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KEY WORDS: Hcc, Hepatocellular Carcinoma, Hepatitis B, Hepatitis C, Alcohol Consumption, Okuda Staging, Alpha-fetoprotein.

CHARACTERISTICS OF HEPATOCELLULAR CARCINOMA: A RETROSPECTIVE STUDY.

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ABSTRACT

AIMS: Hepatocellular carcinoma (HCC) is a primary malignancy of the liver and is apparent as the main cause of death in patients with liver cirrhosis or chronic hepatitis B or C virus infection. It is emerging as a major leading cause of cancer mortality. In India, the mean incidence of Hepatocellular carcinoma is 2.77% for males and 1.38% for females based on the population registry. Our study aims to assess the clinico-etiological profile of HCC at a tertiary hospital in India.

METHODS AND MATERIAL: Cross-sectional, observational and hospital-based retrospective study. Patients diagnosed as HCC from Jan 2014 to Feb 2019, registered in Hepatocellular Cancer Registry and admitted to the hospital, were reviewed. Clinical, biochemical, serological and radiological details were noted from case records and analysed. Out of the total 70 Patients, 57 patients had radiological or pathological evidence of HCC. Out of 57 patients, 53 of them had radiologically confirmed the diagnosis and 44 of them had histopathological report confirmative of HCC.

RESULTS: Age wise, out of 57 HCC patients 45 are males, 12 are females. Median age group is 60 years. The predominant complaint among HCC patients is abdominal pain/discomfort in 56.75% followed by abdominal distension in 40.54%.53 patients out of 57 patients have undergone HIV/HBsAg/Anti HCV serology testing. 5 out of 53 patients screened for HBsAg antigen were positive and 2 patients were anti-HCV antibody positive. Alpha-fetoprotein levels were available in 45 patients, out of which 12 (26.6%) patients had normal levels of alpha-fetoprotein and 20(44.4%) patients have in the diagnostic range of more than 400ng/ml. Patients were classified according to okuda staging and most of the patients belong to Okuda stage I (48.07%). Most of the patients were started on Sorafenib 200mg once daily dose and titrated according to tolerance.

CONCLUSIONS: This data on HCC provides information about tumour characteristics and possible associated risk factors. Study results show that alcohol consumption (40%) is the commonest underlying etiological factor for HCC followed by Hep B (9.43%) and Hep C (3.77%). Hepatitis B positivity in this study is lower than observed in various other studies done in India.

INTRODUCTION:

Hepatocellular carcinoma (HCC) is a primary malignancy of liver and is apparent as main cause of death in patients with liver cirrhosis or chronic hepatitis B or C virus infection. It is emerging as major leading cause of cancer mortality.[1]

Liver cancer is now the fourth leading cause of cancer mortality worldwide in 2018. It is now sixth most commonly diagnosed cancer.[2]

The incidence rates for liver cancer in developing countries are two to three fold higher than in the developed countries. Men are at 2 to 4 times higher risk than women.[3] Liver cancers are major problems in developing countries contributing to high mortality rates, which could be reduced by various early precautions such as immunization against hepatitis B virus infection would reduce the incidence of HCC. The ratio of mortality to incidence in liver cancer is 0.98:1.[4] Primary liver cancer incidence can be reduced by using hepatitis B virus vaccines and screening of blood and blood products for hepatitis B and C viruses.

In India more than one million new cases of cancer are diagnosed every year in population of more than 1.3 billion. Most of the cancers in India are due to avoidable causes such as tobacco use, alcohol consumption and infections. Social factors, especially inequalities, are major determinants of India's cancer burden, with poorer people more likely to die from cancer before the age of 70 years than those who are more affluent.[5]

Data of HCC patients in India is important for early detection and management of HCC.

Early detection of HCC is difficult as it requires use of one or more imaging modality. Serum AFP is used as diagnostic modality but sensitivity and specificity is low. [6] Best diagnostic modality of HCC is Ultrasound guided FNAC of liver lesion. Most of the patients are asymptomatic in the initial phases of the disease. Hence, HCC is strenuous to manage. Majority of the patients present to the tertiary hospital with advanced disease.

The modalities of treatment are confined to early stages of HCC. Some treatment modalities include Liver transplantation, hepatic resection, and early-stage radiofre quency ablation (RFA)are considered potentially curative. However these treatment modalities are useful in early stages of HCC. Advanced HCC treatment options include multikinase inhibitor Sorafenib, systemic chemotherapy and transarterial chemoembolization.Though these treatments have shown modest improvement in overall survival in early stage disease, there is no curative treatment for advanced HCC.[7]

This study provides the clinical features, biological parameters, underlying risk factors, pathological or radiological evaluation and outcomes of treatment of HCC.

METHODS:

SOURCE OF DATA:

The patients admitted to Father Muller Medical College

Hospital and diagnosed as HCC were included in the study.

METHOD OF COLLECTION OF DATA:

STUDY DESIGN - This is a descriptive chart based and time bound study.

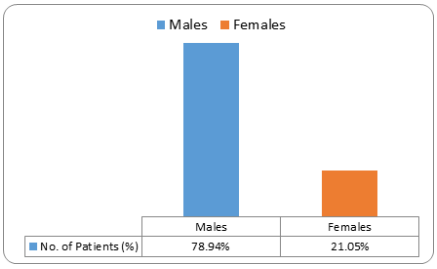
STUDY PERIOD - Over a period of 5 years from Jan 2014 to Feb 2019.

STUDY POPULATION - Patients diagnosed as Hepato cellular carcinoma by pathological or radiological analysis and admitted as inpatient in department of medical oncology at Father Muller Medical College Hospital.

Selection Criteria - Patients with diagnosis of HCC and are registered in cancer registry between Jan 2014 to Feb 2019. Patients with age of >15 years are considered for the study.

RESULTS:

Age wise, out of 57 HCC patients 45 are males, 12 are females. Median age group is 60 years.

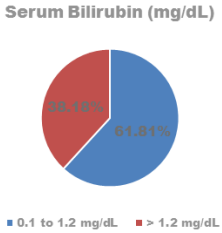


The predominant complaint among HCC patients is abdominal pain/discomfort in 56.75% followed by abdominal distension in 40.54%.

53 patients out of 57 patients have undergone HIV/HBsAg /Anti HCV serology testing. 5 out of 53 patients screened for HBsAg antigen were positive and 2 patients were anti-HCV antibody positive.

HBsAG Antigen positive	**9.43%**
Anti-HCV antibody positive	3.77%

Serum bilirubin values of 55 patients were available, 34 out of 55 patients(61.81%) had normal levels of serum bilirubin (0.1 to 1.2 mg/dL) and 21 out of 55 patients(38.18%) had elevated levels of serum bilirubin (> 1.2mg/dL).



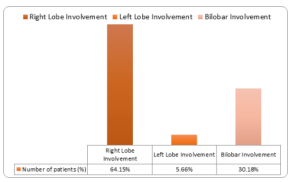
Alpha-fetoprotein levels were available in 45 patients, out of which 11 (24.44%) patients had normal levels of serum alpha-fetoprotein (upto 7 ng/ml), 14 (31.11%) patients had serum alpha-fetoprotein in range of 7 to 400 ng/ml and 20(44.44%) patients have in the diagnostic range of more than 400 ng/ml.

Serum Alphafetoprotein (ng/mL)	No. Of patients (%)
Upto 7 ng/mL	24.44%
7 to 400 ng/mL	31.11%
> 400 ng/mL	44.44%

		Mean	Std. Deviation	Percentiles		
	N			25	Median	75
SERUM BILIRUBIN	55	2.81	10.60	.59	.87	1.66
ALPHAFETOPROTEIN	45	12721.17	23489.49	7.95	291.10	20158.00

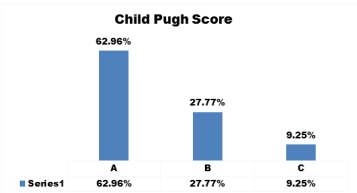
Liver lobe involvement was assessed using ultrasonography. Majority of HCC Lesions are located in the right lobe. 34 (64.15%) patients had right lobe involvement, left lobe was involved in 3 (5.66%) patients and bilobar involvement was seen 16 (30.18%) patients.

Parameter	**Number of patients (%)**
Right Lobe Involvement	34 (64.15%)
Left Lobe Involvement	03(5.66%)
Bilobar Involvement	16 (30.18%)

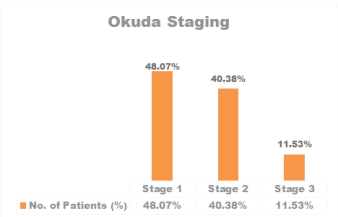


Child Pugh score was calculated in 54 patients. Majority of patients belong to Child Pugh Class A (62.96%). 5 patients out of 54 belong to Child Pugh Class C(9.25%). Mortality was 100% as per data collected in patients with Child Pugh Class C.

Child Pugh Score	Mean	Std. Deviation	Percentiles		
N			25	Median	75
54	6.48	1.82	5.00	6.00	7.00



Okuda staging was possible in 52 patients. Majority of patients i.e. 25 out of 52 were in Okuda stage 1 (48.07%). 21 patients out of 52 were in Okuda stage 2 (40.38%). 6 patients out of 52 were in Okuda stage 3 (11.53%).



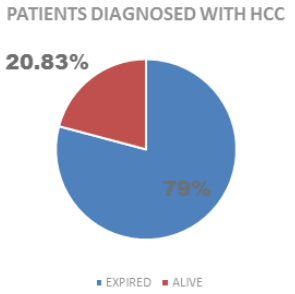
Sorafenib was started at dose 200mg OD and was titrated according to tolerance in 23 patients with HCC. 6 patients have undergone hepatectomy. 5 patients have undergone both hepatectomy and were treated with sorafenib. One patient had undergone Trans Arterial Chemo Embolisation (TACE) and was started on sorafenib later. 22 patients were on supportive care.

Treatment	No. Of Patients
Only on Sorafenib	23
Undergone Hepatectomy	6
Hepatectomy + Sorafenib	5
TACE + Sorafenib	1
Supportive care	22
Total	57

DISCUSSION:

Hepatocellular carcinoma being a primary malignancy of liver, its clinico-etiological profiling in Indian scenario is necessary for further understanding of the cancer. In this study males were affected more than females. Median age

group is 60 years. Most predominant complaint among HCC patients is abdominal pain/discomfort. Alpha-fetoprotein had very less significance, one-fourth of patients had normal levels of alpha-fetoprotein. History of alcohol consumption was noted in 40% of patients. In this study Hepatitis B positivity and Hepatitis C positivity was less than compared to previous studies done in India. Mortality rates are high in patients with HCC, 79.16 % of patients have expired and 20.83% were found to be alive during follow up.



Study done by Wenzel TM et al have described the risk factors of HCC include HCV, HBV infections, alcohol related disorders and rare metabolic disorders. Population-attributable fractions were greatest in alcohol related disorders followed by HCV and HBV infections.[8]

Sarin SK et al have concluded that, In India HBV infection was major cause for HCC, Alcohol and HCV were also found to be one of the causes. A majority of chronic alcoholics had an associated viral infection. Few cases of HCC had undetermined etiology.[9]

Paul SB et al study was done in tertiary care centre in India have noticed Hepatitis B infection as the predominant cause of HCC. Serum Alpha-fetoprotein was of diagnostic value in only one third of patients. Most patients visited tertiary centre when curative therapies were not possible.[10]

Kumar R et al had mentioned HCC in India has few atypical characteristics. The diagnosis of HCC was very late with metastases or vascular invasion. Serum Alpha-fetoprotein has low sensitivity and USG guided FNAC of liver lesion is better diagnostic modality of HCC.[11]

Patient survival with HCC is overall very poor and limited treatment modalities are available in advanced stages. Studies regarding HCC are very essential in detecting the causative factors in early stages. Serum Alpha-fetoprotein was of less significance as one-fourth of HCC patients had normal value. Sorafenib is inhibitor of Raf kinase, Platelet-derived growth factor, VEGF receptor and c-Kit. It has been approved for advanced HCC. Due to adverse reactions with higher doses of Sorafenib in Indian population, patients were started on 200mg once a daily dose and titrated accordingly on follow up based on tolerance.

In our study we found that alcohol was the major cause for Hepatocellular carcinoma followed by Hepatitis B and Hepatitis C compared to previous studies done in India. Alcohol consumption as an etiological factor of HCC was seen in previous studies.

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ETHICAL APPROVAL: The study was approved by the Institutional Ethics Committee

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