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Comparison of quality of life in hepatitis B virus carriers versus chronic hepatitis B virus carriers versus the normal population

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Aim: To compare health related quality of life (HRQOL) in hepatitis B virus (HBV) carriers versus chronic HBV disease carriers versus the normal population.

Materials and methods: The study sample consisted of 2 groups. HBV carriers were recruited from individuals who were regularly followed-up at the Infectious Diseases and Clinical Microbiology outpatient clinic of our setting due to inactivity in HBV infection. The control group was recruited from the same outpatient clinic among patients who had a diagnosis of chronic HBV infection and who were not undergoing active treatment yet. Both groups were requested to fill in the short form 36 questionnaire on HRQOL (HRQOL-SF-36) and a form to gather data about age, gender, and education. We also compared the mean values of the SF-36 domain scores of these 2 groups with published scores of healthy controls derived from the Turkish population.

Results: QOL in HBV carriers was greatly similar to that of patients with chronic HBV disease except for physical role limitation scores and both HBV carriers and patients with chronic disease had lower HRQOL than the normal Turkish population.

Conclusion: When compared with the normal Turkish population, QOL is affected negatively both in chronic HBV infection patients and in HBV carriers.

Key words: Inactive hepatitis B infection, HRQOL-SF-36, Turkey

İnaktif hepatit B hastaları, kronik hepatit B hastaları ve sağlıklı populasyonunun yaşam kalitelerinin karşılaştırılması

Amaç: Bu çalışmada, kliniğimizde ayaktan takip edilen inaktif hepatit B (HBV) enfeksiyonu olan hastalar ile kronik hepatit B hastaları ve normal populasyonun yaşam kalitelerinin karşılaştırılması amaçlanmıştır.

Yöntem ve gereç: Çalışmaya alınacak hastalar iki gruba ayrılmıştır. İlk grubu Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji kliniğine düzenli olarak gelen ve ayaktan takip edilen inaktif HBV hastaları oluşturmuştur. Kontrol grubunda ise, aynı dönemde kronik HBV enfeksiyonu tanısı konulmuş ve henüz tedavi görmeyen hastalar yer almıştır. Her iki grubun da yaş, cinsiyet ve eğitim derecesini sorgulayan bir anket formu ile yaşam kalitesini belirlemek üzere Kısa Form 36 (SF-36) yaşam kalitesi ölçeğini doldurmaları istenmiştir. Bu iki gruptan elde edilen sonuçlar aynı zamanda sağlıklı Türk populasyonunun yaşam kalitesi sonuçları ile karşılaştırılmıştır.

Bulgular: İnaktif hepatit B enfeksiyonu olan hastalar fiziksel rol güçlüğü skoru dışında kronik HBV hastaları ile büyük oranda benzer bulunmuştur. Her iki grubun da yaşam kalitesi skorunun, normal Türk populasyonuna göre daha düşük olduğu saptanmıştır.

Sonuç: Hem kronik HBV enfeksiyonu hem de inaktif HBV taşıyıcılarının yaşam kaliteleri normal populasyona göre olumsuz etkilenmektedir.

Anahtar sözcükler: İnaktif Hepatit B enfeksiyonu, SF-36, Türkiye

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Introduction

Hepatitis B virus (HBV) infection is one of the most important and widespread public health problems in the world. Worldwide HBV is the main cause of hepatitis in approximately 400 million people and it causes 500,000-1,200,000 deaths per year. The illness caused by HBV infection and its complications are among the most common 3 causes of death in Africa, Asia, and the Pacific coasts. The number of the people exposed to HBV is about 2 billion worldwide (1).

In the world, the distribution of HBV infection shows differences according to geographical regions. Turkey is located in the moderate endemic region; and according to the latest reports, there are approximately 4 million HBV carriers in this country (2).

As in all chronic diseases, these infections may lead to psychological health problems. There are numerous studies addressing the psychological well-being, psychosocial stressors related to the disease, quality of life (QOL), and the effect of antiviral treatments on QOL in patients with chronic hepatitis (3-8). The recent studies concerning QOL of patients with chronic viral hepatitis have found a relationship between the QOL and the severity of the disease (6,9,10) or interferon treatment (11,12). The data about the effect of antiviral therapy on QOL are inconclusive. In some studies, it was reported that antiviral therapy reduced QOL (13-15), while some others reported an improvement in the QOL after successful antiviral therapy (5,16,17). In addition to these findings, though some studies have reported differences in terms of QOL in patients with chronic viral hepatitis with respect to virus type (HBV or hepatitis C virus-HCV) (3,10,12), some of them have reported no significant differences (4,6).

This study aimed to evaluate the health related quality of life (HRQOL) in HBV carriers and a control group who had a diagnosis of chronic hepatitis B and had not received any antiviral therapy yet and to compare data of these 2 groups with the published HRQOL of the normal Turkish population.

Methods

The current study was performed in the Department of Infectious Diseases and Clinical Microbiology and Department of Psychiatry, Faculty of Medicine, Ege University, between January and December 2006. The study sample consisted of 2 separate groups. The first group comprised HBV carriers recruited from individuals who were regularly followed-up in the Infectious Diseases and Clinical Microbiology outpatient clinic due to inactive hepatitis B virus infection (IHBV) [Low Hepatitis B DNA levels (under 1×10^3 copies/mL, Robogene Hepatitis B virus quantitation kit, Roboscreen, Germany) and normal biochemical parameters (Aspartate amino transferase-AST, alanine amino transferase-ALT, bilirubin, no human immunodeficiency virus (HIV) or hepatitis C virus infection and no drug abuse] (18,19).

All HBV carriers were informed about the study and invited to participate on their control visits. The second group was recruited from the same outpatient clinic among patients who had a diagnosis of chronic HBV infection [patients who had positive hepatitis B surface antigen for at least 6 months, had hepatic activity index ≥4 in liver biopsy, and whose HBV DNA levels were above 1×10^4 copies/mL (Robogene Hepatitis B virus quantitation kit, Roboscreen, Germany) and AST and ALT levels at least 2-fold higher than normal ranges] and who were not undergoing active treatment yet. Patients who had liver failure, cirrhosis, or another chronic disease, and those that had received any antiviral or interferon treatment were excluded from the study.

Questionnaire

Participants of the study were requested to fill in the short-form 36 questionnaire on HRQOL (HRQOL-SF-36). The questionnaire also included information related to age, gender, marital status, education, and work status.

The questionnaire comprised 36 items and 8 subscales/domains, including physical functioning (PF), role limitations due to physical health problems (RP), bodily pain (BP), general health perceptions (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE), and mental health (MH). Each scale contained 2-10

questions and was graded between 0 and 100 points (14,20). The Turkish version of the SF-36 was translated in 1999 and demonstrated good psychometric properties (21).

Statistical analysis

Data were evaluated by SPSS 14.0. Descriptive statistics such as frequencies were used to summarize demographic characteristics of the study subjects. Educational level of HBV carriers was significantly higher than that of the patients with chronic HBV infection. Therefore, we conducted analysis of covariance (ANCOVA) and controlled educational level as covariate in order to compare QOL between the study groups. Pearson's and Spearman's correlation coefficients were computed for each domain score versus age, gender, and educational level. We conducted logistic regression analysis to define the most important factors in discriminating HBV carriers from patients who had chronic HBV disease. We also compared mean values of the SF-36 domain scores of HBV carriers and patients who had chronic HBV disease with the published scores for healthy controls derived from the Turkish population (20) by Student's t test. A P value less than 0.05 was considered significant.

Results

Demographics and the mean domain scores for health related quality of life

Of the 131 HBV carriers, 128 (50 females, 78 males, mean age 41.42 ± 12.32, Table 1) agreed to participate in the study. Their mean scores for HRQOL were 86.05 ± 15.01, 77.15 ± 35.49, 79.43 ± 21.47, 61.82 ± 19.01, 67.89 ± 19.74, 79.29 ± 19.43, 76.04 ± 34.73, and 66.58 ± 16.89 in the PF, PH, BP, GH, VT, SF, RE, and MH domains of the SF-36, respectively (Table 2).

Of the 38 patients with chronic HBV diseases, 28 (9 males, 19 females, mean age 36.68 ± 10.56, Table 1) agreed to participate in the study. The socio-demographic properties of the other 10 patients were not different from those of the study participants. Their mean scores for HRQOL were 80.7 ± 22.8, 54.4 ± 37.3, 70.2 ± 22.2, 59.5 ± 22.7, 64.5 ± 22.7, 71.4 ± 27.6, 58.3 ± 42.2, and 65.8 ± 22.5 in the PF, PH, BP, GH, VT, SF, RE, and MH domains of the SF-36, respectively (Table 2).

The groups did not show any significant difference in terms of age or gender, though a significant difference was observed in educational level (Table 1).

The relationship between demographics and QOL

We analyzed the relationship between gender, age, and educational status versus QOL domains with Spearman's and Pearson's correlation coefficients. We found significant relationships between gender and physical functioning (rs = –0.260, P = 0.001) and between gender and bodily pain (rs = –0.232, P = 0.004). In terms of age, a significant relationship was found only in role limitations due to physical health problems (r = 0.164, P = 0.004). We also found significant relationships between educational level and role limitations due to physical health problems (r = 0.219, P = 0.006) and between educational level and bodily pain (r = 0.194, P = 0.02).

Table 1. Demographic characteristics of study participants.

	Hepatitis B virus carriers (n = 128)	Patients with chronic hepatitis B virus disease (n = 28)	Statistical analysis
Age (year)	41.42 (12.32)	36.68 (10.56)	F = 0.88 P = 0.06
Educational status year	12.38 (2.86)	10.82 (2.2)	F = 11.31 P = 0.002
Gender (n/%)			
Female	78 (60.9%)	9 (32.1%)	X^2 = 0.47
Male	50 (39.%)	19 (67.9%)	P = 0.49

Means (with standard deviations) and percentages

Table 2. Comparison of quality of life between hepatitis B virus carriers and patients with chronic hepatitis B virus disease not undergoing active treatment.

SF-36 domains	Hepatitis B virus carriers n = 128	Chronic hepatitis B virus infection n = 28	Covariance analysis
Physical functioning	86.05 ± 15.01*	80.71 (22.8)	F = 1.55 df = 1.153 P = 0.22
Role limitation-Physical*	77.15 ± 35.49	54.46 (37.3)	F = 9.52 df = 1.153 P = 0.002
Bodily pain	79.43 ± 21.47*	70.25 (22.2)	F = 2.47 df = 1.153 P = 0.11
General health perception	61.82 ± 19.01*	59.59 (22.7)	F = 0.29 df = 1.153 P = 0.59
Vitality	67.89 ± 19.74	64.58 (22.7)	F = 0.29 df = 1.153 P = 0.59
Social functioning	79.29 ± 19.43*	71.42 (27.6)	F = 2.27 df = 1.153 P = 0.13
Role limitation-emotional	76.04 ±34.73*	58.33 (42.2)	F = 3.64 df = 1.153 P = 0.06
Mental health	66.58 ± 16.89*	65.85 (22.5)	F = 0.00 df = 1.153 P = 0.9

Means (with standard deviations), *P < 0.05

Comparison of the HBV carriers and patients with chronic HBV disease in terms of HRQOL

We compared HRQOL between the groups by testing the effect of educational level with ANCOVA. The test revealed that there was only a statistically significant difference in terms of role limitations due to physical health problems between the study groups (F = 9.52, df = 1.153, P = 0.002, Table 2). With regard to the significant relationships between demographics and some of the HRQOL domains, we performed logistic regression analysis via forward selection to identify the most important predicting factors in discriminating HBV carriers from patients with chronic HBV disease. All variables (age, gender, educational level, SF-36 domains) were entered into the model. The test revealed that the role limitations due to physical health problems domain of SF-36 (β = –0.003, standard error = 0.001, t = –3.086, P = 0.002) and educational level (β = –0.025, standard error = 0.011, t = –2.322, P = 0.022) were the most important factors in discriminating groups from each other (F = 8.59, P < 0.001). The role limitations due to physical health problems domain of SF-36 was first entered into the model and explained 6.9% of the variance.

The role limitations due to physical health problems domain of SF-36 together with educational level explained 10.1% of the variance.

Comparison of HRQOL life scores of the study groups with published scores for healthy controls derived from the Turkish population

When we compared HBV carriers' domain scores of SF-36 with Turkish population standards, HRQOL of patients showed a profile similar to that of the general Turkish population, with normal PF and VT scores, but significantly lower RP, BP, GH, SF, RE, and MH domain scores (Table 3, $P < 0.001$, $P = 0.001$, $P < 0.001$, $P < 0.001$, $P < 0.001$, $P < 0.001$, respectively). Patients with chronic HBV disease not undergoing active treatment showed a profile similar to that of HBV carriers with respect to comparison with Turkish population standards except in mental health domain score.

Discussion

The most important finding of our study was that the QOL profile in HBV carriers was greatly similar to that of the patients with chronic HBV infection not undergoing active treatment except in the role limitations due to physical health problems domain of SF-36.

HBV carriers showed better QOL than the patients with chronic HBV disease in the RP domain of SF-36. In addition, both HBV carriers and patients who suffered from chronic HBV disease showed QOL profiles greatly similar to those of the general Turkish population standards except in the GH domain of SF-36. Although there was not a significant difference between HBV carriers and patients with chronic disease in terms of the GH domain of SF-36, HBV carriers obtained significantly lower scores from the GH domain of SF-36 when compared with the general

Table 3. SF-36 scores of hepatitis B virus carriers and normal Turkish population.

Subscales of SF-36	Turkish population standards	Hepatitis B virus carriers (n = 128)	P value*
Physical functioning	86.6 ± 25.2	86.05 ± 15.01*	t = –0.41 0.68
Role limitation-Physical	89.5 ± 29.6	77.15 ± 35.49	t = –3.63 P < 0.001
Bodily pain	86.1 ± 20.6	79.43 ± 21.47*	t = –3.51 P = 0.001
General health perception	73.9 ± 17.5	61.82 ± 19.01*	t = –7.19 P < 0.001
Vitality	67.0 ± 13.8	67.89 ± 19.74	t = –0.11 P = 0.92
Social functioning	94.8 ± 14.2	79.29 ± 19.43*	t = –8.84 P < 0.001
Role limitation-emotional	94.7 ± 20.9	76.04 ± 34.73*	t = –5.93 P < 0.001
Mental health	73.5± 11.6	66.58 ± 16.89*	t = –4.65 P < 0.001

*t test results

Table 4. SF-36 scores of patients with hepatitis B virus disease not undergoing active treatment and normal Turkish population.

Subscales of SF-36	Turkish population standards	Patients with chronic hepatitis b virus disease (n = 28)	P value*
Physical functioning	86.6 ± 25.2	80.71 ± 22.8	t = –1.37 P = 0.183
Role limitation-Physical	89.5 ± 29.6	54.46 ± 37.30	t = –4.97 P < 0.001
Bodily pain	86.1± 20.6	70.25 ± 22.23	t = –3.77 P = 0.001
General health perception	73.9 ± 17.5	59.58 ± 22.66	t = –3.34 P = 0.002
Vitality	67.0±13,8	64.59 ± 22.66	t = –0.56 P = 0.58
Social functioning	94.8±14.2	71.43 ± 27.61	t = –4.48 P < 0.001
Role limitation-emotional	94.7±20.9	58.33 ± 42.19	t = –4.56 P < 0.001
Mental health	73.5± 11.6	66.86 ± 22.51	t = –1.79 P = 0.08

*t test results

Turkish population standards, but the patients with chronic disease did not.

HBV carriers are regarded as healthy individuals and they are usually referred to as healthy carriers in the literature. However, physicians want them to arrange control visits regularly because there is usually an obvious risk of becoming chronically ill at some time in the future. Importance of giving extensive information about the disease and the need for regular control visits should be explained to the patients to enhance QOL (10,22,23). In our outpatient clinic, standard disease oriented information is given to all patients.

Since QOL is a subjective concept, its definition and measurement are rather difficult (24). In chronic diseases, it is not possible to evaluate the clinical course and the treatment success in a short time. There are some universal factors affecting QOL such as being a woman or being elderly (4). In the present study, we tested those factors by conducting ANCOVA and logistic regression analysis. In addition, there are numerous studies in the literature addressing the effect of psychiatric morbidity on QOL in patients with chronic viral liver diseases and these studies reported that psychiatric morbidity affected QOL negatively (25,26).

To our knowledge, there is no study concerning the effect of psychiatric state on QOL in HBV carriers. Only in one study were psychiatric disorders and functioning evaluated in HBV carriers (7). According to the study results, the authors reported that HBV carriers had significantly higher levels of depression and anxiety and lower level of functioning when compared with healthy controls. They added that worries about contamination and illnesses related to HBV infection were associated with the presence of psychiatric disorder. In the present study, as mentioned above, the HBV carriers had lower scores

in the RP, BP, GH, SF, RE, and MH domains of SF-36 when compared with the Turkish population standards, and patients with chronic HBV disease not undergoing active treatment showed a profile similar to that of HBV carriers except in the MH domain score. The reason that we did not come up with better QOL in HBV carriers may be the fact that we did not evaluate the psychiatric state of participants in the current study. Therefore, an existing psychiatric disease might have affected the results via its direct or indirect effect on QOL (for example, an existing anxiety might have caused misinformation about the disease).

In this study, it was found that patients with chronic HBV disease had worse QOL than carriers in only the RP domain of SF-36. The RP domain of SF-36 is included in the physical aspects of HRQOL. In the literature, one of the reasons for impaired QOL among patients with chronic hepatitis virus infections was reported to be the effect of the disease itself (22,27). With respect to the literature, we suggest that the difference in QOL in terms of role limitations due to physical health problems might have been affected by the HBV disease itself via higher viral load or higher serum liver enzymes than that of HBV carriers.

Although most of the HBV carriers do not have any symptoms, it is possible to encounter one of the non-specific symptoms such as weakness, fatigue, vomiting, upper abdominal pain, or muscle and joint pains in some of them. These symptoms may be the cause of the decrease in the MH and RP domains of SF-36 when compared with the healthy population.

HBV infection leads to cirrhosis in up to 20% of those chronically infected and it is one of the most common indicators for liver transplantation worldwide (11). The disease, its long-term complications, and its economic burden have a significant impact on HRQOL. Although the treatment of the chronic disease has several effects on long-term survival, improvement in the QOL is also necessary.

To our knowledge, this is the first study measuring QOL in HBV carriers in Turkey. We chose the SF-36 health survey because its reliability and validity were shown among different diseases and general population groups (28). The SF-36 is a widely used generic instrument and it has several other advantages, including the measurement of high and low scores and feasibility of a broad range of strategies to be used in the interpretation of the results. Since SF-36 is not specific to chronic HBV, the Chronic Liver Disease Questionnaire (CLDQ) has been developed. On the other hand, it is reported in a study comparing the 2 questionnaires that SF-36 is as effective as CLDQ and that CLDQ does not contribute an extra important benefit (29).

Most of the studies about QOL related to chronic viral hepatitis involve patients with HCV and studies regarding QOL of the patients with HBV are insufficient in the English literature. Foster et al. reported a decrease in MH and GH scores in 30 English patients with HBV compared to healthy volunteers (12). Pojoga et al. found lower QOL scores for every domain of HRQOL (PF, RP, MH, RE, SF, VT, and GH) in 66 Romanian patients (27 with HBV, 38 HCV, 1 HBV+HCV, 3 patients with HBV had high transaminase levels) than the normal population (3). Therefore, our study results with regard to comparison of QOL of in HBV carriers and patients with chronic HBV disease with the Turkish population standards are consistent with the previous study results reporting poor QOL in patients with chronic liver disease when compared with the normal population (3,4,30).

In this study, logistic regression analysis revealed that the RP domain of SF-36 explained 6.9% of the variance by itself while it accounted for 10.1% of the variance together with the educational level. The effect of the RP domain of SF-36 and educational level in discriminating HBV carriers from patients with chronic HBV disease may seem rather low but it reflects our results. We think that if we had included more variables in the study (for example, psychiatric status), the results could have been different.

There are some limitations of our study. First, our sample size with regard to patients with chronic HBV disease was rather small and this might have affected our results. Second, we did not control for the psychiatric state. If we had included some psychiatric measures depending on the existent literature, we would probably have found psychiatric state to decrease QOL.

On the other hand, the importance of this study was that it was the first to assess QOL in HBV carriers. In addition, we invited all patients and healthy virus carriers to participate in the current study in order avoid selection bias.

In conclusion, our study results suggest that the QOL in HBV carriers is greatly similar to that of patients with chronic HBV disease and both groups have lower QOL than the normal Turkish population. Chronic HBV infection may require lifelong follow-up. Regular implementation of HRQOL questionnaires may be helpful to physicians to apply for psychiatric consultancy, when needed.

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