serum AFP levels.

V. CONCLUSION :

In our study conducted in AJIMS among 42 patients 18 patients having significant increase in serum AFP levels . Among them 0 patients in stage A having significant increase in serum AFP levels ,9 (39.1%) patients in stage B and 9 (60%) in stage C have significant increase in serum AFP levels. But there's no certain correlation between the AFP levels and the stage of the disease. Increase in AFP levels do not necessarily explain the stage of hepatocellular carcinoma.

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