Original Article

The Effect of Chronic Hepatitis B on Health-Related Quality of Life: A Cross-sectional Study on Egyptian Patients

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Abstract

Background: Hepatitis B virus infection (HBV) is one of the major public health problems, which in addition to physical disorders, affects patients' quality of life (QoL). In Egypt, the prevalence of HBV is 1% while 87.2% of the liver cirrhosis patients reported poor QoL.
Objective(s): The present study was conducted to investigate the effect of chronic hepatitis B (CHB) on the QoL in Egypt.
Methods: An observational cross-sectional study was conducted in the Clinic of "On State Expenses Treatment" in Alexandria and Cairo for 18 months using WHOQO-BREF 26 questionnaire. It is composed of four domains: physical, social, psychological, and environmental. Each domain included different facets. A total of 294 HBV patients, as well as 64 physicians, as a control, participated in the study. Representation of the different chronic hepatitis B clinical stages was ensured.
Results: The overall 100-format QoL score was low (0.2). The QoL score among Hepatocellular Carcinoma (HCC) patients was the lowest, with the physical domain being greatly impaired, while the QoL score in the Chronic hepatitis B clinical stage was the highest, with the psychological domain showing the greatest impairment. Stepwise multiple regression modeling resulted in three main predictors (classification of the clinical stage, marital status, and smoking). These predictors were responsible for 41% of the variance in the QoL score. The classification of the clinical stage and smoking were inversely correlated to the QoL, the marital status was positively correlated.
Conclusion: The current study highlighted the importance of social support in the management of CHB patients. Moreover, the rehabilitation programs in the late stages of the disease are highly recommended, as the physical aspects become more affected at the end stage of the disease, as well as psychological aspects. The importance of early diagnosis and management of cases is an important priority especially with the fact that the clinical stage is a major predictor of the overall QoL of the patients.

Keywords: Chronic Hepatitis B, health-related Quality of life, Egypt

INTRODUCTION

Hepatitis B virus infection (HBV) is considered as an important public health problem due to its high morbidity and mortality. World Health Organization (WHO) defines chronic hepatitis B (CHB) by the persistence of HBsAg for more than six months.[1] CHB has many serious clinical consequences due to the progression into different clinical stages; cirrhosis, hepatic decompensation, and hepatocellular carcinoma (HCC). Additionally, the course of treatment is lifelong and its main objective is to improve liver function and slow down the disease progression without a cure.[2] This clarifies the high burden of such infection which creates great stress on those infected as well as the health care systems.[3, 4]

Despite this burden, CHB is underestimated and undertreated. In 2016 WHO reported that approximately 240 million people have CHB virus infection worldwide.[5] Additionally, Global Health Sector Strategy (GHSS) service coverage indicators on Viral Hepatitis reported that only 9% of those infected with HBV are diagnosed and only 8% are on treatment. [6] Furthermore, assessing the aspects of quality of life (QoL) among CHB patients received little attention.[7]

According to WHO, QoL is defined as "individuals' perception of their position in life in the context of culture and value systems in which they live and in relation to their goals, expectations, standards and concerns".[8] On the other hand, the term health-related quality of life (HRQOL) is described as: "A term referring to the health aspects of quality of life,

generally considered to reflect the impact of disease and treatment on disability and daily functioning; it has also been considered to reflect the impact of perceived health on an individual's ability to live a fulfilling life. However, more specifically HRQOL is a measure of the value assigned to duration of life as modified by impairments, functional states, perceptions, and opportunities, as influenced by disease, injury, treatment and policy".[9]

Assessment of the health relatedly is an important aspect in tailoring the management plan for the different diseases. It highlights the defective aspects in the overall health of patients and subsequently allow better allocation of resources towards these aspects.[10] Multiple tools have been developed to facilitate assessment of the health-related quality of life. They are classified either as generic or disease-specific instruments.

Regarding Egypt, the prevalence of Hepatitis B infection is 1% according to Egypt Demographic and Health Survey (EDHS), 2014. However, CHB is associated with a 15-25% risk of premature death from liver cancer or end-stage liver disease. [11, 12] Additionally, most of the liver cirrhosis patients in Egypt (87.2%) reported their QoL as poor.[13] There is no published evidence about the QoL of CHB in Egypt despite the disease burden. Thus, the present study was conducted to investigate the effect of chronic hepatitis B on patients' quality of life.

METHODS

Study design
An observational cross-sectional study was conducted.

Study setting
The study was carried out in the Clinic of "On State Expenses Treatment" in Alexandria Main University Hospital, Hepatology department as well as National Liver Institute in Cairo in addition to inpatient wards in Hepatology and Hematology departments, Alexandria Main University Hospital for one and half years.

Data collection tools and techniques
The Arabic version of WHO Quality of Life questionnaire (WHOQOL-BREF 26) was used for estimating the QoL either in the form of interview or self-administrative format. It assesses the overall quality of life across four domains: physical, psychological, social, and environmental domains. Each domain includes different facets as displayed in table 1. Additionally, sociodemographic data as well as HBV risk factors were retrieved from medical records.

Sampling
The questionnaire guidelines recommend including at least 300 respondents; 250 with disease or impairment and 50 well persons. The role of the respondents without the disease, is neutralization of the reported scores of the patients as they always tend to exaggerate their suffering and report a low QoL.

Thus, 294 chronic Hepatitis B patients - from Alexandria and Cairo were interviewed. The representation of the age groups, high-risk groups and clinical stages among the patients was ensured according to the questionnaire's guidelines. Each interview took around 10-15 minutes. Additionally, 64 physicians from Faculty of Medicine, Alexandria University, were contacted and their sample included both specialists and consultants from Hepatology, Emergency, and internal medicine departments.

A pilot study was conducted prior to actual field work to explore accommodation of the aim of the work to actual feasibility and detect various difficulties encountered at the execution of the study. It included 50 respondents: 40 patients and 10 physicians. The main challenge was not being able to use the questionnaire as self-administrative form for patients.

Score calculation and data analysis
The data revealed from the WHOQOL- BREF 26 was coded and checked for completeness of at least 80% of the answers. The SPSS syntax file for automatic checking, recording, and computing the scores of the four domains was used. This file was provided by WHO with the Arabic version of the questionnaire. The four domain scores of the WHOQOL-BREF 26 reflect individuals' perception of QoL in each domain. The higher scores indicate a higher QoL. Each domain produced a separate score through calculating the mean score of questions (3-26). Then, the domain score from the BREF-26 questionnaire was transformed into WHO-100 format using the WHO syntax file.

The overall score was produced through calculating the mean of questions 1, 2 which were examined separately:

o Question 1 asks about the individual's overall perception of QoL.
o Question 2 asks about the individual's overall perception of their health.

The results of the 64 physicians were included in the analysis and calculation of the score and not represented alone.

Moreover, further statistical analysis was done using Microsoft Excel and SPSS system files. Several statistical measures were adopted; descriptive statistics, Kolmogorov – Smirnov test, correlation analysis to test the association between the domains and the overall QoL, as well as regression analysis to identify the relevant determinants of the QoL. A 0.05 level of significance was used for the interpretation of results.

Ethical Considerations

Approval of the ethical committee of faculty of medicine, Alexandria University was obtained. Objectives of the study, the expected benefits, and types of information to be obtained were explained to the participants and an informed oral consent was received. Confidentiality of data was ensured.

Table 1: WHO BREF-26 Domains and Facets included in the questionnaire

Domain	Facets Included		
Physical Health	• Activities of daily living • Dependence on medical substances& medical aids • Energy& fatigue • Mobility		• Pain& discomfort • Sleep& rest • Work capacity
Psychological	• Bodily image and appearance • Spirituality/ Religion/ Personal beliefs • Thinking, learning, memory and concentration, self-esteem		• Negative feelings • Positive feeling • Self-esteem
Social Relationship	• Personal relationships • Social support • Sexual activity		
Environmental	• Financial resources • Freedom, physical safety, and security • Health& social care; accessibility and quality • Home environment • Opportunities for acquiring new information& skills. • Participation in opportunities for recreation/ Leisure activities		• Physical environment • Transport
General Questions	• How would you rate your quality of life? • How satisfied are you with your health?		

RESULTS

The sociodemographic characteristics of CHB patients enrolled in the study are portrayed in Table 2. Males constituted 61.9% of the participants while 38.1% were females. Illiterates were 14.3% while the remaining of the sample were educated. Despite most of the patients included could read the questionnaire, they needed an explanation of the questions included and they preferred to fill the questionnaire in the interview format. Around two-thirds of the patients were rural residents (64.9%) and 35.1 % were urban dwellers. Most of the patients were married (68.7 %). In the current sample, the mean age was (43.4 ± 13.5) years. More than half of the participants (50.7%) were in the age group (20- 40 years). More than half of the patients (58.5%) were in the chronic hepatitis stage, followed by decompensated cirrhosis, compensated cirrhosis, and HCC (21.8%, 15.6%, and 4.1% respectively). The high-risk groups represented 23.8% of the current sample.

Table 3 demonstrates the domains' score, where the social domain was the highly affected one (0.27) while the environmental domain was the least affected (0.76). The overall QoL score was 0.2 reflecting the great impairment in the CHB patients' QoL.

Further, the QoL of the patients according to their clinical stage was calculated and displayed in table 4. The QoL was highly affected in HCC patients (overall score of 0.14) with the physical domain being greatly impaired. On the other hand, the QoL in case of chronic hepatitis clinical stage was the least affected with the psychological domain showing the great impairment due to the psychological trauma of being newly diagnosed with HBV. There was a statistically significant difference between the reported mean score for each domain according to the different clinical stages of the disease.

Spearman correlation test was carried out to test the direction and strength of association between the overall score and the four domains. There was a significant positive correlation between the overall score and the scores of each of the four domains as demonstrated in table 5.

Multiple linear regression model was adopted to clarify the predictors of the QoL score in the current study. The dependent variable was considered as the overall QoL score. The independent variables were considered as follow; gender, education, residence, age, occupation, clinical stage, and being classified as high-risk group.

The model assumptions were fulfilled; the relationship between dependent and independent variables was linear. There was no multicollinearity in data. The collinearity diagnostics test showed that the variance inflation factor (VIF) scores were well below 10 and tolerance scores were above 0.2. The values of the residuals were independent. The variance of

residuals was constant (homoscedasticity). The values of the residuals were normally distributed. No influential cases were biasing the model.

Stepwise multiple regression modeling was adopted. The best fitted model considered three predictors (classification of the clinical stage, the marital status and smoking) as the main predictors of the QoL score in the current sample. These predictors were responsible for 41% of the variance variation in the QoL score ($R^2 = 0.410$). Additionally, the adjusted R^2 showed a fair bit difference (Adjusted $R^2 = 0.404$), so in the general population these predictors would account for 40% of QoL variance variation. ANOVA test concluded that the model parameters improved the ability to predict the QoL score. ($p= 0.000$). The classification of the clinical stage and smoking were inversely correlated to the QoL, the marital status was positively correlated. All the parameters were significant predictors for the QoL. (Table 6)

Table 2: Sociodemographic and clinical characteristics of the enrolled chronic hepatitis B patients for QoL assessment

Characteristic	Chronic hepatitis B patients	
	No.	**%**
Gender		
Male	182	61.9
Female	112	38.1
Education level		
Illiterate	42	14.3
Read& write	78	26.5
Primary/ secondary	97	32.9
University/higher	77	26.2
Residence		
Urban	103	35.1
Rural	191	64.9
Marital status		
Single	46	15.6
Married	202	68.7
Divorced	26	8.8
Widow	20	6.8
Smoking status		
Smoker	234	79.6
Never smoked	32	10.9
Ex-smoker	28	9.5
Age interval (years)		
20-40	149	50.7
40-60	105	35.7
Above 60	40	13.6
Mean ± S.D.	43.4 ± 13.5	
Employment status		
Worker	156	53.1
Clerk	32	10.9
Unemployed	106	36.1
Clinical Stage		
Chronic Hepatitis	172	58.50
Compensated cirrhosis	46	15.65
Decompensated cirrhosis	64	21.77
Hepatocellular Carcinoma	12	4.08
Classification according to High- Risk Group		
Frequent Blood Transfusion	13	4.4
Dialysis Patients	12	4.1
Organ Transplantation	1	0.3
Intravenous drug users	Cannot be accessed	
Household Contacts	28	9.5
People with multiple sexual partners	Cannot be accessed	
Health care workers	16	5.4
Total of high-risk groups	70	23.8
Not classified as high-risk group	224	76.2

Table 3: Quality of life of the studied hepatitis B patients according to WHOQOL-BREF 26, Egypt

Domain	Mean Score	SD	Test of Normality Kolmogorov Test (P-Value)
Physical Domain (WHOQOL-BREF 26)	15.8	3.4	0.142 (0.000)
100-format score of the physical domain	0.63	0.13	0.141 (0.000)
Psychological Domain (WHOQOL-BREF 26)	14.2	3.4	0.147 (0.000)
100-format score of the psychological domain	0.56	0.13	0.148 (0.000)
Social Domain (WHOQOL-BREF 26)	6.8	1.2	0.183 (0.000)
100-format score of the social domain	0.27	0.07	0.177 (0.000)
Environmental Domain (WHOQOL-BREF 26)	19.1	2.8	0.116 (0.000)
100-format score of the environmental domain	0.76	0.11	0.114 (0.000)
100-format mean score of the four domains	**0.56**	**0.10**	**0.135 (0.000)**
Overall, 100-format score (Questions 1,2)	**0.2**	**0.06**	**0.254 (0.000)**

Table 4: Quality of life of Hepatitis B patients sample according to the clinical stage

Clinical stage	Physical domain Average (Min- Max)	Psychological Domain Average (Min- Max)	Social Domain Average (Min- Max)	Environmental Domain Average (Min- Max)	Overall score Average (Min- Max)
Chronic Hepatitis	0.57 (0.33- 0.72)	0.42 (0.37- 0.75)	0. 59 (0.43- 0.83)	0.43 (0.25- 0.59)	0.54 (0.10- 0.78)
Compensated cirrhosis	0.34 (0.25- 0.46)	0.41 (0.38- 0.50)	0.21 (0.10- 0.67)	0.37 (0.28- 0.44)	0.46 (0.25- 0.75)
Decompensated cirrhosis	0.16 (0.11- 0.21)	0.27 (0.21- 0.33)	0.41 (0.33- 0.50)	0.38 (0.31- 0.47)	0.27 (0.13- 0.63)
Hepatocellular carcinoma	0.16 (0.11- 0.21)	0.36 (0.29- 0.42)	0.33 (0.22- 0.46)	0.28 (0.25- 0.34)	0.14 (0.10- 0.25)
Test of significance Kruskal Wallis (P- Value)	96.6 (0.000)	159.2 (0.000)	77.2 (0.000)	46.7 (0.000)	18.2 (0.000)

Table 5: Spearman's Correlation test between the overall scores and the four domains

		Physical domain	Psychological Domain	Social Domain	Environmental Domain
Overall Score	Correlation Coefficient	0.492[**]	0.513[**]	0.326[**]	0.408[**]
	Sig. (2-tailed)	0.000	0.000	0.000	0.000

Table 6: The coefficient and significance of the predictors of QoL among chronic hepatitis B patients in the multiple regression model

	Unstandardized Coefficients		Stand. Coefficient			95.0% Confidence Interval for B	
	B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound
(Constant)	.205	.005		41.116	.000	.195	.215
Clinical classification	-.075	.005	-.621	-13.754	.000	-.085	-.064
Marital status	.017	.006	.137	3.032	.003	.028	.006
Smoking	-.014	.006	-.102	-2.257	.025	-.002	-.027

DISCUSSION

The current study revealed great impairment in the overall QoL score among CHB in Egypt 0.2, where the social domain was the highly affected one (0.27) while the environmental domain was the least affected (0.75).

The finding of the current study regarding physical limitation in the late stages of the disease was similar to the findings of a study carried out in Turkey, 2010,[15] where the physical impairment was associated with the disease progression.

On the other hand, the current study reported a lower QoL score than what was reported in a study carried out in Assiut University Hospital [16], where around half of the patients in the sample (n=385 patients) reported moderate impairment in the QoL.

The differences between the studies' results are due to using different QoL assessment tools. The current study adopted WHOQOL-BREF26

questionnaire which assesses the QoL according 26 questions in four domains; physical, psychological, social, and environmental while the study in Assiut University adopted CLDQ with 29 questions in six domains; abdominal symptoms, fatigue, systemic symptoms, activity, emotional function, and worry.

Additionally, the results of the current study were different from a study in China using the same tool of the current study. The mean score was 22.78 for the physical domain, 19.57 for the psychological domain, 10.31 for the social domain, and 26.25 for the environmental domain.[17] However in the current study the mean scores were (15.8, 14.2, 6.8, 19.1) for the same domains respectively. Despite the differences in the mean scores between the two countries, the rank of the four domains was the same.

Furthermore, the current study findings were different from a study carried out in India, [10] where the mean scores were:, (43.78±13.08, 46.65±11.86, 54.67±10.36, 50.58±10.02) for the physical, psychological, social, and environmental scores respectively. The highest score was obtained in the social domain and the lowest was in the physical domain. By using the same scale, the current study reported a score of (63±13, 56±13, 27±7, 76±11) for the same domains respectively where the highest score was obtained in the environmental score and the lowest score was in the social domain.

The differences between the studies were attributed to carrying out the study of India in a tertiary health care facility for 103 patients without a control group. The WHO questionnaire guidelines recommend recruiting a sample of at least 250 patients in different clinical stages of the disease and 50 respondents free from the disease as a control.

Moreover, the current study findings were different from another study carried out in India about the prevalence and impact of Hepatitis on the QoL of patients using both WHOQOL-BREF26 and Short Form (SF-36) health survey questionnaire. The scores reported were as follow: physical domain (42±8), psychological domain (51.1±13.5), social domain (44.7±22.7), and environmental domain (41.5± 9.5). The environmental domain was the highly affected one. These findings were the opposite of our study results. The differences are explained by the discrepancy in the patient samples in both studies. The Indian study examined the QoL among 65 patients (30 control and 35 patients). Among the patients, 31 were Hepatitis C Virus (HCV) and only four were HBV. The current study examined the QoL among 294 respondents with patients in different clinical stages of the disease.

In addition, the results of the current study were different from that reported in a study carried out in Pakistan. which examined the QoL among 120 chronic hepatitis patients (55 HBV patients and 65 HCV patients).[18] The study of Pakistan used WHOQOL-100 questionnaire. The reported mean scores for physical, psychological, social, and environmental domains were as follow 39.2, 46.18, 61.14 and 40.1 respectively. The reported scores were different from that of the current study due to the differences in the data collection tool, sample size between the two studies, in addition, the study of Pakistan examined both HBV and HCV patients together.

As regards, the QoL scores among different CHB clinical stages, the current study reported that the QoL is highly affected in HCC patients (overall score of 0.14) with the physical domain being greatly impaired. On the other hand, the QoL in case of chronic hepatitis clinical stage is the least affected with the physical domain showing the great impairment. There was a statistically significant difference for the reported mean score of each domain according to the different clinical stages of the disease.

The current study findings were consistent with a study carried out in Singapore, 2008, about the QoL in CHB patients using SF-36 Health survey and the EQ-5D self-report questionnaire.[19] The development of chronic hepatitis was associated with decrease in general health and mental dimension. The development of advanced liver disease was associated with physical impairment.

Additionally, our results were similar to what was reported in a study [20] about the overall health related QoL in patients with end stage liver disease where the overall score is significantly low in the late stages of liver disease in comparison to early stages of the disease.

On the other hand, the scores reported in the current study were lower than that reported in a study in Toronto. [21] The reported QoL for non-cirrhotic CHB, compensated cirrhosis, decompensated cirrhosis, HCC and post-transplant patients were as follow 0.89, 0.87, 0.82, 0.84 and 0.86 respectively. The study used SF-36 and EQ5D to assess the QoL among 433 patients. The current study reported scores of 0.54, 0.46, 0.27, 0.14 for the same clinical stages respectively.

The lower scores for the health related QoL among CHB patients were explained by challenges that face the Egyptian health care system in the detection and management of chronic hepatitis cases. [22] Additionally, the differences in the QoL in general between the developed and the developing countries played a major role in the final score especially in the environmental domain. [23]

The current study reported a significant positive correlation between the scores of the four domains of the questionnaire and the overall QoL score. This finding was consistent with what was reported in the study of   China [17], where the correlation between QoL and the four domains was

positive and significant.

The regression model in the current study showed that three predictors (classification of the clinical stage, the marital status and smoking status) were the main determinants of the QoL score. These predictors were responsible for 41% of the variance in the QoL score ($R^2 = 0.410$).

This finding was different from what was reported in the study of China [17], where stigma, disclosure, depression and anxiety were the predictors of interest. The Chinese study focused mainly on the relation between the psychological factors and the overall QoL. Additionally, it used a specific tool to measure the psychological status (stigma, anxiety, depression) and its relation to the overall QoL score.

The current study has two main limitations; collecting data from 294 CHB patients with consideration of representation of different clinical stages as well as high- risk groups took a long time. Additionally, many patients were excluded during the data collection phase due to being unable to classify them according to the clinical stages, only those with complete clinical data were included.

CONCLUSION AND RECOMMENDATIONS

The current study highlighted the importance of social support in the management of CHB patients. Organizing a social support program for CHB patients tailored according to their needs is a must. This includes emotional support to overcome the various psychological stresses of the disease and informational support through being well informed with the correct knowledge about the disease progression and treatment options.

Additionally, great concern about the rehabilitation programs in the late stages of the disease is highly recommended, as the physical aspects become more affected at the end stage of the disease as well as the psychological aspects. The importance of early diagnosis and management of cases is an important priority especially with the fact that the clinical stage is a major predictor of the overall QoL of the patients.

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