

## HEALTH-RELATED QUALITY OF LIFE AMONG HEPATITIS C PATIENTS IN PAHANG STATE, MALAYSIA: A CROSS-SECTIONAL STUDY

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### ABSTRACT

Measurement of health-related quality of life (HRQOL) among hepatitis C patients is crucial in assisting health care providers to understand the complex psychosocial impact of disease on patients, thus facilitating a more patient-centred care. There is still scarcity of data on this matter, not adequately explored and nor has it been empirically studied in Malaysia. Thus, this study aims to measure the HRQOL among hepatitis C patients attending a tertiary hospital in Pahang, Malaysia. This was a cross-sectional study conducted among 195 hepatitis C patients attending Hospital Tengku Ampuan Afzan (HTAA), the main public tertiary hospital in Pahang. HRQOL was assessed using the 36-item short-form survey (SF-36v2). Respondents had lower scores in physical (mean score =  $48.88 \pm 8.9$ ) and mental (mean score =  $47.70 \pm 9.1$ ) health components of HRQOL than normal population (mean score > 50). Those who completed treatment had higher scores in both physical and mental health component, compared to those who was not treated or on treatment. There were no significant association between HRQOL and gender, age, marital status, employment status and education level. Our findings showed that patients with hepatitis C, in general, have poor HRQOL in both physical and mental health components. Thus, this study highlight a pressing need for a holistic disease management by taking into account patients' quality of life as part of the inter-disciplinary approach.

**Keywords:** Health-Related Quality of Life (HRQOL); hepatitis C; Malaysia

## 1.0 INTRODUCTION

The burden of hepatitis C virus infection is not limited to cirrhosis and hepatocellular carcinoma. Hepatitis C virus infection is widespread and associated with high economic costs and reduced quality of life [1]. Previous research also found that hepatitis C virus infection is associated with reduced health-related quality of life (HRQOL), even in the absence of cirrhosis [1–4].

Various studies had indicated that the diagnosis of hepatitis C and its treatment could provoke negative emotional responses that impair quality of life. HCV Quest, a global survey conducted among almost 4000 people with hepatitis C, with 131 responses recorded from Malaysians found that 47% of respondents from Malaysia reported interruption in their work. Of these, 11% claimed their work had been impacted ‘significantly,’ while 26% felt uncomfortable talking about their disease with their boss, colleagues or with staff at their school or university. Though most respondents said their relationships with their colleagues had not been affected by hepatitis C, 12% said the relationship had been negatively affected. About 16% experienced discrimination [5].

HRQOL is an important measure that provides insight into a patient’s experiences while coping with diseases and treatments. HRQOL is a multi-dimensional concept and can be defined as the patients’ subjective perception of the impact of their disease and its treatment on their daily life, and their physical, psychological and social functioning [6]. It has become a common and standard practice by researchers to measure HRQOL when assessing a patient’s experience with illness and receiving healthcare [7], as HRQOL can be an indicator of treatment effectiveness.

HRQOL studies in patients with hepatitis C have never been done in Malaysia. This study was designed to assist public health experts and policymakers in developing programs and interventions that can improve the quality of life among hepatitis C patients. Also, it helps healthcare providers in enhancing service delivery and quality of care, for instance, by promoting a multi-disciplinary engagement in the clinical setting that can increase patients’ psychological well-being.

## 2.0 METHODOLOGY

### 2.1 Design and study population

A cross-sectional study was conducted from April 2019 to August 2019 at Hospital Tengku Ampuan Afzan (HTAA) which is located in Pahang capital city, Kuantan. Respondents were recruited through convenience sampling based on the following inclusion criteria: a) aged 18 years or older; b) diagnosed with hepatitis C using serological test, and; c) attended gastroenterology clinic or was admitted to medical ward in HTAA. Patients with overt encephalopathy (grade II or more) and those proved or suspected to have hepatocellular carcinoma (based on ultrasounds, CT scan and/or alpha-fetoprotein levels) were excluded.

## 2.2 Tools and Measurements

Data collection was performed using a structured self-administered questionnaire which was given to respondents during their clinic visits. The questionnaire was available in Malay and English languages. The researcher directly approached the potential respondents and invited them to join the study. Upon agreement, each respondent received a thorough explanation about the study and had their written consent taken.

The questionnaire comprised the following sections: a) questions on socio-demographics, treatment status and clinical status; b) the SF-36v2 scale to measure HRQOL; c) other potential confounders such as comorbidities and social support. Social support was assessed using the Duke Social Support Index (DSSI).

Demographic characteristics included age, gender, marital status, employment, monthly income, educational level, comorbidity, cirrhotic status and treatment status. Marital status was categorized into 'married/ living with partner' or 'single' (including divorced, widowed or separated). Educational level assessed the highest education attained by the respondent. Monthly income was initially categorised into seven groups: <RM499, RM500-RM999, RM1000-RM1499, RM1500-RM1999, RM2000-RM2499, RM2500-RM2999 or >RM3000. Subsequently, it was collapsed into: a) B40 < RM3000, and; b) M40 + T20 > RM3000 [8]. Comorbidity was categorized into 'yes' (having any other chronic illness) or 'no'. Treatment status classified into 'treatment-naïve', 'on treatment' and 'completed treatment'. Cirrhotic status was categorized into 'yes' (cirrhotic) or 'no' (not cirrhotic). Cirrhosis is defined as an advanced stage of liver disease characterized by extensive hepatic fibrosis, nodularity of liver, alteration of liver architecture and disrupted hepatic circulation [9].

For HRQOL, the Optum™ SF-36v2® Health Survey entails 36 questions in order to measure functional health and well-being [10]. The validated Medical Outcomes Study 36-item Short-Form Health Survey (SF-36v2) in English (IQOLA SF-36v2 Standard, (English)) and Malay version (IQOLA SF-36v2 Standard, Malaysia (Malay)) were used in this study. The Malay version of SF-36v2 was validated before, with a Cronbach's alpha over 0.70 for all scales except for social functioning [11]. The SF-36v2 covers eight domains of HRQOL: physical functioning (PF, 10 items), role physical (RP, 4 items), role-emotion (RE, 3 items), bodily pain (BP, 2 items), vitality (VT, 4 items), social functioning (SF, 2 items), general health (GH, 5 items) and mental health (MH, 5 items). These eight domains are subsequently summarized into physical component summary (PCS) and mental component summary (MCS). Scoring was performed by the QualityMetric Health Outcomes™ Scoring Software 4.0. [12].

## 2.3 Analytical Approach

Statistical analyses were performed using the SPSS 21.0 for Windows. Continuous data were reported in means and standard deviations (SD) while categorical data were reported in percentages. Ethnicity and religion were excluded from bivariate and multivariate analyses as over 90% of the sample fit a Malay Muslim profile. With regards to continuous data, differences between two groups were tested by independent sample t-tests and differences between three groups or more were tested using one-way ANOVA. Association between each

variable and HRQOL was analysed using t-test, one way ANOVA and Pearson correlation. P-value below 0.05 denoted as statistically significant.

## 2.4 Ethical Approval

Ethical approval was obtained from the National Medical Research Register (NMRR), Malaysia Research Ethics Committee (MREC) and the Clinical Research Centre (CRC) of HTAA (Ethics No: NMRR-18-3536-42688).

## 3.0 RESULTS AND DISCUSSION

Hepatitis C infection is a severe public health problem because it is associated with illnesses such as chronic hepatitis, cirrhosis and hepatocellular carcinoma. Research on HRQOL is based on the fundamental concept of wellness by the WHO as a state of total physical, emotional, and cultural wellbeing, not just the absence of the disease [7].

### 3.1 Demographic and Clinical Characteristics of Study Participants

From 200 patients who were recruited, 195 respondents agreed and joined the study. The response rate was 97.5%. Age of participants ranged between 21 and 76 years old. The demographic of the subjects are shown in Table 1. However, most respondents had no genotype result as it was not tested due to limited resources. Most respondents were in a treatment naive group (53.3%). The majority were non-cirrhotic (77.9%). 48.7% of the respondents had comorbidities.

**Table 1 Demographic** characteristics of study respondents

<b>Variables</b>	<b>N</b>	<b>%</b>
<b>All patients</b>	<b>195</b>	<b>(100%)</b>
<b>Age, mean <math>\pm</math> SD</b>	195	45.6 $\pm$ 9.7
<b>Sex</b>		
Male	162	83.1%
Female	33	16.9%
<b>Marital Status</b>		
Married/ Living with partner	122	62.6%
Single	73	37.4%
<b>Employment Status</b>		
Employed	135	69.2%
Unemployed	60	30.8%
<b>Income</b>		
B40 (<RM3000)	165	84.6%
M40 + T20 (>RM3000)	30	15.4%
<b>Education Level</b>		
No formal education	1	0.5%
Primary education	37	19%
Secondary education	136	69.7%
Tertiary education	21	21%
<b>Comorbidity</b>		
Yes	95	48.7%

No	100	51.3%
<b>Cirrhosis Status</b>		
Cirrhosis	43	22.1%
Non Cirrhosis	152	77.9%
<b>Treatment Status</b>		
Treatment naive	104	53.3%
On Treatment	44	22.6%
Completed Treatment	47	24.1%
<b>Hepatitis C Virus Genotype:</b>		
Genotype 1	19	9.7%
Genotype 2	55	28.2%
Genotype 3	3	1.5%
Genotype 4	1	0.5%
Genotype 5	0	0%
Genotype 6	1	0.5%
Indeterminate	1	0.5%
Unknown/Not available/ Not tested	116	59.5%

### 3.2 Distribution of Study Participants Based on Lifestyle

Table 2 showed the lifestyle information of the participants. Here, we observed that most of the participants were current smokers, and contracted hepatitis C *via* intravenous drug; however, 60% of them were on a recovery program.

**Table 2** Lifestyle information of the participants

Lifestyle variables	Frequency, n	(%)
<b>Smoking Status</b>		
Current smoker	118	60.5%
Never smoke	49	25.1%
Ex-smoker	28	14.4%
<b>Alcohol Consumption</b>		
Yes	6	3.1%
No	128	65.6%
Used to	61	31.3%
<b>Drug Abuse</b>		
Yes	8	8 (4.1%)
No	70	70 (35.9%)
On recovery program	117	117 (60%)
<b>Mode of Transmission</b>		
Intravenous Drug User	116	116 (59.5%)
Intranasal Illicit Drug Use	9	9 (4.6%)
Recipients of blood/ blood product/ clotting factor/ concentrate / recipients of organ transplant	33	33 (16.9%)

On long term hemodialysis	1	1 (0.5%)
Tattoo/ Ear piercing	1	1 (0.5%)
Needle sticks injury	3	3 (1.5%)
Sexual Transmission	15	15 (7.7%)
Vertical Transmission	2	2 (1.0%)
Unknown	15	15 (7.7%)

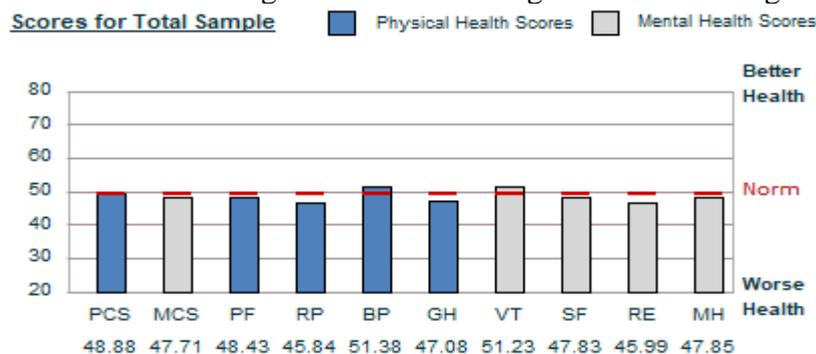
### 3.3 Significant Reduction of SF36v2 Scores Among Hepatitis C Patients

Results of the research show that all domains and summary physical and mental health scores of generic SF-36v2 in Pahang’s hepatitis C patients are below the standard (50) except for vitality and bodily pain. Table 3 displays the SF-36 quality of life dimensions scores profile. For all measurements, a wide range of scores were recorded. While the overall mean scores in all domains were below 50.00 except bodily pain and vitality, domains related to both physical and mental health status showed a comparatively lower score compared to normal population.

**Table 3** Overall scores of SF36v2 quality of life dimensions

	Physical Component Score (PCS)				Mental Component Score (MCS)			
	Physical Functioning (PF)	Role-Physical (RP)	Bodily Pain (BP)	General Health (GH)	Vitality (VT)	Social-Functioning (SF)	Role-Emotional (RE)	Mental Health (MH)
Mean	48.43	45.84	51.38	47.08	51.23	47.83	45.99	47.85
Standard Deviation (SD)	8.90	9.50	9.41	10.10	8.90	9.40	10.00	9.50
Minimum	10.00	0.00	0.00	0.00	12.5	25	8.33	25
Maximum	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00

\*Scores range from 0-100 with higher scores indicating better functioning



**Figure 1:** Average summary measure and scale

Figure 1 displayed the average summary measure and scale scores for the sample. From left to right, the physical and mental summary measures were presented followed by physical health scores and mental health scores with higher scores indicating better functioning and well-being. Underneath the graph, there is a table that lists the average scale and summary measure score.

### 3.4 Physical and Mental Quality of Life in Respond to Patient and Clinical Characteristics and Social Support

We further analysed the study cohort based on the physical and mental quality of life. Here, we found that social support and treatment status have a strong positive influence on physical and mental domain of the quality of life as stated in Table 4.

**Table 4** Univariate analysis of associations between patient and clinical characteristic, social support and HRQOL

	Physical quality of life	P-value	Mental quality of life	P-value
<b>Gender</b>				
Male	48.63±7.88	0.333 <sup>a</sup>	47.47±9.24	0.432 <sup>a</sup>
Female	50.09±7.73		48.84±8.38	
<b>Marital Status</b>				
Married	49.56±7.56	0.109 <sup>b</sup>	48.46±9.38	0.106 <sup>b</sup>
Divorced	45.55±7.73		44.45±8.60	
Widowed	51.09±10.15		52.86±8.30	
Single	48.67±8.25		46.91±8.19	
<b>Employment Status</b>				
Employed	49.31±7.34	0.287 <sup>a</sup>	47.65±8.98	0.899 <sup>a</sup>
Unemployed	47.91±8.91		47.83±9.41	
<b>Income Range</b>				
<3000	48.45±7.91	0.081 <sup>a</sup>	47.11±9.18	0.035 <sup>a</sup>
>3000	51.14±7.26		50.86±8.00	
<b>Cirrhotic Status</b>				
Cirrhosis	47.51±7.84	0.197 <sup>a</sup>	46.54±9.65	0.342 <sup>a</sup>
Non-Cirrhosis	49.27±7.84		48.04±8.93	
<b>Comorbid</b>				
Yes	47.89±8.11	0.088 <sup>a</sup>	47.49±8.71	0.746 <sup>a</sup>
No	49.81±7.53		47.91±9.48	
<b>Age</b>				
1-50	49.06±7.60	0.623 <sup>a</sup>	47.47±8.93	0.579 <sup>a</sup>
51-100	48.45±8.47		48.26±9.51	
<b>Social Support (DSSI)</b>	0.269	0.000 <sup>c</sup>	0.357	0.000 <sup>c</sup>
<b>Treatment Status</b>		0.034 <sup>b</sup>		0.008 <sup>b</sup>
On treatment	47.71±7.72		46.97±8.24	
Treatment naïve/untreated	48.21±7.89		46.42±9.14	
Completed treatment	51.45±7.49		51.24±8.99	
<b>Education Level</b>		0.379 <sup>b</sup>		0.921 <sup>b</sup>
No Formal	58.52		52.05	
Primary Education	49.06±8.56		48.37±10.01	
Secondary Education	48.47±7.81		47.52±9.05	
Education	50.76±6.74		47.53±8.13	

Tertiary Education				
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<sup>a</sup>Independent t-test, <sup>b</sup>ANOVA, <sup>c</sup>Pearson Correlation

It was not surprising to find that the patient who already completed treatment will have a better PCS and MCS score in univariate analyses. This may imply that the eradication of hepatitis C virus will improve the HRQOL. Pegylated Interferon in conjunction with Ribavirin has for years stayed the cornerstone of hepatitis C virus treatment however it was associated with lots of side effect and often deceptive therapy results. In comparison, extremely effective comparatively secure direct-acting antivirals for hepatitis C virus therapy were introduced, interferon-based regimens were replaced, and therapy prospects were changed, resulting in improved effectiveness. Most of our patient who already completed treatment received direct-acting antivirals (81% from those who received/completed treatment) that resulted in improvement of HRQOL similar to recent study finding [13].

The patient that completed treatment and tested negative hepatitis C virus RNA received many benefits. Cure of hepatitis C leads to reduce risk of cirrhosis, disappearance of esophageal varices, and reduce the risk of progression to liver cancer. It was proven that all this lead to improvement of QOL [14]. Besides that, the main public health concern of the danger of sexual and perinatal transmission disappears with cure of hepatitis C [15]. This in turn, removed the perceived hepatitis C virus infection-related stigma that leads to elevated rates of anxiety and exaggerated transmission fear that lead to a significant cause of social isolation and decreased relationship [15]. Removing psychological, family and social stigma is a tremendous advantage to all. Stigma is a fact that must be considered when setting up hepatitis C treatment and also when considering the disease's true burden.

Ample evidence points to the positive effects of social support on QOL. Supporting family and friends can enhance the physical, emotional, and function of the patient. Our study found that that social support was associated with better QOL. The higher the social support, the greater the QOL. It's also worth noting that the measured HRQOL and the patient's perception of QOL may differ. Individual beliefs, cultural variety, and personal adaptive capability may all play a role.

Nearly 60% of the participants in our study contracted hepatitis C *via* intravenous drug. In one study on social support among drug addicts in Malaysia, showed that the highest social support perceived by the addicted participants came from significant others such as wife, ex-wife, children, girlfriends etc., while the lowest perceived social support came from the father [16]. It was also discovered that drug addicts particularly perceived lower social support from their family especially mothers, fathers and siblings compared to non-addicts. This was true for all aspects of the social support investigated in the research - socializing, emotional, practical aid, economic aid, advice and instruction [16].

With prolonged detachment from the most immediate source of social support, they might have grown accustomed to it. Thus the impact of social support among this particular

group could be out-performed by other more important factors. A qualitative study will be helpful in exploring the context of social support in hepatitis C infected patient.

On the other hand, our study showed that lower-income was associated with lower mental component summary (MCS). Lower-income have been proven to be associated with an increase in mood, anxiety or substance use disorders due to continuing stress of employment insecurity, sudden and unexpected dismissals and the effects of work loss (economic, social and psychological) [17].

In comparison to other studies, the present research unable to establish strong connection between gender, age, marital status, employment status, education level with patient's HRQOL status. However, other study involving a cohort of 1817 chronically sick individuals in US (median and 12 months follow-up) showed that marriage conditions positively influenced mental wellness through personal assistance, but do not immediately impact physical or mental fitness [18].

In our study, we did not find any associations between gender and QOL. It could be due to the very small sample size of females, compared to males – which could have made it very difficult for us to find substantial difference. The reason behind it is due to most of our Hepatitis C patients in Pahang is male patient who contracted Hepatitis C via intravenous drug usage. Furthermore, other studies have disclosed that women with chronic hepatitis C tend to be more tired and depressed, which may be the reason why their HRQOL was reported to be worse than men [19].

This study hindered by several limitations. The comorbidities and cirrhosis status not significantly impaired HRQOL in Pahang population, contradicting with other studies [20]. We speculated that it could be due to qualitative approach to evaluate and categorize comorbidities. For which, the quantifying process was based on 'yes' (presence of comorbidity/ cirrhotic) and 'no' (absence of comorbidity/ cirrhotic) classification. Hence, it does not capture the whole spectrum of how existing chronic diseases can affect QOL. This warrant further analyses using the Charlson Comorbidity Index (CCI) that quantifies an individual's burden of disease and corresponding 1-year mortality risk. Comorbidity indexes usually recognize current comorbid illnesses and then apply weights or severity ratings for these illnesses [21].

#### **4.0 CONCLUSION**

This study has shown that patients with hepatitis C in Pahang, Malaysia have relatively poor quality of life pertaining to both physical and mental health components. HRQOL is influenced by both socio-demographic and clinical factors in hepatitis C patients. Remarkably, we highlighted the importance of treating hepatitis C infection and enhance the role of social supports in improving the patients' care and HRQOL. This study advocate that treating physician should incorporate multidisciplinary interventions programs based on scientific evidence to help improving quality of life in hepatitis C patients. For example, the #MYmissingmillions campaign that was announced during the World Hepatitis Day 2019 would best benefit this vulnerable group.

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