Health-Related Quality of Life among a Sample of Chronic Hepatitis B Patients in AL-Najaf Province, Iraq.

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Abstract

The effect of physical and mental health on the feelings of personal welfare are known as health-related quality of life. Infection with hepatitis B virus is a major global health problem. Health-related quality of life was emerged as an important consideration in the care of patients with chronic hepatitis B infection. The aim of the current study was to measure health-related quality of life among a sample of chronic hepatitis B patients in AL-Najaf city/Iraq. The current study was cross-sectional study carried out on (104) already diagnosed chronic viral hepatitis B patients who attended the Gastroenterology and Hepatology Center/Al-Sader Medical City/Najaf during November 2018 to May 2019. In addition, (100) apparently healthy subjects were included as a control group. Health related quality of life was measured using the Arabic version of the Short Form 36. The health-related quality of life of patients with chronic hepatitis B infection was affected by the disease in a highly significant manner where the median scores for all health-related quality of life domains were significantly lower in patients than in controls. Physical functioning score was negatively correlated to age, significantly higher in male patients, significantly higher in highly educated patients, significantly higher in single patients, and significantly higher in patients with no children. Role limitation due to physical health score was negatively correlated to age, significantly higher in those with no children. Energy/fatigue score was negatively correlated to age, and significantly higher in male patients. Social functioning score was significantly higher in male patients. Pain score was negatively correlated with age. Physical functioning score was negatively correlated to serum albumin. Social functioning and general health score were negatively correlated to viral load. In conclusion, chronic hepatitis B patients showed significantly lower health-related quality of life scores in various domains compared to healthy control subjects in AL-Najaf province/Iraq.

Keywords: Health-Related Quality of Life, Hepatitis B, Short Form 36, AL-Najaf, Iraq.

Journey of the healthcare electronic health record (EHR) in the Najaf city/

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Introduction

Hepatitis B virus (HBV) infection is one of the widespread and most important public health problems worldwide (1). Globally, about 2 billion people have been infected with hepatitis B virus, and about 5% of them have chronic infections (2). In Iraq, the prevalence rate of hepatitis B surface antigen (HBsAg) in apparently healthy individuals was 1.6% (3). Hepatitis B virus infection is transmitted by perinatal, sexual, or percutaneous exposure; sharing of household items such as razors and toothbrushes; and close person-to-person contact with open cuts and sores (4). Infants born to mothers infected with actively replicating HBV have a 70%-90% risk of acquiring the infection (5). Chronic hepatitis B (CHB) infection is characterized by the persistence of HBsAg and serum HBV-DNA levels detectable for more than 6 months (6). There are about 250 million individuals with CHB around the world (7). Patients with CHB have to cope with many recurrent symptoms in their long-term disease histories and are at higher risk of developing end-stage liver diseases such as liver failure, cirrhosis, and hepatocellular carcinoma (HCC) (8).

Quality of life is a concept that reflects the negative and positive aspects of the life of an individual. The impact of mental and physical health on the feeling of well-being is known as health-related quality of life (HRQoL) (9). Health related quality of life is a multifactorial construct that describes individuals’ perceptions of their psychological, physical, and social functioning. Thus, HRQoL is a more holistic assessment than clinical parameter, especially in chronic disease in which mortality is not an immediate concern, because it also considers a patient’s functional health and well-being. This is particularly important in CHB, in which the natural history is complex and includes a number of phases (6). HRQoL was found to be decreased in chronic diseases like diabetes mellitus and hypertension (10). There have been some studies focusing on HRQoL of CHB patients (11-13).

The aim of the current study was to measure HRQoL among a sample of chronic hepatitis B patients in AL-Najaf province /Iraq.

Patients and Methods

Patients

The current cross-sectional study was carried out on (104) already diagnosed patients with chronic hepatitis B who were admitted the Gastroenterology and Hepatology center/Al-Sader Medical City/Najaf during November 2018 to May 2019. In addition, (100) apparently healthy subjects were included as a control group.

Inclusion criteria

The inclusion criteria for the current study were:
1-Patients having chronic hepatitis B, who were aged 18 years or more of either sex and who were accepted to participate in the study.
2-Disease duration (since diagnosis) of at least 6 months or more.

Exclusion criteria

The exclusion criteria for this study were:
1-Patient who had a hearing, speech or cognitive deficits that would impair understanding of the questions.
2-Patient who had liver cancer or clinical evidence of decompensated liver cirrhosis (ascites, history of hepatic encephalopathy, or history of variceal bleeding).
3-Concomitant medical illness (such as chronic renal failure, chronic lung disease, hypertension, heart disease, DM, stroke).
4-Patient who take antidepressant drugs, or being on treatment for any neurological or psychological diseases.
5-Pregnant and lactating women.
6-Patients providing incomplete information during completion of the questionnaire also will excluded from the study.

Method

The questionnaires

In the current study, health related quality of life was measured using the Arabic version of the Short Form 36 (SF-36). The Short Form 36 (SF-36) is a widely used self-administered questionnaire which provide a reliable assessment of HRQOL (14). It includes eight items: general health, role limitations due to physical problems, mental health, physical functioning, vitality, social functioning, role limitations due to emotional problems, and bodily pain. Items with higher scores indicate better health conditions (15).

Administration of questionnaires

The data related to the study were collected by the researcher herself. When the patients arrived to the hospital to made their programmed laboratory data and receive their treatment, they were asked if they accept to participate in the study, if they accepted to participate, a complete explanation to the questions in the questionnaire was done and each patient spent about 5 minutes to fill the research questionnaire completely.

Statistical analysis

Data were collected, summarized, analyzed using two software programs, statistical package for social sciences (SPSS) version 23 and Microsoft Office Excel 2010. Categorical variables were presented as number and percentage. Quantitative variables were initially analyzed for normality distribution Kolmogorov-Smirnov test. Therefore, quantitative variables were described as mean ± standard deviation or median (interquartile range). Comparison of mean values between any two groups carried out using independent sample t-test or Mann Whitney U test in case of normally distributed data or not normally disturbed data, respectively, whereas Kruskal Wallis test was used to evaluate difference among three groups or more. Association between any two categorical variables was done using Chi square test. Spearman correlation test was used to assess variables. P-value was considered significant when it is equal or less than 0.05 and highly significant when it is equal or less than 0.001.
**Results**

Demographic characteristics of patients with hepatitis B and control subjects are shown in table 1. While the disease characteristics and investigations in patients with HBV are shown in table 2.

Table 1. Demographic characteristics of patients with chronic hepatitis B infection compared to that of control group.

| Characteristics          | Control | Hepatitis B | P value |
|--------------------------|---------|-------------|---------|
| Age                      | N       | Mean ± SD   | N       | Mean ± SD   |         |
| Age                       | 100     | 40.81±11.6  | 104     | 42.6±15.8   | 0.368†  |
| Gender                   | N       | %           | N       | %           | P value |
| Male                      | 53      | 53          | 57      | 54.8        | 0.796¥  |
| Female                    | 47      | 47          | 47      | 45.2        |         |
| Education level           | N       | %           | N       | %           |         |
| Illiterate                | 19      | 19          | 29      | 27.9        | 0.352¥  |
| Primary                   | 32      | 32          | 35      | 33.7        |         |
| Secondary                 | 32      | 32          | 28      | 26.9        |         |
| University                | 17      | 17          | 12      | 11.5        |         |
| Social status             | N       | %           | N       | %           |         |
| Single                    | 11      | 11          | 10      | 9.6         | 0.881¥  |
| Married                   | 79      | 79          | 86      | 82.7        |         |
| Divorced                  | 4       | 4           | 4       | 3.8         |         |
| Widow                     | 6       | 6           | 4       | 3.8         |         |
| Children                  | N       | %           | N       | %           |         |
| Yes                       | 83      | 83          | 84      | 80.8        | 0.679¥  |
| No                        | 17      | 17          | 20      | 19.2        |         |
| Residency                 | N       | %           | N       | %           |         |
| Urban                     | 75      | 75          | 75      | 72.1        | 0.640¥  |
| Rural                     | 25      | 25          | 29      | 27.9        |         |

Data were expressed as either mean±standard deviation (SD) or number (%); ID: Iraqi dinar; †: independent samples t-test; ¥: Chi-square test; NS: not significant at P ≤ 0.05.

Table 2. Disease characteristics and investigations in patients with chronic hepatitis B infection.

| Characteristic | N    | %    | Characteristic | N    | %    |
|----------------|------|------|----------------|------|------|
| Biopsy         | 2    | 1.9  | Treatment      | 10   | 9.6  |
| Other family member | 17  | 16.3 | Entecavir     | 28   | 26.9 |
| Mode of transmission | 17  | 16.3 | Interferon    | 1    | 1    |
| Blood transfusion | 17  | 16.3 | Interferon + Ribavirin | 41  | 39.4 |
| Surgery        | 23   | 22.1 | Not treated   | 24   | 23.1 |
| Tooth extraction | 18  | 17.3 | Tenofovir     | 10   | 9.6  |
| Shaving        | 4    | 3.8  | Treatment experience | 29  | 27.9 |
| Needle         | 5    | 4.8  | Naive         | 29   | 27.9 |
| Tattoo         | 14   | 13.5 | Experienced   | 75   | 72.1 |
| Unknown        | 3    | 2.9  | Hospital admission | 5   | 4.8  |
| Vertical       | 16   | 15.4 |               |      |      |
| Sexual         | 2    | 1.9  |               |      |      |

| Characteristic                  | Minimum | Maximum | Median | IQR   |
|---------------------------------|---------|---------|--------|-------|
| Duration of disease             | 0.50    | 7.00    | 1.25   | 2.50  |
| Duration of treatment           | 0.00    | 3.50    | 0.00   | 1.00  |
| HBV DNA (IU/ml)                 | 0.00    | 200000000.00 | 4140.0 | 29100000.00 |
| ALT (U/l)                       | 5.00    | 179.00  | 17.25  | 15.12 |
| AST (U/l)                       | 3.00    | 95.00   | 15.00  | 13.65 |
| Albumin (g/dl)                  | 3.60    | 39.00   | 4.64   | 1.32  |
| INR                             | 1.00    | 2.30    | 1.15   | 0.42  |
| Total bilirubin (mg/dl)         | 0.40    | 42.10   | 0.75   | 0.45  |

 HBV: hepatitis B virus; DNA: deoxyribonucleic acid; ALT: alanine aminotransferase normal range (up to 12) U/l; AST: aspartate aminotransferase normal range (up to 12) U/l; INR: international normalized ratio (1.0); Total bilirubin normal range (0.3-1.2) mg/dl; Serum albumin (35-52) g/l.
In general, the HRQoL of patients with hepatitis B was affected by the disease in a highly significant manner where the median scores for all HRQoL domains were significantly lower in patients than in controls \((P <0.001)\) as shown in table 3.

### Table 3. Comparison of median values related to short form domain average scores between patients with chronic hepatitis B infection and control group.

| Domain                                | Control n = 100 |                  | HBV n = 104 |                  | \(P^†\) |
|---------------------------------------|-----------------|-----------------|-------------|-----------------|--------|
|                                       | Median Score    | IQR             | Median Score| IQR             |        |
| Physical functioning                  | 100             | 5               | 80          | 45              | <0.001 |
| Role limitation due to physical health| 100             | 0               | 0           | 75              | <0.001 |
| Role limitation due to emotional problems | 100           | 0               | 0           | 33.3            | <0.001 |
| Energy Fatigue                        | 95              | 25              | 30          | 54              | <0.001 |
| Emotional well being                  | 96              | 12              | 20          | 52              | <0.001 |
| Social functioning                    | 100             | 25              | 50          | 50              | <0.001 |
| Pain                                  | 100             | 20              | 80          | 51.8            | <0.001 |
| General health                        | 90              | 29              | 40          | 35              | <0.001 |

\(n\): number of cases; IQR: inter-quartile range; \(†\): Mann Whitney U test. PF: Physical functioning; RLPH: Role limitation due to physical health; RLEP: Role limitation due to emotional problems; EF: Energy Fatigue; EWB: Emotional wellbeing; SF: Social functioning; P: Pain; GH: General health; * significant at \(P \leq 0.05\); **significant at \(P \leq 0.01\).

Distribution of short form domain scores to demographic characteristics of patients with hepatitis B are shown in table 4. Physical functioning score was negatively correlated to age, significantly higher in male patients, significantly higher in high educated patients, significantly higher in single patients, and significantly higher in patients with no children. Role limitation due to physical health score was negatively correlated to age, significantly higher in those with no children. Energy/fatigue score was negatively correlated to age, and significantly higher in male patients. Social functioning score was significantly higher in male patients. Pain score was negatively correlated with age. Role limitation due to emotional problems, emotional wellbeing and general health scores were unaffected by any of the demographic characteristics of patients with CHB infection.

Correlations between short form domain scores and disease characteristics of patients with HBV are outlined in table 5. Patients with previous liver biopsy had significantly higher pain score than those who have never performed liver biopsy. While other domains were unaffected by any of disease characteristics of CHB patients. Correlations between short form domain scores and laboratory investigations of patients with HBV are shown in table 6. Physical functioning score was negatively correlated to serum albumin. Social functioning and general health score were negatively correlated to viral load. While other domains were unaffected by any of laboratory investigations of CHB patients.
### Table 4. Distribution and correlation of short form domain scores and demographic characteristics of patients with chronic hepatitis B infection.

| Characteristic | PF | RLPH | RLEP | E/F | EWB | SF | P | GH |
|----------------|----|------|------|-----|-----|----|----|----|
| **Age**        |    |      |      |     |     |    |    |    |
| r              | 0.021* | 0.021* | 0.021* | 0.021* | 0.021* | 0.021* | 0.021* | 0.021* |
| Sex            |    |      |      |     |     |    |    |    |
| Female         | 0.033* | 0.033* | 0.033* | 0.033* | 0.033* | 0.033* | 0.033* | 0.033* |
| Education      |    |      |      |     |     |    |    |    |
| Illiterate     | 0.016* | 0.016* | 0.016* | 0.016* | 0.016* | 0.016* | 0.016* | 0.016* |
| Social         |    |      |      |     |     |    |    |    |
| Children       | 0.007* | 0.007* | 0.007* | 0.007* | 0.007* | 0.007* | 0.007* | 0.007* |
| Residency      |    |      |      |     |     |    |    |    |
| PF: Physical functioning; RLPH: Role limitation due to physical health; RLEP: Role limitation due to emotional problems; EF: Energy Fatigue; EWB: Emotional wellbeing; SF: Social functioning; P: Pain; GH: General health; * significant at P ≤ 0.05; **significant at P ≤ 0.01; IQR: inter-quartile range; med: median; r: spearman correlation coefficient; €: Kruskal Wallis test. |
**Table 5. Correlations between short form domain scores and disease characteristics of patients with chronic hepatitis B infection.**

| Characteristic               | PF          | RLPH        | RLEP        | EF          | EWB         | SF          | P           | GH          |
|------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
|                              | r           | P           | r           | P           | r           | P           | r           | P           | r           | P           |
| Duration of disease          | -0.085      | 0.389       | -0.009      | 0.927       | -0.066      | 0.502       | -0.090      | 0.363       | -0.074      | 0.454       | 0.028       | 0.779       | 0.074       | 0.456       | 0.003       | 0.978       |
| Biopsy                       | 0.067       | 0.499       | 0.102       | 0.304       | -0.073      | 0.460       | -0.129      | 0.192       | 0.023       | 0.814       | -0.140      | 0.157       | 0.213       | 0.030*      | 0.130       | 0.189       |
| Other family member          | -0.027      | 0.788       | -0.147      | 0.137       | 0.022       | 0.826       | 0.020       | 0.840       | -0.004      | 0.965       | 0.002       | 0.985       | 0.020       | 0.839       | -0.010       | 0.923       |
| Mode of transmission         | 0.168       | 0.088       | -0.052      | 0.602       | 0.037       | 0.712       | 0.073       | 0.464       | 0.028       | 0.776       | 0.091       | 0.357       | -0.006      | 0.952       | 0.162       | 0.101       |
| Treatment                    | -0.114      | 0.251       | -0.046      | 0.642       | -0.024      | 0.807       | -0.061      | 0.535       | 0.034       | 0.733       | -0.071      | 0.472       | -0.121      | 0.220       | -0.056       | 0.574       |
| Duration of treatment        | -0.098      | 0.321       | -0.037      | 0.712       | -0.028      | 0.775       | 0.067       | 0.497       | 0.000       | 0.994       | -0.027      | 0.782       | 0.007       | 0.945       | -0.036       | 0.716       |
| Previously treated           | -0.123      | 0.214       | -0.057      | 0.566       | -0.047      | 0.635       | -0.022      | 0.828       | -0.002      | 0.986       | -0.087      | 0.379       | -0.014      | 0.885       | -0.136       | 0.170       |
| Hospital admission           | 0.100       | 0.314       | 0.094       | 0.340       | 0.041       | 0.676       | 0.171       | 0.083       | -0.052      | 0.601       | 0.109       | 0.269       | 0.104       | 0.292       | 0.027        | 0.785       |

PF: Physical functioning; RLPH: Role limitation due to physical health; RLEP: Role limitation due to emotional problems; EF: Energy Fatigue; EWB: Emotional wellbeing; SF: Social functioning; P: Pain; GH: General health; * significant at $P \leq 0.05$; **significant at $P \leq 0.01$; r: spearman correlation coefficient.

**Table 6. Correlations between short form domain scores and laboratory investigations patients with chronic hepatitis B infection.**

| Characteristic | PF          | RLPH        | RLEP        | EF          | EWB         | SF          | P           | GH          |
|----------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
|                | r           | P           | r           | P           | r           | P           | r           | P           | r           | P           |
| HBV DNA        | 0.038       | 0.705       | -0.183      | 0.063       | -0.174      | 0.078       | -0.175      | 0.075       | -0.136      | 0.168       | -0.234      | **0.017*    | -0.131      | 0.184       | -0.291       | **0.003**    |
| ALT            | 0.010       | 0.916       | -0.072      | 0.470       | 0.142       | 0.149       | 0.034       | 0.735       | 0.129       | 0.193       | 0.131       | 0.183       | 0.047       | 0.635       | 0.129       | 0.191       |
| AST            | -0.020      | 0.840       | -0.116      | 0.240       | 0.050       | 0.615       | -0.031      | 0.757       | -0.008      | 0.939       | -0.030      | 0.765       | 0.002       | 0.986       | 0.038       | 0.701       |
| Albumin        | -0.468      | **0.050*    | -0.097      | 0.701       | 0.101       | 0.689       | 0.113       | 0.655       | 0.165       | 0.512       | 0.150       | 0.553       | -0.118      | 0.640       | 0.031       | 0.903       |
| INR            | -0.071      | 0.472       | -0.064      | 0.521       | 0.035       | 0.722       | -0.116      | 0.241       | -0.078      | 0.434       | 0.014       | 0.887       | 0.035       | 0.727       | -0.009       | 0.930       |
| Bilirubin      | -0.068      | 0.495       | 0.005       | 0.957       | 0.026       | 0.790       | -0.061      | 0.538       | 0.040       | 0.689       | 0.050       | 0.617       | -0.013      | 0.897       | 0.026       | 0.791       |

PF: Physical functioning; RLPH: Role limitation due to physical health; RLEP: Role limitation due to emotional problems; EF: Energy Fatigue; EWB: Emotional wellbeing; SF: Social functioning; P: Pain; GH: General health; * significant at $P \leq 0.05$; **significant at $P \leq 0.01$; r: spearman correlation coefficient.
Discussion

The impact of the disease and treatment on patient’s HRQoL has become an important medical concern. The current study showed that HRQoL of patients with CHB infection was affected by the disease in a highly significant manner where the median scores for all HRQoL domains were significantly lower in patients than in controls (table 3). A study from Singapore showed that HRQoL was significantly decreased in CHB patients and further decreased with disease progression (11). Another study from Hong Kong of China showed that all individuals with CHB infection had significantly decreased HRQoL compared to general population even among those without any clinical and biochemical abnormalities (16). Impairment in HRQoL in CHB patients (with or without cirrhosis) was also documented in several other countries (12, 13, 17).

Many other studies have shown HRQoL to be impaired in patients with chronic liver diseases (HBV, HCV, alcoholic liver disease), and many physical and psychological factors (depression, anxiety, illness understanding, social stigma, worry about family situation, fear of complications, problems with concentration and memory, and loneliness) have been associated with this impaired HRQoL in patients with chronic liver diseases (18-22). Although the previous studies from other countries showed impaired HRQoL in CHB patients (11-13, 16, 17), almost all showed the impairment on some but not all dimensions (11, 13, 16, 17). It may be that the stress of having a serious, and potentially life-threatening illness makes CHB patients having reduced HRQoL.

Health related quality of life of CHB patients may vary according to their socio-demographic properties. Physical functioning, role limitation due to physical health, energy/fatigue and pain scores were negatively correlated to age. Similar findings were reported among Saudi hepatitis B patients (23). In addition, it was found that physical functioning, social functioning and energy/fatigue score were significantly lower in female in comparison with male. Similar finding was reported among turkeys’ CHB patients (24). It is well known that women, in many countries, receive less social support compared to men if they experience chronic diseases. Additionally, women access to medical care is generally delayed compared with men and they are either obliged to work or take over their responsibilities even before they get complete recovery (20). These variations between male and female may cause HRQoL to be worse in female patients with CHB. Regarding education level, the current study showed that physical functioning score was significantly higher in single compared to married patients and this disagree with that reported in Turkey where married CHB patients had better HRQoL than singles (24). Regarding to children, the current study showed that in patients who do not have children, physical functioning and role limitation due to physical health were significantly higher than in those with children, this may be due to fearfulness of parents from disease transmission when become in contact with their children. While residency do not have any significant effect on HRQoL scores and this result disagree with a study in Pakistan which showed that rural HBV patients are in worse condition as compared to urban patients (28).

Also, the study showed that no correlations between disease characteristics and SF-36 domains with exception that patients with previous liver biopsy had significantly higher pain score than those who have never performed liver biopsy. The percentage of patients who had had a liver biopsy in the current study was low (1.9%), which makes us unable to clearly understand the positive correlation between biopsy and HRQoL pain score.

The current study showed that social functioning and general health scores were negatively correlated to viral load. This might be due that these patients are frequently called back for control visits to check the activity of the disease which may lead to an increase in anxiety among these patients. Physical functioning score was negatively correlated to serum albumin. In Saudi CHB patients, albumin correlated with physical functioning, role limitation due to physical health, social functioning, pain, and general health suggesting that active liver disease or perhaps significant fibrosis was more likely affecting the HRQoL domain score rather than the virus itself (23). The current study showed that the duration of disease and the period of therapy did not affect SF-36 scores at all. Similar findings were reported among CHB patients in Turkey (24).

Showing attention to some limitations of our study regarding the planning process could be helpful for future studies. One limitation is the cross-sectional design of this study rather than prospective which allow studying the effect of treatment on patients’ HRQoL. Future study about the same topic can be conducted as multi-center studies to enroll patients from different centers in Iraq. In conclusion, our sample of chronic hepatitis B patients show significantly lower HRQoL scores in various domains compared to control healthy subjects.

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