

# FACTORS AFFECTING THE HEALTH-RELATED QUALITY OF LIFE AMONG PATIENTS WITH CHRONIC LIVER DISEASE SEEN AT THE UP-PGH GASTROENTEROLOGY CLINIC

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## ABSTRACT

**SIGNIFICANCE:** The biopsychosocial model of disease encourages that physicians not only treat the physical aspect of disease. As the burden of CLD remains to be high, knowing how it impacts health-related quality of life (HRQOL) is important in aligning physician goals and patient expectations. Knowing the factors that affect HRQOL may help individualize management.

**METHODOLOGY:** HRQOL among CLD patients was determined by administering the SF36 and CLDQ. Demographic and clinical data were extracted and statistical analyses were used to ascertain factors that affect the HRQOL.

**RESULTS:** HRQOL among CLD patients is decreased in all domains of SF36 with physical component score of 45.36 and mental component score of 47.3. Mean CLDQ score was 5.36. Univariate statistics showed that severity of CLD is not associated with decreased HRQOL. Factors associated with poor scores are; etiology: ALD, HBTB and schistosomiasis, presence of ascites, repeated EVL and presence of multiple co-morbidities.

**CONCLUSION:** Improving the HRQOL of CLD patients must be part of the holistic approach to management with care on addressing the etiology disease and alleviating symptoms that impair function.

Keywords: cross-sectional survey, HRQOL, CLD, HBV, HCV, ALD, NAFLD, cirrhosis, SF36, CLDQ

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## INTRODUCTION

The World Health Organization (WHO) in 1948 defined health as a state of complete physical, mental and social well-being – not merely the absence of disease, or infirmity.<sup>1</sup> While the traditional measures of health (e.g. life expectancy, mortality rates, causes of death, etc.) have been useful as key indicators of population health, they do not offer information about the quality of the physical, mental and social domains of life.<sup>2</sup> Beginning in 1995, the WHO recognized the importance of evaluating and improving people's quality of life (QOL) and defined it as individuals' perception of their position in life, in the context of the culture and value systems in which they live in, in relation to their goals, expectations, standards and concerns. It is a complex concept affected by the person's physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to their environment.<sup>3</sup> When taken in the context of health and disease, it is commonly referred to as health-related quality of life (HRQOL).<sup>2</sup> It is multidimensional and multifactorial, going beyond the presence and severity of disease or side effects of treatment but also examining how patients perceive and experience these manifestations in their daily lives.<sup>4</sup>

Assessing HRQOL is done by using standardized and scientifically well-validated questionnaires. Generic and disease-specific questionnaires are available that have been adequately validated in different countries worldwide. Generic questionnaires are comprehensive and wide in scope and can be used for comparisons between conditions. Disease-specific surveys on the other hand are more relevant to its target population, and the clinician in terms of treatment outcomes.<sup>4</sup>

The Short Form 36 (SF36) is a generic, multi-purpose, short-form survey with 36 questions that yields an 8-scale profile of functional health and well-being scores as well as psychometrically-based physical and mental health summary measures and a preference-based health utility index developed in the early 1990s by the Medical Outcomes Trust. It has been proven useful in comparing the relative burden of diseases and in differentiating the health benefits produced by different treatments.<sup>5</sup> This survey has been translated into 140 languages and is used globally in population-based studies.

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<sup>1</sup> (World Health Organization 2014)

<sup>2</sup> (U.S. Department of Health and Human Services 2010)

<sup>3</sup> (World Health Organization 1997)

<sup>4</sup> (Glise 2002)

<sup>5</sup> (Ware n.d.)

Recently, the group of Professor Castillo-Carandang validated the Tagalog version of SF36 and concluded that it is a reliable instrument for measuring health status among tested subjects.<sup>6</sup>

The Chronic Liver Disease Questionnaire (CLDQ) is a 29-item survey that was developed in 1999 to specifically address HRQOL studies for chronic liver disease (CLD). It was the first disease-specific questionnaire developed for CLD, and was found to correlate with SF-36 scores but reflecting more responsiveness with clinical deterioration.<sup>7</sup> In 2010, the CLDQ was translated and validated by Dr. Lei-Mercado into Filipino and was found to be a valid and reliable quality of life tool which can be used among Filipinos with CLD.<sup>8</sup>

The burden of CLD in the Philippines is unknown. While the nationwide prevalence of chronic hepatitis B virus (HBV) infection remains high<sup>9</sup> and the overall prevalence of chronic hepatitis C virus infection (HCV) remains unknown, lifestyle-related diseases such as alcoholic liver disease (ALD) and non-alcoholic fatty liver disease (NAFLD) have also been recognized as major contributors to this burgeoning health problem.<sup>10</sup> Physical sequelae of chronic liver disease may range from mild nonspecific symptoms to overt manifestations of liver cirrhosis such as debilitating fatigue, pruritus, ascites, encephalopathy, bacterial peritonitis and variceal bleeding.<sup>11</sup> These complications may also give negative impact on a patient's well-being, and quality of life.

This study aims to to ascertain the biomedical and psychosocial factors that affect the health-related quality of life of Filipinos with chronic liver disease, to be able to add insight on the holistic management of CLD and the psychosocial burden of this disease.

## **METHODS**

### *Ethics and setting*

We conducted a cross-sectional study reviewed and approved by the University of the Philippines Manila Review and Ethics Board, involving patients diagnosed with chronic liver disease seen at the University of the Philippines-Philippine General Hospital Gastroenterology Clinic from October to December 2015.

### *Population*

All patients were adult patients diagnosed with CLD, defined as the presence of a liver condition that leads to destruction and regeneration of liver parenchyma resulting in fibrosis, and/or, cirrhosis. Adult

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<sup>6</sup> (Castillo-Carandang 2013)

<sup>7</sup> (Younossi 1999)

<sup>8</sup> (Lei-Mercado 2010)

<sup>9</sup> (Gish 2015)

<sup>10</sup> (De Lusong 2008)

<sup>11</sup> (Afendy 2009)

patients who were able to provide consent and did not have, a diagnosed psychiatric condition, overt encephalopathy, mental retardation and active malignancy were included in the study.

### *Data Collection*

At the end of patient consult, inclusion in the study was discussed to a candidate patient. Once consent is given, a standardized data collection form was used using number codes to conceal identity. Demographic data such as age, sex, and marital status, geographical area of habitation, educational attainment and monthly household income were noted. Clinical profile was also taken which included etiology of CLD, severity of CLD using the Child-Turcotte-Pugh score, aminotransferase levels, creatinine level, presence of esophageal varices, previous history of variceal bleeding and history of repeated sessions of endoscopic variceal ligation when available. Presence of co-morbid illnesses were also noted.

### *HRQOL Surveys*

We administered the Filipino versions of the SF36 version 2 (SF36v2) (see Appendix A) under license from Optuminsight Life Sciences Inc. The Filipino version of SF36v2 consists of 36 questions targeting 8 domains, which can be further simplified into 2 summary scores, namely the Physical Component Score (PCS) and the Mental Component Score (MCS). The PCS represents the overall physical health of a patient and is measured using the domains on physical function (PF), carrying out physical roles (RP), severity of bodily pain (BP) and general sense of well-being (GH). The MCS on the other hand is composed of the social and emotional health of the patient represented by sense of vitality (VT), social functioning (SF), emotional roles (RE) and mental health (MH). SF36v2 scores were interpreted using the SF Health Outcomes Software Version 4.5 provided by Optuminsight.

To ascertain disease-specific HRQOL, we also administered the CLDQ under license from the Center for Outcomes Research in Liver Diseases (COR-LD) (see Appendix B). It includes domains on abdominal symptoms (AS), fatigue (FA), systemic symptoms (SS), activity (AC), emotional function (EF), and worry (WO). CLDQ scores were tabulated according to its scoring and interpretation manual.

### *Statistics*

Unpaired t-test was done to compare mean SF36v2 scores between healthy Filipino subjects and CLD patients. Univariate analysis of variance (ANOVA) was used to test the difference in SF36v2 and CLDQ scores with respect to severity of CLD. P values <0.05 were noted to be statistically significant differences. Linear regression analysis was used to demonstrate the association of demographic and clinical factors (e.g. age, sex, household income, severity of CLD) to different HRQOL domain scores. Results were deemed statistically significant if a threshold p value of <0.1 was derived.

## RESULTS

Tables are shown in Appendix C.

### *Demographic data*

Of the 68 recruited patients, 41 (60.29%) were males and 27 (39.71%) were females. The mean age was 45.9 years with median age of 49 and mode of 55 years. Forty seven (69.12%) patients live in the urban setting. Most patients recruited were below the poverty line with monthly household income of less than five thousand pesos (35 or 51.47%). The most common cause of CLD was HBV (51.47%) followed by ALD (20.59%), NAFLD (13.24%), hepatobiliary tuberculosis (HBTB) (8.82%), HCV (1.47%), schistosomiasis (1.47%). Two patients (2.94%) were still undergoing workup to ascertain etiology of CLD. Thirty two (47.06%) patients were cirrhotic, with equal number of Child A and Child B disease severity. There were no Child C patients recruited in the study. Esophageal varices were present in 24 (35.29%) of patients with 17 (25%) having history of upper gastrointestinal bleeding. Eighteen patients underwent repeated endoscopic variceal ligation (EVL) sessions. Ascites was observed in 13 (19.12%) of CLD respondents. The most common co-morbid illness was hypertension followed by type 2 diabetes mellitus and pulmonary tuberculosis. Seven patients had more than 2 co-morbidities. Table 1 summarizes demographic data.

### *HRQOL of CLD patients*

Tables 2 and 3 summarizes the mean SF36v2 and CLDQ scores of respondents respectively. SF36v2 scores among CLD patients were noted to be decreased among all domains and were statistically different from a previously conducted survey among healthy normal Filipinos. The mean CLDQ score was 5.36, fatigue garnering the lowest score (5.06) followed by emotional function (5.26), worry (5.36), activity (5.45), abdominal symptoms (5.49) and systemic symptoms (5.63). Univariate ANOVA shown in Table 4 demonstrates numerically decreasing trends in HRQOL scores in general with progressing liver disease severity, but these were statistically significant only in the RP, GH, RE domains of SF36 and none in the domains of CLDQ.

### *Factors affecting HRQOL*

Tables 5 and 6 shows linear regression analysis of variables that may affect HRQOL when applied to SF36 and CLDQ respectively.

Age, was not shown to be correlated to SF36 domains. Male sex shows a positive correlation to the BP, GH and MH domains. Better education also shows positive correlation to PF and MH. Negative association is noted among ALD patient in terms of GH, MH and MCS. HBTB on the other hand is associated negatively to VT and SF. Schistosomiasis is negatively associated with RP and RE. Weak negative association is noted with increasing AST to RP and RE, while positive association is noted in

PF, RP and RE with regard to increasing ALT. Having 2 or more co-morbidities negatively impacts on RP, BP, GH, MH, and MCS. Ascites shows negative association to HRQOL in terms of BP, GH, SF, RE and PCS.

Only AST levels and repeated EVL sessions showed negative association to CLDQ domains (WO and FA, respectively).

## DISCUSSION

Our data shows that patients with CLD have impaired HRQOL in all domains of the SF36 compared to healthy Filipinos.<sup>6</sup> These findings are consistent with other studies done in different countries.<sup>11, 12, 13, 14, 15</sup>

Since this is the first study to employ the recently validated CLDQ, the mean score of this questionnaire may be used as a baseline for future comparison studies. Parkash<sup>16</sup> in 2011 used the cutoff of 5 to categorize HRQOL among patients with cirrhosis in Karachi, with patients scoring  $\geq 5$  as having better HRQOL than those scoring  $< 5$ . Our data probably represents well-compensated CLD patients most of whom are non-cirrhotics, as such, validating the previously noted utility of CLDQ as a more sensitive tool in progressing liver disease.<sup>7</sup>

Several studies have demonstrated factors that may affect HRQOL among CLD patients, with inconsistent results. Many studies have shown that HRQOL is impaired as disease severity progresses in terms Child-Turcotte-Pugh scores.<sup>12,15,17,18</sup> This was not observed in our data, despite numerically decreasing scores in SF36 and CLDQ in general, these differences were not statistically significant. Moreover, our data set did not include Child C patients who may have exhibited worse clinical scores.

Etiology of CLD have also not been consistently observed to affect HRQOL. One study showed association of HBV<sup>12</sup> to impaired HRQOL, while others have shown that NAFLD were related to decreased scores.<sup>11,14, 19</sup> In our study, negative impact was noted among ALD patients in GH, MH and MCS. HBTB was seen to correlate with decreased vitality and social function, probably still reflecting the social stigma associated with tuberculosis, while schistosomiasis was noted to affect physical role functioning and emotional role functioning. These findings were not previously noted in reviewed

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<sup>12</sup> (Zhi-Jun 2007)

<sup>13</sup> (de Souza 2015)

<sup>14</sup> (Thiele 2013)

<sup>15</sup> (van der Plas 2003)

<sup>16</sup> (Parkash 2011)

<sup>17</sup> (Gao 2012)

<sup>18</sup> (Lam 2009)

<sup>19</sup> (Dan 2007)

literature. In terms of CLDQ however, our study has not shown that the etiology of CLD is associated with decreased HRQOL as with other authors.<sup>13, 17, 18, 20, 21</sup>

Consistent with the findings of Gao, recurrent variceal ligation also negatively impacts HRQOL. Moreover, ascites as reported in similar studies has been showed to affect physical and emotional perceptions of CLD patients.<sup>17</sup> The presence of 2 or more co-morbidities greatly impacts HRQOL, but this may not purely reflect that caused by CLD itself. Interestingly, level of education has positive correlation to physical functioning and mental health.

Our study has attempted to demonstrate the use of HRQOL questionnaires to ascertain factors that may complement holistic clinical management of CLD. It has shown that the SF36 and CLDQ are quick and reliable tools by which clinicians may integrate psychosocial aspects in the approach to care for CLD. We have limitations in our study however, which include, low sample size, the absence of severe liver cirrhosis from the analysis and lack of CLD patients from other rarer etiologies. In addition, since the study setting is at a tertiary, charity hospital, located in the city, potential selection bias may have occurred. A larger, probably a nationwide study, may be instituted to further elucidate the true psychosocial burden of CLD.

In summary, our study has shown that HRQOL is decreased among patients with CLD. Etiology of CLD may affect certain aspects of the HRQOL, as well as the presence of ascites, recurrent variceal ligation and multiple co-morbidities. Managing these aspects of CLD may help improve the psychosocial outlook of patients of CLD.

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<sup>20</sup> (Kalaitzakis 2008)

<sup>21</sup> (Sumskiene 2006)

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