

## Validation of the Brazilian version of the hepatitis B quality of life evaluation instrument - HBQOL, and its application to patients with chronic hepatitis B in Cascavel – PR

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The objective of this study is to validate the specific questionnaire for Hepatitis B HBQOL (Hepatitis B Quality of Life Instrument, version 1.0) for the Brazilian version, in addition to testing its applicability in patients with hepatitis B under treatment and comparing the quality of life between patients using first-line drugs (tenofovir and entecavir). For the validation, the back-translation technique was used in a sample of 47 patients. Factor analysis was performed between the items in each domain of the questionnaire and the internal consistency was calculated using Cronbach's  $\alpha$  coefficient. In assessing the applicability of the validated questionnaire, interviews were carried out with 124 patients. Sociodemographic and treatment data were collected to characterize the sample and perform correlation analyzes. The results demonstrate that the Brazilian version of the questionnaire was successfully validated. In the analysis carried out among the 124 patients, the domains psychological well-being and stigma obtained the highest scores in quality of life and the lowest level of education conferred better results in these two domains. The comparison between tenofovir and entecavir showed no significant difference in patients' quality of life. The use of this validated instrument can make therapeutic decisions more rational.

**Keywords:** Quality of life. Chronic hepatitis B. Therapeutics.

### INTRODUCTION

Hepatitis B is one of the most common viral infections in the world. It is estimated that approximately 2 billion people have already been infected by the virus, and about 350 to 450 million are chronic carriers of this

etiologic agent (Mutimer, Oo, 2011; Trépo, Chan, Lok, 2014). The most serious complications of the disease are related to the development of cirrhosis and hepatocellular carcinoma (CHC), which in general cause between 0.5 and 1.2 million deaths per year worldwide (Saffari *et al.*, 2015).

There are currently seven drugs for the treatment of the disease; five of them orally administered: lamivudine, adefovir, entecavir, telbivudine and tenofovir, and two subcutaneously: interferon alpha and pegylated interferon alpha (DeFrancesco *et al.*, 2015).

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The first line consists of the nucleoside/nucleotide analogs entecavir (ETV) and tenofovir (TDF). These two drugs are powerful antiviral agents and present a minimal risk of developing resistance (Chao, Hu, 2013; Cholongitas, Tziomalos, Pipili, 2015). Drug therapy aims to reduce the risks of developing cirrhosis and CHC while increasing the survival and quality of life of patients (Almeida *et al.*, 2012).

The term quality of life has gained relevance in recent years, with a growing interest in health-related quality of life (HRQoL) (Qiao *et al.*, 2012). It refers to the subjective assessment made by patients regarding their physical, mental, and social well-being (Strauss *et al.*, 2014). In addition to clinical and economic data, HRQoL has proven to be important information in the treatment and decision of therapeutic choice (Abdo, 2012).

Patients with chronic liver disease, including viral hepatitis, cirrhosis, and CHC, may have losses in their HRQoL (Lam *et al.*, 2009). Therefore, to assign a value to this parameter, several generic and specific instruments have been proposed (Strauss *et al.*, 2014). Generic instruments are those used in general populations and assess several domains, which can be applied in a variety of health states and diseases. On the other hand, the specific ones respond better to small changes in specific diseases, filling gaps left by generic instruments (Che *et al.*, 2014).

In 2007, Spiegel and collaborators developed and validated the HBQOL (Hepatitis B Quality Of Life Instrument, version 1.0), a questionnaire to assess HRQoL in patients with chronic hepatitis B (HBC) and non-cirrhotic hepatitis. Until this date, there was no specific instrument for HBC, only for liver diseases (Poorkaveh *et al.*, 2012).

The HBQOL consists of 31 items that assess six domains, including psychological well-being, anticipatory anxiety, vitality, stigma, vulnerability, and transmission. It also has an extra domain, the viral response, which is generated from the combination of the domains of transmission and vulnerability (Spiegel *et al.*, 2007).

Few studies in the world evaluate the HRQoL of these patients through the specific HBQOL questionnaire. This tool is also extremely important in Brazil, where

treatment for this disease is provided free of charge by the government.

The objective of this study was to validate the Brazilian version of the HBQOL and evaluate the HRQoL of patients with HBC undergoing treatment with antivirals provided by the Unified Health System (SUS) using the validated version of this questionnaire. Another aim was to compare the HRQoL of patients using the first line of treatment.

## MATERIAL AND METHODS

### Validation of the questionnaire

In the validation process of the specific HBQOL v 1.0 questionnaire for the Brazilian version in Portuguese, we used the technique of translation by health professionals followed by reverse translation by an English-speaking teacher. After translation, patients over 18 years of age with HBC who were admitted to the Hospital das Clínicas of the Federal University of Paraná in the city of Curitiba during the research period between 2010 and 2011 were recruited, totaling 47 patients. The interviews were conducted by a trained interviewer in a quiet and illuminated room. All items of the questionnaire followed the Likert scale, ranging from 1 to 5. To measure these domains, a score was established for each item according to the participants' response, where 1 (score 100) constituted the best scenario, that is, a better quality of life, and 5 (score 0) the worst scenario, consequently a worse quality of life. In addition, to characterize the sample in question, data such as gender, age, education, marital status, drug treatment, and comorbidities were collected.

The analyses were performed considering the domains of the original HBQOL, in order not to make the mistake of dissociating the construct validity from the theoretical content, which would refer to statistical empiricism without meaning. The item response theory (TRI) was used, in which each item of the questionnaire can be independently excluded if it is not assigned validity within the domain.

Factor analysis (AF) was performed among the items of each domain separately, seeking to identify common factors that refer to the underlying latent traits.

The method of analysis of the main components (MC) was used, which has the advantage of not requiring the normal distribution of variables. Besides, we opted for the oblique rotation technique because it works with less simplified data, getting closer to reality.

The number of MC was determined by the Kaiser criterion, which discards factors that have a lower degree of explanation than for any single item. Items with communalities lower than 0.5 with such MC were considered inadequate.<sup>16</sup>

The internal consistency of the instrument was calculated before and after the AF filtering process by determining Cronbach's  $\alpha$  coefficient for each domain individually, and values above 0.6 were considered acceptable. Statistical calculations were performed using the SPSS software version 17.0, with a significance level of 5%. Regarding the analyses, for the instrument as a whole and each domain, the Kaiser-Meyer-Olkin coefficient and Bartlett's sphericity test for the data matrix were calculated (Hair, 1998).

### **Evaluation of the quality of life of patients with HBC employing the HBQOL v 1.0 instrument for the Brazilian version in Portuguese**

We interviewed patients older than 18 years of age, with HBC, under treatment, and monitored by SUS, from June to December 2014. The exclusion criteria established were HIV, hepatitis C or D viruses co-infections, and severe psychiatric disorders.

The collection instrument used was HBQOL v 1.0 already validated for the Brazilian version. The questionnaires were self-administered; however, three trained interviewers guided the participants about the research, without influencing the choice of responses. As in validation, data were also collected from medical records, such as age, marital status, comorbidities, education level, treatment time, and medications used.

The approaches to individuals took place at the 10th Regional Health Department of Paraná in the city of Cascavel-PR, where medications for the treatment of HBC are dispensed and also at the Specialized Center for Infectious-Parasitic Diseases (CEDIP), where medical appointments are previously scheduled.

The 10th Regional Health Department made available in advance a list of people who were undergoing treatment for HBC and during the survey period, the interviewers were waiting for patients at the time of medication withdrawal. The interviews carried out at the 10th Regional Health Department took place on random days and times, whenever a trained interviewer was available. The interviews at CEDIP were carried out after the medical consultation, where an interviewer was waiting for the patient because the research team was aware of the day and time of the consultation.

The treatment time was calculated from the moment the patient started the therapy until the date of the questionnaire application. In the end, individuals who did not answer all the questions or did not meet the established criteria were excluded.

For comparison between the impact of pharmacotherapies with TDF and ETV on HRQoL, only individuals who used these drugs alone and without having had other therapy for HBC previously were evaluated.

The statistical analyses were performed through the "R" program (R Core Team, 2015). Descriptive analyses, such as mean and sample standard deviation, were applied in the characterization of the seven domains of the questionnaire. In the correlation tests, Spearman's method was used, which evaluates linear relationships between the data. Comparison analyses were performed using the Wilcoxon test (Mann-Whitney) for independent samples. The Chi-square test was used to relate the level of education to the domains of the questionnaire, and the Wilcoxon test (Mann-Whitney) was used again to determine which level of education was significant. The level of significance adopted for all analyses was 5% ( $p < 0.05$ ).

This study was approved by the Research Ethics Committee of the Federal University of Paraná (CEP/SD: 819.154.09.10) for the questionnaire validation stage and also by the Ethics Committee of the Western Paraná State University (opinion no. 667.253) to evaluate the quality of life of patients with chronic hepatitis B. All participants signed the informed consent form.

## RESULTS

### Validation of the questionnaire

The validation of the Brazilian version of the HBQOL v 1.0 - Brazil instrument included 47 adult patients (36.2% women and 63.8% men) diagnosed with chronic hepatitis B. The average age was  $47.3 \pm 11.3$  years. Of the patients included, most were married (51.1%) and had incomplete primary education (40.4%). The most frequent comorbidity was arterial hypertension (25.5%).

Regarding treatment, 24 (51.1%) of them were not taking any drugs. As for those who were on drug therapy, most were being treated with lamivudine (14.9%), followed by tenofovir (12.8%) and entecavir (10.6%) (Table I).

Regarding the analyses, for the instrument as a whole and each domain, we calculated the Kaiser-Meyer-Olkin coefficient and Bartlett's sphericity test for the data matrix, which were adequate in all cases. This reflects that the sample of 47 patients was sufficient for AF.

In HBQOL global AF (Brazil), ten MC were extracted, accounting for 76.9% of the items variance, and none of these items presented communality below the limit of 0.5 in relation to the MC set (Table II).

The items individually excluded in each domain, according to the TRI, do not measure the latent trait or psychological construct, mathematically represented by the MC, targeted by the assessed domain, and should be considered as not belonging to the same in the Brazilian cultural reality. Table III shows the Cronbach's alpha coefficients before and after the filtering performed by AF.

**TABLE I** - Sociodemographic characteristics of participants in the HBQOL validation in the city of Curitiba – PR

Characteristics	N	%	Mean ± SD
Gender			
Female	17	36.2	-
Male	30	63.8	-
Age (years)			
20 – 30	3	6.4	
30 – 40	9	19.2	
40 – 50	16	34.0	$47.3 \pm 11.3$
50 – 60	12	25.5	
60 – 70	5	10.6	
70 – 80	2	4.3	
Marital status			
Married	24	51.1	-
Single	23	48.9	-
Education level			
Incomplete elementary school	19	40.4	-
Complete elementar school	10	21.3	-

**TABLE I** - Sociodemographic characteristics of participants in the HBQOL validation in the city of Curitiba – PR

Characteristics	N	%	Mean ± SD
Incomplete high school	1	2.1	-
Complete high school	15	32.0	-
Graduated	1	2.1	-
Not reported	1	2.1	-
<b>Comorbidities</b>			
Arterial hypertension	12	25.5	-
Diabetes <i>mellitus</i>	2	4.3	-
Alcoholism	2	4.3	-
Dyslipidemia	1	2.1	-
Chronic gastritis	1	2.1	-
<b>Drug treatment</b>			
Lamivudine 150 mg	7	14.9	-
Tenofovir 300 mg	6	12.8	-
Entecavir 0,5 mg	5	10.6	-
Adefovir 10 mg	1	2.1	-
Lamivudine 150 mg and Adefovir 10 mg	3	6.4	-
Tenofovir 300 mg and Entecavir 0.5 mg	1	2.1	-
<b>Time Treatment</b>			
Lamivudine 150 mg	-	-	42.7 ± 38.7
Tenofovir 300 mg	-	-	16.8 ± 28.5
Entecavir 0.5 mg	-	-	5.2 ± 3.0
Lamivudine 150 mg and Adefovir 10mg	-	-	76.0 ± 48.5

**TABLE II** - Factor Analysis between the items in each domain of the questionnaire

Domains	Items	Number of main components (MC)	Variance	Communality between items
Psychological Well-Being	F6 (Anxiety) F4 (Frustration) F3 (Sadness) F7 (Irritation) F10 (Less useful life) F13 (Scared) F19 (Bad) F8 (Isolated)	3	70.7%	None of the items presented communality lower than 0.5
Antecipation Anxiety	C1 (Failure) C2 (Cancer) C15 (Worsening of health) C12 (Occurrence of something serious) C9 (Survival) C5 (Worsening of the disease)	1	67.1%	None of the items presented communality lower than 0.5
Vitality	P1 (Tiredness) F5 (Exhaustion) P3 (Muscle pain) P2 (Memory problems) F12 (Lack of productivity)	1	54.8%	P3 and P2 presented communalities lower than the qualitative cut-off point.
Stigma	C14 (Embarrassment) F1 (Ashamed) C10 (Excessive concern) C11 (Social isolation) C3 (Relative to the boss) F2 (Stigmatized)	2	67.2%	All presented communalities above the cut-off value
Vulnerability	C13 (Diet) C6 (Ease of falling ill) C8 (Regarding medications)	1	56.7%	C8 presented insufficient communality
Transmission	C7 (Sexual transmission) C4 (Transmission to children) F11 (Difficulty in having sexual intercourse)	1	41.7%	Only C7 presented sufficient communality
Viral Response	C7 (Sexual transmission) C4 (Transmission to children) C13 (Diet) C8 (Regarding medications)	1	43.6%	C4 and C13 did not reach enough communalities to be considered valid in the domain

**TABLE III** - Internal consistency of HBQOL domains and their cross-culturally adapted version for Brazil before and after AF filtering

Domains	HBQOL <sup>a</sup>	HBQOL Brazil <sup>b</sup>	HBQOL Brazil <sup>c</sup>
Psychological Well-Being	0.90 (8)	0.77 (8)	0.77 (8)
Anticipation Anxiety	0.88 (6)	0.90 (6)	0.90 (6)
Vitality	0.90 (5)	0.78 (5)	0.78 (3)
Stigma	0.89 (6)	0.77 (6)	0.77 (6)
Vulnerability	0.82 (3)	0.61 (3)	0.64 (2)
Transmission	0.73 (3)	0.30 (3)	- (1)
Viral Response	0.75 (4)	0.56 (4)	0.60 (2)
Total	0.96 (31)	0.91 (31)	0.91 (27)

Reliability analysis using Cronbach's coefficient  $\alpha$  (number of domain items in brackets). <sup>a</sup>Original HBQOL version; <sup>b</sup>HBQOL-Brazil before AF filtering; <sup>c</sup>HBQOL-Brazil after AF filtering.

### Evaluation of the quality of life of patients with HBC by the HBQOL v 1.0 instrument for the Brazilian version in Portuguese

In the evaluation of the quality of life carried out after the questionnaire was validated for the Brazilian version, 124 patients were interviewed, most of whom were male (66.9%). The general average age was  $49.6 \pm 11.1$  years and the predominant marital status was married (80.6%). Regarding the level of education, most respondents had only incomplete elementary

school (41.1%). The most frequent comorbidity among respondents was arterial hypertension (23.4%).

Concerning the use of drugs provided by the CEAF (Specialized Pharmaceutical Assistance Component), it was observed that most patients used the first line of treatment. Lamivudine was the third most used drug and had the highest average treatment time because it was the first oral nucleoside analog to be approved for HBC treatment. The mean treatment time of all patients evaluated was  $33.3 \pm 35.9$  months (Table IV).

**TABLE IV** - Sociodemographic characteristics of the participants in the evaluation of quality of life in the city of Cascavel - PR

Characteristics	N	%	Mean $\pm$ SD
Gender			
Female	41	33.1	-
Male	83	66.9	-
Age (years)			
>18 - 20	1	0.8	
20 - 30	5	4.0	

**TABLE IV** - Sociodemographic characteristics of the participants in the evaluation of quality of life in the city of Cascavel – PR

Characteristics	N	%	Mean ± SD
30 – 40	15	12.1	
40 – 50	39	31.5	49.6 ± 11.1
50 – 60	39	31.5	
60 – 70	22	17.7	
70 – 80	3	2.4	
Marital status			
Married	100	80.6	-
Single	24	19.4	-
Education level			
Incomplete elementary school	51	41.1	-
Complete elementary school	21	16.0	-
Completo high school	40	32.3	-
Graduated	12	9.7	-
Comorbidities			
Arterial hypertension	29	23.4	-
Alcoholism	7	5.6	-
Dyslipidemia	6	4.8	-
Depression	6	4.8	-
Renal insufficiency	5	4.0	-
Diabetes <i>mellitus</i>	4	3.2	-
Smoking	4	3.2	-
Hypothyroidism	3	2.4	-
Drug treatment*			
Tenofovir 300 mg	77	48.1	-
Entecavir 0,5 mg	42	26.2	-
Adefovir 10 mg	3	1.9	-
Lamivudine 150 mg	22	13.7	-
Pegylated Interferon 2a 180 mcg	2	1.3	-
Interferon 2b 3 millions of UI	4	2.5	-



**TABLE IV** - Sociodemographic characteristics of the participants in the evaluation of quality of life in the city of Cascavel – PR

Characteristics	N	%	Mean ± SD
Interferon 2b 5 millions of UI	10	6.3	-
<b>Time treatment (months)</b>			
Tenofovir 300 mg	-	-	22.4 ± 13.9
Entecavir 0,5 mg	-	-	21.9 ± 14.3
Adefovir 10 mg	-	-	48.0 ± 2.6
Lamivudine 150 mg	-	-	75.6 ± 19.7
Pegylated Interferon 2a 180 mcg	-	-	12.0 ± 0.0
Interferon 2b 3 millions of UI	-	-	8 ± 6.9
Interferon 2b 5 millions of UI	-	-	11.4 ± 1.9

\*The total is greater than the number of individuals interviewed because the same patient used different drugs at different times or concomitantly.

Regarding the descriptive analysis of the domains of the questionnaire in the 124 patients evaluated, it can be determined that the psychological stigma and well-

being dimensions obtained the highest means (88.2±14.9; 82.5±19.1), respectively. In contrast, vulnerability and viral response were the lowest means (Table V).

**TABLE V** - Results of the analysis of the quality of life domains of the 124 patients with HBC and the co-variables gender, marital status, comorbidities, age and time of treatment

Comparatos	PWB <sup>1</sup>	APA <sup>2</sup>	VIT <sup>3</sup>	STM <sup>4</sup>	VUL <sup>5</sup>	TSM <sup>6</sup>	VRS <sup>7</sup>
General Quality of life							
Mean ± SD	82.5 ± 19.1	67.0 ± 25.3	72.9 ± 24.3	88.2 ± 14.9	57.8 ± 23.0	66.5 ± 23.9	53.7 ± 24.6
Gender							
Female (Mean ± SD)	83.5 ± 20.0	69.5 ± 25.4	71.5 ± 26.4	88.2 ± 15.8	55.7 ± 26.1	74.4 ± 25.0	57.2 ± 27.5
Male (Mean ± SD)	82.0 ± 18.8	65.7 ± 25.2	73.7 ± 23.2	88.3 ± 14.5	58.8 ± 21.3	62.6 ± 22.5	52.0 ± 23.1
<i>p</i> -value	0.544	0.361	0.894	0.585	0.6533	0.007*	0.155
Marital Status							
Married (Mean ± SD)	82.0 ± 19.7	66.8 ± 25.5	72.6 ± 24.5	88.6 ± 13.9	56.5 ± 22.8	66.3 ± 22.7	52.9 ± 24.1
Single (Mean ± SD)	84.8 ± 16.6	67.9 ± 24.9	74.4 ± 23.8	86.6 ± 18.7	63.2 ± 23.3	67.4 ± 29.1	57.0 ± 27.1
<i>p</i> -value	0.569	0.942	0.831	0.936	0.225	0.638	0.479
Comorbidities							
Presence (Mean ± SD)	83.9 ± 17.5	68.8 ± 25.4	71.4 ± 25.3	89.2 ± 11.0	59.7 ± 22.5	69.5 ± 25.1	57.9 ± 23.3

**TABLE V** - Results of the analysis of the quality of life domains of the 124 patients with HBC and the co-variables gender, marital status, comorbidities, age and time of treatment

Comparatos	PWB <sup>1</sup>	APA <sup>2</sup>	VIT <sup>3</sup>	STM <sup>4</sup>	VUL <sup>5</sup>	TSM <sup>6</sup>	VRS <sup>7</sup>
Absence (Mean ± SD)	81.6 ± 20.2	65.8 ± 25.3	74.0 ± 23.6	87.6 ± 17.0	56.5 ± 23.3	64.4 ± 23.1	50.8 ± 25.2
<i>p</i> -value	0.543	0.445	0.590	0.552	0.605	0.186	0.200
Age							
Correlation (r)	0.253	0.206	0.067	0.279	-0.024	0.083	0.138
<i>p</i> -value	0.005*	0.022*	0.458	0.002*	0.798	0.359	0.126
Education level							
<i>p</i> -value	0.044*	0.541	0.931	0.002*	0.505	0.955	0.748
Treatment time							
Correlation (r)	0.091	0.072	0.036	0.152	0.082	0.149	0.128
<i>p</i> -value	0.317	0.425	0.691	0.091	0.365	0.099	0.155

<sup>1</sup>PWE psychological well-being, <sup>2</sup>APA anticipation anxiety, <sup>3</sup>VIT vitality, <sup>4</sup>STM stigma, <sup>5</sup>VUL vulnerability, <sup>6</sup>TSM transmission, <sup>7</sup>VRS viral response, \*Significant at 5%.

When comparing the socio-demographic variables with the seven domains of the questionnaire, we observed that the item transmission negatively affects more women than men ( $p=0.0073$ ). On the other hand, age has a linear tendency to provide higher scores for psychological well-being ( $p=0.005$ ), anxiety by anticipation ( $p=0.022$ ), and stigma ( $p=0.002$ ) according to the increase in years of life.

In addition, the psychological well-being ( $p=0.044$ ) and stigma ( $p=0.002$ ) domains were significantly associated with the level of education. In an in-depth comparative analysis between these two domains and the educational levels of the research participants, it was observed that the incomplete elementary level was statistically significant with  $p=0.015$  for the psychological well-being and  $0.034$  for the stigma. This analysis determines that the scores of these two domains are higher in individuals with incomplete elementary education.

Spearman's linear correlation for the treatment time of 124 patients with the seven domains was not significant ( $p>0.05$ ). The variables marital status and comorbidities

also showed no significant values when compared to the HRQoL scores obtained (Table V).

When comparing the HRQoL of patients with HBC who used one of the first-line therapeutic options in a single and isolated way, 59 patients who used only TDF, with an average treatment time of  $22.2 \pm 13.3$  months and 38 patients who used only ETV, with an average treatment of  $22.2 \pm 14.0$  months.

In the analysis of the domains according to the use of these two alternatives, it was possible to observe that there was no significant difference between the two drugs ( $p > 0.05$ ). The correlation of treatment time with each of the seven domains was not significant for patients who used ETV ( $p > 0.05$  for all domains). For TDF, the psychological well-being domains ( $p=0.007$ ), anxiety by anticipation ( $p=0.047$ ), stigma ( $p=0.008$ ), and vulnerability ( $p=0.029$ ), had significant correlation, i.e., the means for these domains increased linearly with the increase in treatment time (Table VI).

**TABLE VI** - Results of HRQoL domain analyzes of patients with HBC according to the use of ETV and TDF and correlation with treatment time

Domains	TDF <sup>8</sup>		Correlation with treatment time	ETV <sup>9</sup>		Correlation with treatment time	TDF $\chi$ ETV
	Mean	SD	( <i>p</i> )	Mean	SD	( <i>p</i> )	( <i>p</i> -value)
PWE <sup>1</sup>	82.5	19.2	0.347 (0.007) *	84.6	16.9	-0.261 (0.114)	0.603
APA <sup>2</sup>	64.7	25.8	0.260 (0.047) *	72.0	23.6	-0.228 (0.168)	0.136
VIT <sup>3</sup>	75.5	22.0	0.170 (0.198)	70.1	27.2	0.020 (0.907)	0.450
STM <sup>4</sup>	86.9	17.1	0.344 (0.008) *	90.4	9.1	-0.016 (0.922)	0.937
VUL <sup>5</sup>	57.4	23.9	0.284 (0.029) *	58.8	21.2	-0.281 (0.088)	0.967
TSM <sup>6</sup>	66.7	23.9	0.203 (0.122)	63.8	24.4	0.069 (0.679)	0.610
VRS <sup>7</sup>	52.0	26.0	0.254 (0.052)	55.2	23.4	-0.048 (0.774)	0.688

<sup>1</sup>PWE psychological well-being, <sup>2</sup>APA anticipation anxiety, <sup>3</sup>VIT vitality, <sup>4</sup>STM stigma, <sup>5</sup>VUL vulnerability, <sup>6</sup>TSM transmission, <sup>7</sup>VRS viral response, TDF<sup>8</sup> tenofovir, ETV<sup>9</sup> entecavir, \*Significant at 5%.

## DISCUSSION

Some socio-demographic characteristics such as education and comorbidities both in the sample of patients in the validation and in the application of the HBQOL v 1.0 questionnaire corroborate the averages found in the Brazilian population (Brasil, 2014b; Brasil, 2019). Bearing this in mind, the translation and validation of this instrument in this work not only translated HBQOL v 1.0, but also adapted it to the Brazilian reality, trying to make it clear and applicable to this population.

However, in a country as diverse as Brazil, cultural, demographic and epidemiological issues can achieve different results in each region. It is known that the southern region of Brazil, has some parameters such as education, access to culture, average wages and unemployment rate, better than other regions such as northeast and north for example (Brasil, 2014a).

In view of the above, it can be said that one of the limitations of the present work is that the validation and application of HBQOL-Brazil took place only in the State of Paraná and future work should be carried out, with its application in different regions of Brazil to compare its applicability in the country.

The validation of HBQOL-Brazil presented similar results when compared to the original instrument (Cronbach's coefficient  $\alpha > 0.9$  in the general evaluation and  $\geq 0.6$  in the evaluation of individual domains). The "viral response" domain had the lowest internal consistency values for both the original and the Brazilian versions of the HBQOL.

Two questions of the "vitality" domain had low communalities (P2 and P3). The same occurred with question C8 of the "vulnerability" domain, C7, C4, and F11 of the "transmission" domain, and C4 and C13 of the "viral response" domain. For this reason, these items were excluded from the final version of HBQOL-Brazil. Questions C8, C7 and C4 remained in the questionnaire in the "viral response" domain; question C13 remained in the questionnaire in the "vulnerability" domain.

The question F11 was not present in any of the domains, and its low communality value probably reflects the socio-demographic characteristic of the cohort of patients included in the study since this question is related to the sexual difficulty presented by the patient with HBC. Considering that more than 60% of patients are male and that the mean age of patients was almost 50 years, it can be inferred that cultural factors may have generated poor quality results for this issue.

In the statistical analysis of the 124 patients who used the translated and validated instrument, it showed that the psychological well-being and stigma domains had the best HRQoL scores. The vulnerability and viral response domains were the lowest scores. A result similar to this was found by another study that used the same questionnaire translated and validated on another continent (Poorkaveh *et al.*, 2012).

Concerning the socio-demographic variables, the female gender obtained the lowest scores for the transmission domain when compared to the male gender. This indicates that women are more concerned with questions related to the transmission of the disease to other people, including children, and also with the sexual transmission of the virus.

The age variable, in turn, showed significant results for the psychological well-being, anticipatory anxiety, and stigma domains, indicating that over time, these items tend to have better HRQoL results. For Lam *et al.*, 2009 age advancement was also associated with a positive effect on HRQoL.

The level of incomplete elementary schooling, on the other hand, gave higher scores for the psychological well-being and stigma domains. These results demonstrate that the lower the degree of knowledge, the less concerns and impacts individuals have on their HRQoL. However, this outcome may bring some concerns to health professionals regarding adherence to treatment and also issues inherent to the transmission of viral diseases, due to the lack of knowledge on the subject. This reinforces the importance of health education in the quality of life.

Some studies have also achieved similar results, Haq *et al.*, 2014 associated the level of knowledge of patients with HBC about their disease with HRQoL. As a result, knowledge had a negative impact on this parameter. Fear of developing cirrhosis and CHC affects the daily activities of patients and results in the worsening of health states. The same occurred in the study by Kim *et al.* (2015), which analyzed the influence of socio-demographic variables in patients with HBC in South Korea. They described that individuals with higher education have lower HRQoL scores compared to the general population.

Another telling result is that there were no differences in HRQoL between patients treated with

tenofovir and entecavir. Some authors have assessed HRQoL with the use of certain medications. Marcelin *et al.*, 2008 compared patients with HBC treated with peginterferon-alfa 2a, to patients with chronic hepatitis C also treated with this drug and found that the treatment reduces HRQoL, but to a greater extent in patients with chronic hepatitis C. For Lam *et al.*, 2009 antiviral treatment was also associated with worse results in HRQoL, however the drugs used were not specified by the authors.

However, treatment for HBC has evolved with the launch of oral nucleotide / nucleoside analogs. It is known that the oral route is safer and offers greater convenience to the patient than the subcutaneous route used for the administration of peginterferon-alfa 2a. In addition, adverse events in the first line of treatment are less aggressive than those of the drug in question (Buti, 2014). For this reason, we found no differences between individuals treated with the first line of treatment (tenofovir and entecavir), however other studies can be carried out based on this result, such as cost studies that may demonstrate the advantages of one drug over another.

Another study that evaluated patients with HBC before and after a comprehensive intervention, which included, medical assistance, antiviral treatment, monthly follow-up, educational lectures, among other strategies, demonstrated that these interventions contribute to an increase in the HRQoL of these patients (Chao *et al.*, 2013).

As the present study evaluated only patients under treatment, it is not possible to conclude if the therapy has a positive impact on HRQoL. But, as in the research by Chao *et al.*, 2013 the patients participating in this research also had a wide range of assistance offered by the government, including antiviral therapy, specialized medical assistance, monitoring with imaging tests and laboratories, in addition to quarterly or semiannual consultations depending on the complexity of each case.

Another important outcome found, when the variable comorbidity with the questionnaire domains was analyzed in isolation, was that the presence of diseases did not influence the HRQoL scores. For Lam *et al.*, 2009, the presence of psychological diseases had a

negative impact on this measure. The fact that the present research used a specific questionnaire for HBC may have contributed to this result since the questions are related to a single disease, minimizing interference from other comorbidities in the assessment of HRQoL.

Some authors also describe that patients who have been living with the disease for many years may create coping mechanisms, contributing to a better HRQoL (Poorkaveh *et al.*, 2012). Our research could not collect data on the time of the disease diagnosis, but when correlated with the treatment time with the domains of the questionnaire of 124 patients, it was not significant.

When the first line of treatment was compared, the domains of psychological well-being, anticipatory anxiety, stigma, and vulnerability were significantly correlated with the treatment time for TDF, indicating that HRQoL scores tend to be higher over time. For the ETV, this correlation was not significant, demonstrating that the values do not depend on the time in which the patient uses this medication. It is worth mentioning that this result does not depend on the number of patients who used each medication.

Most studies assessing HRQoL in patients with HBC use generic instruments or the combination of a generic instrument with a specific one for liver diseases (Abdo, 2012; Chao, Hu, 2013; Dan *et al.*, 2008; Lam *et al.*, 2009; Zhuang *et al.*, 2014). The use of a specific questionnaire such as HBQOL allows a more accurate assessment of small changes characteristic of the disease, better portraying the real HRQoL of these patients. This is the first Brazilian study that assesses the quality of life of patients with HBC through the specific questionnaire HBQOL in the routine of clinical practice and other studies can be carried out in different regions of the country with this research instrument already validated for the Brazilian version.

Due to the lack of computerized data and information in the medical records of the participants of this research, both in Curitiba and in Cascavel, some socio-demographic variables and laboratory results could not be collected and analyzed as to their impact on HRQoL. The lack of computerized systems in Brazil ends up limiting the development of research, since there is not the necessary support for this practice.

## CONCLUSION

The benefits of the treatment of HBC, in general, are long-term, preventing the patient from evolving into more severe conditions. However, these patients may also have short-term benefits, not only physical but also mental health. To this end, evaluating the quality of life is of fundamental interest. The results obtained demonstrate that the HBQOL v 1.0 questionnaire was translated validated for the Brazilian version.

In the analysis of the applicability of this instrument, the psychological well-being and stigma domains had the best HRQoL scores evaluated and individuals with the lowest level of education obtained the highest scores in these two domains. Regarding gender, women were more concerned than men about the transmissibility of the disease. The research also shows that advancing age gives significant results in the areas of psychological well-being, anticipation anxiety and stigma, providing higher scores on HRQoL. With regard to the first line of treatment, it was possible to determine that there were no significant differences between patients treated with these two drugs. The outcomes obtained in this study can be useful in making therapeutic decisions.

## ACKNOWLEDGMENTS

The authors thank the 10th Regional Health Region of Paraná and the Specialized Center for Parasitic Infectious Diseases (CEDIP) for their contribution to the development of the research, and the Coordination for the Improvement of Higher Level Personnel (CAPES) for the scholarship granted.

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Received for publication on 07<sup>th</sup> April 2019

Accepted for publication on 08<sup>th</sup> September 2020