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EPIDEMIOLOGICAL AND CLINICAL CHARACTERISTICS OF EGYPTIAN PATIENTS WITH HEPATOCELLULAR CARCINOMA: A SINGLE CENTER STUDY

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ABSTRACT

Background: Hepatocellular carcinoma is a common malignancy, which usually develops on top of cirrhosis of viral origin; it is responsible for more than one million deaths worldwide per year. Aim: This study was conducted to identify the epidemiological and clinical characteristics of HCC patients attended Menofia oncology unit in the duration from 2003-2012, Egypt. Methodology: A retrospective analysis of records of 1500 HCC patients attended the Menofia oncology unit .The results: Of the 1500 studied HCC patients, 74.4% (1116) were male, and mean age was 54.98 years. HCV, HBV infection was reported to be 69.8 %, 17.2%, respectively, and 18.6 % were positive for Bilharziasis. Cirrhosis was present in (58.93%) of patients and was classified as Child-A (64.47%), Child-B (26.53 %) and Child-C (9 %). Hepatocellular carcinoma was multifocal/ diffuse in (51.26 %) of patients. 59.8% of patients were presented with metastatic disease. As regard to therapy; (59.6 %) of patients received palliative treatment, meanwhile about 28.1%, 12.3 % underwent other lines of treatment, no treatment, respectively. Conclusion: According to the results of this study, we concluded that most of HCC patients presented at Menofia oncology unit were of advanced stage and poor survival. More effort is needed to discover early HCC cases with high risk factors.

Keywords: Hepatocellular carcinoma, Epidemiology, Treatment, Egypt.

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Contribution/ Originality

This study contributes in the existing literature, Egyptian Patients with HCC. This study uses a new estimation methodology.

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1. INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common primary malignant tumor of the liver. HCC accounts for about 90% of primary liver cancers and causes more than one million deaths worldwide per year [1] it ranks the 5th and 7th most common cancer among men and women [2] and the 4th in annular mortality rate [3]. There is a clear predominance of males worldwide, ranging from 8: 1 in countries with high incidence of HCC to approximately 2: 1 to 3: 1 in population with low frequency [4].

Liver cancer incidence and mortality rates vary considerably across different geographical areas, with much of this variability related to the global distribution and natural history of infection with hepatitis B virus (HBV) and hepatitis C virus (HCV) [5]. High incidences (more than 20 cases per 100.000 populations) are found in Eastern and South Eastern Asia, some of the western pacific islands, and eastern Africa [6].

Chronic infection with HBV and HCV, aflatoxin ingestion and excessive alcohol consumption contribute to significant inter-country variations of incidence in hepatocellular carcinoma around the world. Although other factors, such as genetic/family history, diet and tobacco smoking, have been implicated in disease development, their contribution to disease causation remains uncertain [7, 8].

People with chronic HBV or HCV infection are at 20 to 200-fold greater risk of developing HCC than those uninfected [9, 10]. According to a World Health Organization report published in 2004, an estimated two billion people worldwide were infected with HBV (with approximately 350 million chronically infected) and 170 million people were infected with HCV. Some 500,000 – 1.2 million deaths each year are caused by HBV infection, with 320,000 deaths due to liver cancer [11].

The overwhelming majority of HCC cases occur in patients with chronic liver disease [12]. Approximately 80% have cirrhosis, and most of the remainder have moderate to advanced Fibrosis. Cirrhosis of any cause can result in HCC, but chronic viral hepatitis accounts for more than 80 % of cases worldwide [13].

Egypt shows one of the world's highest prevalence rates of HCV with about 10% prevalence of chronic HCV infection among persons aged 15–59 years [14]. The prevalence of HBsAg in Egypt is of intermediate endemicity (2%–8%) and nearly 2 to 3 million Egyptians are chronic carriers of HBV [15].

In Egypt, 4.7 % of chronic liver disease patients suffer from HCC. The development of HCC is mainly due to high rates of hepatitis C and B infections among Egyptian patients [16].

According to the report of the population-based cancer registry of Gharbiah , the incidence of liver cancer is ranked as the second highest in men and the seventh in women during 2000–2002 [17]. Moreover, there has been an alarming increase in incidence of liver cancer in Egypt, which is now three times higher than that in the USA [18].

This study aims to identify the epidemiological and clinical characteristics of HCC patients attended Menofia oncology unit in the duration from 2003-2012, Egypt.

2. METHODOLOGY

This retrospective study has been conducted in the duration from the beginning of December 2013 to the end of April 2014 where records of all hepatocellular carcinoma patients (n=1500) attended the oncology unit in Menofia University Hospital in the duration from 2003-2012 have been reviewed.

Diagnosis of HCC was based on histopathological examination and/or detection of hepatic focal lesions by two imaging techniques (ultrasonography and dynamic CT) plus α-fetoprotein level above 200 ng/mL [19].

The following data have been collected from records; demographic data, medical history, results of clinical examination with stress on jaundice, ascites, lower limb edema, liver and spleen sizes, results of laboratory investigations; markers of liver injury (SGOT, SGPT), viral markers (HBsAg, Anti-HCV), Liver function tests (Serum bilirubin and albumin, Prothrombin time (PT), Prothrombin concentration, and International normalizing ratio {INR}), and tumor markers (Alpha-fetoprotein), radiological investigations (Abdominal ultrasonography, Computed tomography {CT}), received lines of treatments, and history of metastasis.

3. STATISTICAL ANALYSIS

Data has been collected and entered to the computer using SPSS (Statistical Package for Social Science) program for statistical analysis, (version 17; Inc., Chicago. IL). Data from records was entered as numerical or categorical, as appropriate. Two types of statistics have been done: 1) Descriptive statistics; where quantitative data was shown as mean, SD, and range, and qualitative data has been expressed as frequency and percent. 2) Analytical statistics: Chi- square test was used to measure association between qualitative variables, while Mann Whitney test have been used to compare mean and SD of 2 sets of quantitative not normally distributed data. P-value was considered statistically significant when it is less than 0.05.

4. RESULTS

The male to female ratio of the HCC patients was 2.9 :1, 74.4% were males (n=1116) while 25.6% were females (n=384), their ages ranged between 20 and 86 years with Mean ± SD equal to 54.98 ± 10.01 .More than half of patients were resident in urban areas (66.2%). Smoking have been reported in 42.2 % of patients (n=633), 6.86 % of patients (n=103) were found to be alcoholic, 49.73% were diabetic (n=746), 23.20 % were hypertensive (n=348), and 18.6 % were found to have history of Bilharziasis (n=279) {Table 1}. Nearly two thirds of patients were infected with Hepatitis C virus {Figure 1}.

The main complain among patients was the abdominal pain (76.8 %), and more than two thirds have been presented with hepatomegaly (87.2%), while ascites, jaundice and lower limb edema have been reported in 46.53 % of patients. More than half of patients (58.93%) have been diagnosed as having cirrhotic liver by Ultrasound. The size of the lesion was less than 2

centimeters in 48.2 % of patients and more than one third of lesions (44.2%) were present in right hepatic lobe. Multiple lesions and portal vein thrombosis were found in 51.26 %, 24.74 % of our patients respectively. Metastasis has been reported in 59.8 % of patients, nearly one third of patients got abdominal metastatic lesions (39 %) {Table 2}.

Regarding cirrhosis, 64.47 % of patients were Child-A classification (n=967), while 26.53 % were Child-B classification (n=398), and 9% were Child-C classification (n=135) with no significant difference between males and females (p>0.05). Received treatment line didn't differ significantly between male and female patients and it was mainly palliative therapy in 59.6 % of patients {Table 3}.

No significant differences (p>0.05) have been found between male and female patients regarding Serum Glutamic-Oxaloacetic Transaminase, Serum Glutamic Pyruvic Transaminase, and Alfa Fetoprotein levels {Table 4}.

5. DISCUSSION

Hepatocellular carcinoma (HCC) is considered as one of the 130 major causes of morbidity and mortality in the world [20].

In Egypt, Hepatocellular carcinoma is the second most common malignant tumor [21] accounting for about 7.2% of chronic liver disease patients [22].

The prognosis of Hepatocellular carcinoma is generally grave [23] approximately 75% of patients with hepatocellular carcinoma present with advanced, unresectable disease with element of hepatic dysfunction [24] and in Egypt most patients presented in late stage in 85% of cases [21].

This study has been conducted to identify the epidemiological and clinical characteristics of HCC patients attended Menofia oncology unit in the duration from 2003-2012, Egypt.

In this study, HCC has been commonly presented in males74.4% more than females 25.6% (male to female ratio is 2.9:1). This is in agreement with Kew [25] who concluded that male predominance is more obvious in population at high risk with male to female ratio 3.7:1 [25] however, other studies [26, 27] had pronounced male predominance of hepatocellular carcinoma through the world, ranging from male to female ratio 4:1 in low incidence areas and up to 9:1 in high incidence areas.

In Egypt, male predominance may be explained by the higher prevalence of viral hepatitis and high susceptibility to environmental carcinogens. In Egypt, especially in rural areas, males are more exposed to carcinogens and environmental factors as they participate more in outdoor activities than females. Also, androgenic hormones and increased genetic susceptibility may also increase risk among males [28].

The mean age in the current study is 54.98 years, ranging from 20 years to 86 years. This is nearly similar to the age of 56 years found in other Egyptian studies [29, 30].

The clinical picture of HCC is very variable [27] and dramatically different in different parts of the world [31]. In this study, the presenting symptoms mostly were abdominal pain, weight

loss, abdominal enlargement and elevated body temperature. These results were constantly with that reported by Mohamed, et al. [32]. The prominent physical signs in our patients were hepatomegaly and hard liver, this goes in agreement with Di Bisceglie [33] who stated that, at physical examination the liver is often enlarged and may be hard [33].

More than one third of our study patients have been reported to be smokers (42.2%). Badawi and Michael [34] stated that factors associated with an increased risk of HCC in Egypt were age over 60 years-old, farming, cigarette smoking and occupational exposure to chemicals such as pesticides Badawi and Michael [34]. El-Zayadi, et al. [22] reported that smoking yields chemicals with oncogenic potential that increase the risk of HCC[22], however, the role of smoking was not clear in our study.

In this study, 69.8% of patients were found to be anti-HCV positive, while 17.2% were positive to HBsAg, 9.7% had mixed infection and 3.3% were free of infection.

El-Zayadi, et al. [22] reported the proportions of HCV antibodies and HBsAg among HCC cases were 86.9% and 28.4% respectively El-Zayadi, et al. [22]. While, Abdel-Wahab, et al. [35] reported that the proportion of HCV were 79.6%, HBV 6.9% and among them 3.6% with mixed hepatitis B and C virus markers, while 17.1% were negative for HCV and HBV markers [35].

This could be attributed to the high prevalence of chronic HCV infection among general Egyptian population which has been estimated to be approximately 10% among persons aged 15–59 years [14].

This study shows that 18.6 % of cases have history of Bilharziasis**.** Hassan, et al. [36]; El-Zayadi, et al. [22] concluded that both HCV and HBV infection increase risk of HCC in Egyptian patients, whereas isolated schistosomal infection does not [22, 36].

In the current study, most of the patients with HCC (64.47%) were Child I, followed by Child II (26.53%) then Child III (9 %). This is in agreement with study of Mohamed, et al. [32] who reported that (49.5%) of cases were Child **I**, followed by Child **II** (47.5%) then Child **III** (3%) [23] but this is not in agreement with Rex [37] who reported that most HCC (60-70%) are diagnosed at an advanced stage [37].

The right lobe was predominantly more affected (44.2%) than left lobe (23.1%) in the this study. This is in agreement with Rosen and Nagorney [38] who stated that HCC occurs most frequently in the right hepatic lobe [38].

El-Zayadi, et al. [22] reported that 70.9% of lesions were in the right lobe and 81% of lesions smaller than 3 cm [22].

6. CONCLUSION

The current study showed that most of HCC patients who have been presented to the Oncology unit at Menofia University hospitalin the duration from 2003-2012 were of male gender, infected with HCV and/or HBV, and of advanced stage at presentation, which raise the issue of the importance of developing screening programs for early detection of HCC in high risk patients at a national level and searching for new approaches in management; which will

definitely improve the patient outcome. Health education programmes are needed to raise the awareness of publics about the modes of transmission and risks of hepatitis B and C.

6.1. Abbreviations

Hepatocellular Carcinoma (HCC), Hepatitis B virus (HBV), Hepatitis C virus (HCV).

Table-1. Demographic data, social habits, and medical history of the studied group of patients (n: 456).

Studied Variables	No	%
Sex:		
-Male	1116	74.4
-Female	384	25.6
Residence:		
- Urban	993	66.2
-Rural	507	33.8
Positive history of smoking:	633	42.2
Positive history of alcoholism:	103	6.86
Positive history of diabetes:	746	49.73
Positive history of hypertension	348	23.20
Positive history of Bilharziasis	279	18.6
Age:		
-Mean ± SD	54.98± 10.01	
-Range	20-86	

Table-2. Clinical features of the studied group of patients (n: 456).

Studied Variables	No	%
Presentation Symptoms:		
Abdominal pain	1152	76.80
Abdominal swelling	422	28.13
Yellowish color of skin	455	30.33
General manifestations (fatigue, weight loss, fever)	837	55.80
Presentation Signs:		
Shrunken liver	548	36.53
Hepatomegaly	1173	87.2
Splenomegaly	396	26.4
Abdominal mass	297	19.8
Ascites, Jaundice, or L.L. edema	698	46.53
Positive portal vein thrombosis	371	24.74
Positive Triphasic focal lesion	1176	78.4
Performed CT guided biopsy	145	31.81
Positive liver Cirrhosis by U/S	884	58.93
Size of the lesion:		
<2 cm	732	48.2
2-5 cm	451	30.67
≥5 cm	317	21.13
Site of the lesion:		
Right lobe	663	442
Left lobe	347	23.1
Bilateral	490	32.7

Multiple number of lesions:	769	51.26
Metastasis:	897	59.8
-Abdominal	585	39
- Lung	165	11
- Bone	107	7..1
- LN	40	2.7

Table-3. Child Classification and received treatment among studied patients distributed by their gender.

Studied Variables	Males (n=1116)		Females (n=384)		Total (n=1500)		P-Value
	No	%	No	%	No	%	
Child Classification:							
- A	708	63.4	259	67.4	967	64.46	>0.05
- B	304	27.2	94	24.5	398	26.53	
- C	104	9.4	31	8.1	135	9.00	
Type of treatment:							>0.05
Palliative treatment	654	58.6	240	62.5	894	59.6	
-Trans-arterial interventions	130	11.6	38	9.9	168	11.2	
-Percutaneous ablative therapy	107	9.6	31	8.1	138	9.2	
-Surgery	80	7.3	36	9.4	116	7.73	
-No treatment	145	12.9	39	10.1	184	12.26	

Table-4. Distribution of SGOT, SGPT, and AFP regarding gender.

Studied Variables	Male (n=1116) Mean ±SD	Female (n=384) Mean ±SD	Total (n=1500) Mean ±SD	P-Value
SGOT(u/l)*	549.32±1176.02	532.53±1019.7	542.11±1147.85	>0.05
SGPT(u/l)*	547.47±1198.26	541.02±1027.42	545.95±1172.21	>0.05
AFP (ng/ml)*	1996.13±4205.01	2412.66±5873.24	2245.21±1342.24	>0.05

*SGOT: Serum glutamic oxaloacetic transaminase, **SGPT:** Serum Glutamic Pyruvic Transaminase, **AFP:** Alfa Fetoprotein.

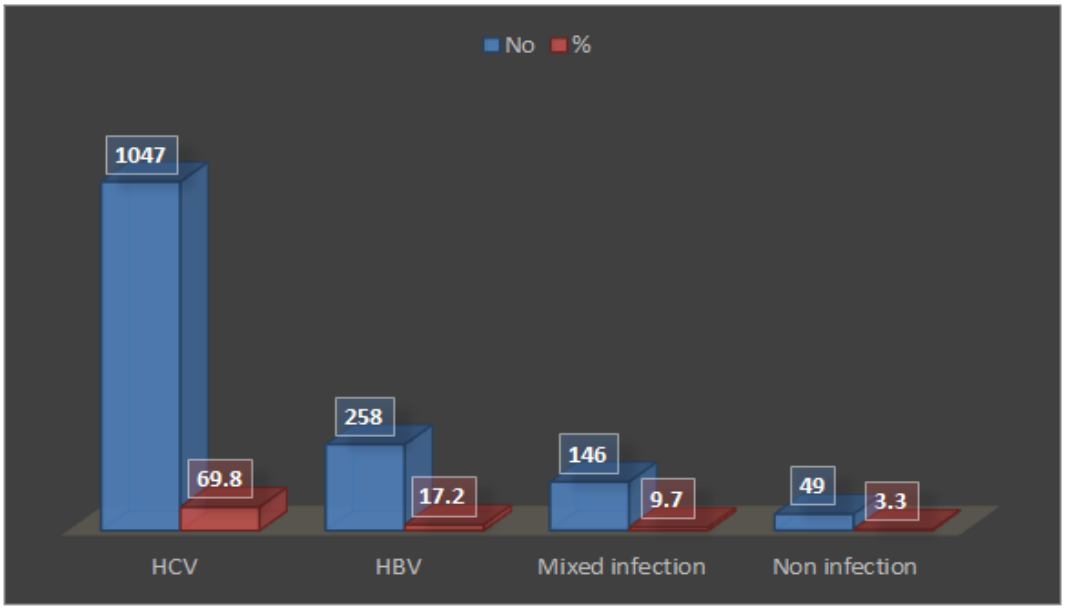

Figure-1. Distribution of Hepatitis viral markers among studied group of patients.

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