Knowledge of Hepatitis, Hepatocellular Carcinoma and Hepatocellular Carcinoma Screening Guidelines among Cirrhotic Patients at El- Ragehy Hospital, Assiut University

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Abstract

Purpose: To assess the knowledge of Hepatitis, HCC and HCC screening among cirrhotic patients presented at El-Ragehy Hospital, Assiut University.

Patients and Methods: This is a cross-sectional hospital- based study conducted from 1st November 2017 up to 30thJune 2019 at outpatient clinics of El-Ragehy Hospital, Assiut University. The study included 404 cirrhotic patients. Data were obtained using standardized questionnaire.

Results: Age of patients ranged from 36.0 to 79.0 with a mean of 58.91± 9.39 years. Male to female ratio was 1:1 and 70% of patients came from rural areas. More than 30% were not working and about 2/5th of patients (39.9%) were illiterate. Family income/month was ≤2000 Egyptian pounds in 69.3% of patients (more than 2/3 were below poverty line). Family history of HCC was reported in 15.10% of patients. For evaluating specific knowledge of hepatitis, HCC, and HCC screening guidelines, results showed that most patients were knowledgeable about mode of HBV and HCV transmission but dissatisfied level of knowledge about HCC, and HCC screening, with a median knowledge score of 4 (0 to 15). Knowledge was related to patients' demographics including age, residence, working job, level of education, and monthly income. Also it was related to family history of HCC, hepatitis or cirrhosis.

Conclusion: Promoting education in Upper Egypt and health education at all levels of health care delivery system could increase knowledge about HCC and HCC screening, as well as promoting screening adherence and earlier diagnosis.

Key words: hepatocellular carcinoma, screening, knowledge, cirrhotic patients.

Introduction:

Liver cancer is the fifth most common cancer in men worldwide, 7.9% of all cancers, and the seventh most common cancer in women, 6.5% of all cancers. Liver cancer has a high mortality rate, with most of the burden is in developing countries, where almost 85% of the cases occur, this according to the International Agency for Research on Cancer IARC, **[1]**.

Hepatocellular carcinoma (HCC) represents the main complication of cirrhosis, and shows an increasing incidence in Egypt, which may be the result of a shift in the relative importance of hepatitis B virus (HBV) and hepatitis C virus (HCV) as primary risk factors, **[2]**.

In Egypt, HCC was found to be the first among men and the third among women**, [3]**. So assessing knowledge and understanding the reasons for the lack of HCC screening among cirrhotic patients could assist health care professionals to develop more effective intervention methods for early detection. Because screening helps to detect HCC at an early stage, effective treatments may be offered to achieve better chances of survival.

Screening guidelines published by the Peking University Medical Press and expert consensus established by the Chinese Anti-Cancer Association Society of Liver Cancer, Chinese Society of Clinical Oncology, and Chinese Society of Hepatology Liver Cancer Study Group, recommend biannual screening with a combination of serum a-fetoprotein (AFP) and abdominal ultrasound at 6-month intervals for high-risk individuals **[4]**.

Knowledge is usually assessed to evaluate how patients' knowledge corresponds to biomedical concepts. Questions included in knowledge assessment

are related to causes, symptoms, transmission and management of the disease or infection condition under investigation concepts, **[5]**.

Although numerous studies have surveyed different populations to understand the knowledge of cervical, breast, and colorectal cancer screenings, it is difficult to find similar studies conducted for HCC and HCC screening guidelines in Egypt. Furthermore, although no population-based data have been published about HCC screening rates in Egypt, studies have suggested that screening rate may be low because of a lack of knowledge and awareness among the general Egyptians and even among health care providers,**[6].**

Hassan, El-Ghitany [7] assess the knowledge, attitude, risky behaviors and changes of lifestyle among group of Egyptian chronic HCV patients. They found that 49.3% of them had poor knowledge about hepatitis C. Another study by **Doa'a, Amr [8]** revealed misconceptions about the modes of transmission of HCV (e.g. polluted air and water) and lack of knowledge about pesticides.

An Egyptian study conducted by**, Hassany, Moustafa [9]** aimed at assessing the physicians' knowledge and attitude towards different aspects of HCC screening, including screening modalities, as well as awareness of published guidelines .The study found that 71 % of the physicians do not know about guidelines for the management of HCC. Results of the same study found that the majority of doctors do not implement or recommend HCC surveillance according to international guidelines.

Low levels of awareness and knowledge about HCV have been identified as a big challenge to prevention and care, **[10].**

Because there is a strong association between knowledge and educational level and according to what was reported by the Central Agency for Public Mobilization and Statistics (CAPMAS) in Egypt, where it is reported that Assiut, suffered the highest rate of illiteracy which was 34.6% and Upper Egypt had the highest rates of illiteracy in 2017 **(www.egyptindependent. com).** We expect a low level of knowledge of HCC and HCC screening among cirrhotic patients at El-Ragehy Hepatology Hospital Assiut University; so, it is important to assess the specific knowledge of hepatitis, HCC, and HCC screening guidelines among patients with liver cirrhosis and examine the association of socio-demographic and clinical factors with HCC screening knowledge.

Patients and Methods:

This is a cross-sectional hospital -based study conducted from 1st November 2017 up to 30th June 2019 at outpatient clinics of El-Ragehy Hepatology Hospital, Assiut University.

Assessing knowledge of patients was done via using a standardized questionnaire. The questionnaire was designed by **[11, 12]** based on hepatology experts' opinions and previous studies on the screening practices and knowledge of cervical cancer, breast cancer, and HBV infection.

The questionnaire consisted of 2 sections.

Section 1 (socio-demographic and clinical characteristics)

Section 2 (Knowledge Questions): Consisted of 8 yes-or-no questions, 5 multiple-choice questions and 2 open ended questions that examined the patients' knowledge concerning viral hepatitis, HCC, and HCC screening guidelines. Two of the multiple-choice questions had 2 correct answer choices. The knowledge score (range: 0-15) was calculated by giving 1 point for each correct answer and 0 for an incorrect answer or an answer of "I do not know."

Sample size estimation:

The study sample was estimated based on prevalence of 0.5 according to,(**Xu, Watanabe-Galloway [13]** with width of 0.1 and 95% confidence interval, the sample size was 384 patients and increased to 404 to guard against drop out .

Sampling technique:

We recruited the study cases who met the eligibility criteria from the outpatient clinics of El-Ragehy Hospital, those patients were diagnosed as liver cirrhotic patients who attended the outpatient clinic either for follow-up or for preparation for liver transplantation. The diagnosis of liver cirrhosis was based on both clinical and radiologic (ultrasound) or laboratory investigation (alpha-feto protein). Male patients were eligible if age is ≥35 years and ≥45 years for women according to Chinese liver cancer screening recommendations, **[14]**. Patients with chronic hepatitis or not confirmed to be cirrhotic were excluded and formal verification for final diagnosis was performed through electronic medical record systems. . Recruitment of patients started on 1st November 2017 up to 30th June 2019 and was done during the working days of the clinic which were 3 days / week from 9 am to 12 pm. The questionnaire was designed to collect relevant data through personal interview with face to face approach by the researcher and took an average of 15 minutes to be completed.

Statistical methods:

Data analysis was carried out using SPSS (statistical package for the social science; SPSS Inc. Chicago, IL, USA) version 23.0. Continuous data was expressed in form of mean ± standard deviation (SD) or median and range when not normally distributed while nominal data was expressed in form of frequency (percentage). To investigate the association of knowledge with socio demographic and clinical factors, Mann Whitney U test and Kruskall-Wallis test with post-hoc for pair-wise comparisons were utilized. P-value is always 2 tailed set significant at 0.05 level.

Ethical issues:

Approval of Institutional Review Board (IRB) was obtained before start of the study, the data of the patients was presented anonymously with protection of privacy and confidentiality, and an informed consent was taken from the patients after discussing with them the aim and methods of the study.

Results:

Age of patients ranged from 36.0 to 79.0 with a mean of 58.91± 9.39 years. Less than 6% of patients were <45 years and more than 2/3 were ≥55 years. Male to female ratio was 1:1 and 70% of patients came from rural areas. About 2/5th of patients (39.9%) were illiterate, and 73.3% were married. More than 75% of patients have a family size between 4-6 persons and consanguinity was reported in 30.5%.Family income/month was ≤2000 Egyptian pounds in 69.3% of patients (more than 2/3 were below poverty line).None of the females with liver cirrhosis were smokers either current or ex-smoker with a total prevalence of 15.6% of current and 3.8% ex-smokers among both genders.

Average duration of hepatitis in the whole study group was 4.58±2.2 years. Family history of hepatitis was found in 33.4% of patients while family history of cirrhosis was positive in 6.30% of patients. Family history of HCC was reported in 15.10% of patients all of them had only one relative with HCC. For co-morbidities 61.1%of patients reported to be treated from hypertension, 31.2% from diabetes and 19.3% had cardiac disease. Patients with uncompensated liver cirrhosis were around 2/3 of all patients (64.6%).

For evaluation of Specific knowledge of hepatitis, HCC, and HCC screening guidelines, questions are presented in (table **1**). The question with the highest percentage of overall correct response **(**70%) was Q3-can HBV or HCV be transmitted through sexual intercourse? (Correct: yes). The second and third correct knowledge questions were (Q7 and Q8) with percentage (64.6% and 55.4%) respectively. The 3 questions with the lowest percentage of overall correct responses were Q15-when should patients with chronic hepatitis start to undergo HCC screening? (Correct: men at age 35 and female at age 45) (2%), Q14-how often should patients with chronic hepatitis undergo HCC screening? (Correct: at least every half year) (7.9%), and Q13-which of the two choices are the most common tests used for HCC screening AFP or CBC? (Correct is AFP) (14.6%). Median knowledge score (given a point for every correct answer) was 4 with range from 0 to 15.

Table 2 illustrates the association between knowledge scores with the different socio-demographic characteristics. It was found that older patients aged >65 years had lower knowledge score (median = 2) compared with all other age groups, p<0.001. Gender was not found to affect knowledge but patients living in urban areas has better knowledge than rural patients (median 7 vs. 4 respectively), p<0.001. As the education level improves the total knowledge score also increase, p <0.001. It was found that widow patients had lower knowledge than married and single patients and pair-wise comparisons yielded p values of 0.001 and 0.002 respectively. On other hand it was found that patients with monthly income >2000 L.E had better knowledge score than those with income <1000 L.E and those with income between 1000 and 2000 L.E, p<0.001

Current smokers, those with positive family history of HCC, hepatitis or cirrhosis and patients with compensated cirrhosis were found to have higher knowledge score compared to their counter groups, p < 0.001 for all comparisons. On the other hand presence of co-morbidities of hypertension, diabetes or cardiac disease had a negative impact on the level of knowledge of cirrhotic patients, p<0.001. (Table 3)

Table (1) Correct knowledge of patients about liver cirrhosis and HCC screening *(correct answer between brackets)* El- Ragehy Hospital, Assiut University 2019

Question	No	%
Q1- Prior to participation did you know the purpose of liver AFP (tumor marker)? (yes)	70	17.3
Q2- Is HBV or HCV commonly transmitted through consuming contaminated food? (no)	202	50.0
Q3- Can HBV or HCV be transmitted through sexual intercourse? (yes)	283	70.0
Q4- Is excessive alcohol or smoking consumption considered a risk factor for HCC?(yes)	187	46.3
Q5- Have you heard of aflatoxin and its carcinogenic role in HCC?(yes)	61	15.1
Q6- Does hepatitis have to cause cirrhosis before developing HCC?(no)	75	18.6
Q7- Can HCC metastasize to other organs in the body?(yes)	261	64.6
Q8- Do symptoms usually show up in the early stage of HCC?(no)	224	55.4
Q9- Which of the choices are common symptoms of HCC abdominal pain, red eye, leg pain?(abdominal pain)	196	48.5
Q10- Which of the choices are common symptoms of HCC unexplained weight loss, skin rash, and red eye? (unexplained weight loss)	215	53.2
Q11- Which of the following life styles are important to prevent HCC: smoking cessation, alcohol drinking cessation, limit the intake of salty foods, consumption of high fruit and vegetables, HBV vaccine, or all of above? (all of above)	224	55.4
Q12- Which of the two choices are the most common screening test used for HCC screening ultrasound or urine analysis? (ultrasound)	109	27.0
Q13- Which of the two choices are the most common tests used for HCC screening AFP or CBC ?(AFP)	59	14.6
Q14- How often should patients with chronic hepatitis undergo HCC screening?(at least every half year)	32	7.9
Q15- When should patients with chronic hepatitis start to undergo HCC screening?(men at age 35 and female at age 45)	8	2.0
Total knowledge score, median (range)	4	(0 – 15)

Table (2) Relationship between total knowledge score and socio-demographic characteristic of cirrhotic patients **(n=404)**

	knowledge score		p-value
	Median	Range	
Age (years)			
- 35-	7.00	(3-13)	
- 45-	7.00	(1-15)	<0.001
- 55-	5.00	(1-15)	
- >=65	2.00	(0-14)	
Gender			
- Male	5.00	(0-14)	0.118
- Female	4.00	(0-15)	
Residence			
- Urban	7.00	(1-15)	<0.001
- Rural	4.00	(0-15)	
Occupation			
- Not working	3.00	(0-13)	
- Employee	9.00	(3-15)	<0.001
- Labor worker	4.00	(1-14)	
- Horse wife	4.00	(1-15)	
Educational level			
- Illiterate	2.00	(0-9)	
- Low level education	6.00	(1-14)	<0.001
- High level education (university)	11.00	(6-15)	
Marital status			
- Single	7.00	(2-14)	
- Married	5.00	(0-15)	<0.001
- Widow	3.00	(1-15)	
- Divorced	4.00	(0-15)	
Consanguinity			
- Yes	4.00	(1-14)	0.100
- No	4.00	(0-15)	
Family size (persons per households)			
- 1-3	6.00	(2-15)	0.060
- 4-6	5.00	(0-15)	
- >=7	4.00	(0-14)	
Family income			
- <1000	4.00	(1-10)	
- 1000-2000	3.00	(0-15)	<0.001
- >2000	9.00	(2-15)	

Table (3) Relationship between total knowledge score of cirrhotic patients and family history of liver diseases, and co-morbidities

	Knowledge score		p-value
	Median	Range	
Current smoking			
- No	4.00	(0-15)	<0.001
- Yes	7.00	(1-14)	
Family history of HCC			
- No	4.00	(0-150	<0.001
- Yes	10.00	(1-15)	
Family history of hepatitis			
- No	4.00	(0-15)	<0.001
- Yes	7.00	(0-15)	
Family history of liver cirrhosis			
- No	4.00	(0-15)	<0.001
- Yes	7.00	(1-15)	
Hypertension			
- No	4.00	(0-15)	<0.001
- Yes	6.00	(1-15)	
Diabetes mellitus			
- No	3.00	(0-15)	<0.001
- Yes	6.00	(0-15)	
Cardiac disease			
- No	3.00	(0-12)	<0.001
- Yes	5.00	(0-15)	
Cirrhotic status			
- Compensated	7.00	(1-15)	<0.001
- Non compensated	4.00	(0-15)	

Discussion:

Although numerous studies have surveyed different populations for perception and understanding the knowledge and barriers for cervical, breast, and colorectal cancer screenings, it was difficult to find similar studies that were conducted for HCC screening in Egypt.

In Egypt, HCC was found to be the first among men and the third among women, **[3]**.so understanding the reasons for the lack of HCC screening among cirrhotic patients could assist health care professionals to develop more effective intervention methods for early detection. Because screening helps to detect HCC at an early stage, effective treatments may be offered to achieve better chances of survival.

The results of the present study showed that the mean age of the whole study group (n=404) was 58.91± 9.39 years and ranged from 36.0 to 79.0 years which was comparable with the result of Shaw, Patidar [15] that was done in Spain and included 69 cirrhotic patients with a mean age of 59.0±8.41.Another study done by **Ziada, El Sadany [16]** that aimed to assess the prevalence of HCC among chronic HCV and cirrhotic patients in Mid Delta, Egypt at Tanta University showed that the age of the patients ranged between 29-78 with an average age of 55.13±9.82 years.

The result of the present study showed that 50.70% of the patients were males and 49.30% were females and this was more or less similar to the results of the study that included patients with cirrhotic hepatitis C and hospitalized at the Tropical Medicine Department, Sohag University Hospital which showed that 52.5% of the patients were male and 47.5% were females **[17]** and was comparable with result of **Ahmed, Taha [18]** that was conducted in tropical medicine and gastroenterology units at Zagazig University Hospitals on 115 liver cirrhotic patients show that Males were 51.3% and females were 48.7% of patients.

In relation to patient's residence this study showed that 70% of patients were from rural areas and this was consistent with the results of a study by **Khalil, Youssef [19]** which was conducted in the Tropical Medicine and Gastroenterology department at Assiut University

Hospital and found that 85% of cirrhotic patients were from rural areas. **Rao, Naficy [20]**, reported that; in Egypt, liver cirrhosis was more common in rural than urban regions because rural regions presented a suitable environment for developing a schistosomal infection due to exposure to water canals that would be polluted by snails that harbor the schistosomal parasite. In the period between 1950 to 1980, public health programs for getting rid of bilharziasis by injection of tartar emetic using contaminated needles led to wide spread of HCV infection in Egypt, **[21]** and because the majority of the people working as farmers in rural areas in Egypt were more susceptible to be infected by HCV during this period which is a major risk factor for development of liver cirrhosis and HCC, **[22].** Also decreased educational level and wealth, poor infection control and bad equipment sterilization procedures used in rural medical and dental settings also contributed to the ongoing iatrogenic HCV infections in rural areas in Egypt, **[23].**

For the educational level the present study showed that 39.9% of the patients were illiterate, 45.3% low level/middle and 14.9% had high level of education. This finding is consistent with what was reported by the Central Agency for Public Mobilization and Statistics (CAPMAS) in Egypt, where it is reported that Assiut, suffered the highest rate of illiteracy which was 34.6% and Upper Egypt had the highest rates of illiteracy in 2017 (**www.egyptindependent. com).** A study conducted at the Tropical Medicine and Gastroenterology department at Assiut University to assess the nutritional status of patients with liver cirrhosis showed that 68.3 % were illiterate, **[19]**.

Present study showed that 30.7% of males were smokers, which is considerably high percent among cirrhotic patients. This value was a mid-way between that by **Ziada, El Sadany [16]**, who found that 42% of cirrhotic patients were smokers and **Mohamed, Bassiony [24]** who showed that 24% of cirrhotic patients were smokers. And this indicates the high percentage of smokers among cirrhotic patients.

Present study showed that family history of HCC was present in 15% of patients and this was comparable with result of **Ziada, El Sadany [16]**that was conducted at the Department of Tropical Medicine and Infectious Diseases at Tanta University Hospital, Egypt and aimed at assessing the prevalence of HCC among chronic HCV patients where they found that 12.2% of the patients had a family history of HCC. Also **Zipprich, Garcia-Tsao [25]** found that family history of liver diseases was 16.7% in patients with suspected cirrhosis.

In our study the mean duration of hepatitis was 4.58±2.20 years and this is consistent with the results of **Hassan, El-Ghitany [7]** who found that the mean duration of HCV infection was 4.5±3.6 years.

Most patients were knowledgeable about mode of HBV and HCV transmission where 70% gave correct response that is transmitted by sexual intercourse. On the other hand majority of the patients gave dissatisfied level of knowledge about HCC, and HCC screening, the high illiteracy rate, and low public awareness in general and viral hepatitis, HCC and HCC screening specifically could explain these findings. **Ibrahim and**

Madian [26], found that the great majority of patients gave unsatisfactory level of knowledge about HCV; general knowledge about HCV (poor 26.3% and average 24.3%), mode of transmission (poor 22.0% and average 55.3%), which factor which do further damage to liver (poor 20.5% and average 41.0%), how to protect themselves from getting HAV and HBV infection (poor 91.7% and average 8.0%) as well as their knowledge about the healthy diet needed by HCV patients (poor 97.0% and average 2.7%). Another study by **Sultan, YacoobMayet [27]** for assessing the level of knowledge and available sources of information about hepatitis C infection among HCV-infected Egyptians, revealed that correct knowledge of the modes of transmission of HCV among Egyptian HCV-infected patients was unsatisfactory in most of the participants, 50.3% of participants had an equal to or below median knowledge score of HCV infection.

Sultan, Yacoob Mayet [27] also found that 3/4 of patients were not frequently receiving information on how to follow up once HCV is detected, how often to do a liver function test and an ultrasound to assess liver status and the presence of any liver cancer, and where and when to seek HCV treatment. **Doa'a, Amr [8]** evaluated the knowledge and perceptions of HCV infection and pesticides use in two communities in rural Egypt and found that there was a considerable lack of knowledge pertaining to the adverse health effects of pesticides and basic prevention and treatment of HCV infection and found that 22% of participants did not know what causes HCV infection, 81% mentioned incorrect modes of transmission, and 45% did not know the disease manifestations. In Alexandria **Hassan, El-Ghitany [7]** assessed the knowledge, attitude and lifestyle changes among chronic hepatitis C patients and reported that it was significantly low, as 49.3% of the patients had poor knowledge regarding all aspects of HCV in addition to wrong concepts.

Older patients aged >65 years had lower knowledge score (median = 2) compared with all other age groups. Patients living in urban areas had better knowledge than rural patients. Concerning occupation employees were found to be more knowledgeable than those not working, patients with labor work and house wives. As the educational level improves the total knowledge score also increased. On the other hand it was found that patients with a monthly income >2000 L.E had better knowledge score than those with income <1000 L.E and those with an income between 1000 and 2000 L.E.

Sultan, Yacoob Mayet [27] found a significant association between educational levels, the frequency of visiting the physicians and knowledge of HCV infection. The participants with a lower education level were at least 2 times more likely to have below or equal median knowledge score of HCV infection than those with college graduates. **Farvardin, Patel [28]** studied patient-reported barriers that were associated with lower HCC surveillance rates in patients with cirrhosis which include 541 cirrhotic patients at the University of Texas, Dallas Country. The researcher found that factors associated with higher levels of overall knowledge included English as primary language, HCV- related

cirrhosis, Child Pugh A cirrhosis (compensated), receipt of hepatology subspecialty care, higher educational level, and high perceived likelihood of dying from HCC. Living alone and lack of insurance were associated with lower levels of knowledge. **Xu, Watanabe-Galloway [13]** found that patients from age group 35-44 had better knowledge than patients aged 55-65 years. Patients living in urban areas with higher monthly income also exhibited better knowledge. Moreover, patients with a college education or above had better knowledge than patients with degrees of high school and middle school or below.

In conclusion current findings suggest that appropriate and effective educational programs should be established. Egyptian health care practitioners and community health promotion leaders should play an active role to implement and use educational programs as an intervention to improve high-risk patients' awareness, knowledge, and perceptions about HCC screening. These educational programs should target patients with low socioeconomic status, patients who reside in rural areas, and middle aged and older patients.

Recommendations:

As found in the current study, there is lack of knowledge, and awareness about HCC screening that is aggravated by poverty, so the authors recommend the following:

1- Promoting education in general especially in Upper Egypt

2- Health education using different methods as group discussion, brochures, face to face education, or home visits at all levels of health care delivery with involvement of health care professional and community leaders in a national health program (like 100 million healthy lives campaign) with stress on:
  - Magnitude of hepatitis problem
  - Causes and consequences of cirrhosis
  - Ways of protection against hepatitis
  - HCC if early detected could be a treatable disease

3- Scheduling system for follow up with reminders for the patients and utilities for facilitating transportation from and to homes

4- Subsidizing patients for cost of investigations for HCC screening

5- Social support especially for bread winner's women

6- Banning smoking among chronic liver patients

Conclusion:

Promoting education in Upper Egypt and health education at all levels of health care delivery system could increase knowledge about HCC and HCC screening, as well as promoting screening adherence and earlier diagnosis.

Authors' contributions

All authors carried out study design, data collection, analysis, interpretation of data, manuscript editing, the sequence alignment, and in the decision to submit the manuscript for publication.

Conflicts of interest

There are no conflicts of interest.

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