

Electronic Physician (ISSN: 2008-5842)

August 2015, Volume: 7, Issue: 4, Pages: 1214-1219, DOI: 10.14661/2015.1214-1219

Health-related quality of life (HRQOL) in children with chronic liver disease in North East Iran using PedsQLTM 4.0

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Type of article: Original

Abstract

Background: Health-related quality of life (HRQOL) is a concept that relates to an individual's perception of health status in relation to the culture and value systems in which they live, in addition to their expectations, goals, concerns, and living standards. Considering the size of the population affected by Chronic Liver Diseases (CLDs) and the severity and chronic nature of the symptoms, there is an emerging need to evaluate the quality of life of patients using a standard protocol. The aim of this study is to assess the HRQOL in children with CLD based on child self-report and parent proxy-report forms.

Methods: A total of 164 children, 55 CLD and 109 healthy children (aged 6-17 years), upon referral from the Pediatric Department at Ghaem Hospital in Mashhad from 2010 to 2014 were enrolled in this case-control study. We used the PedsQLTM 4.0 generic score scale to assess the HRQOL in children with CLD compared to the control group based on child self- and parent proxy reports.

Results: According to the child self-reports, the total HRQOL in the case group (89.93 ± 9.63) was significantly lower than control group (93.05 ± 9.28) (p=0.006). We found significant differences in emotional functioning based on the CLD child self-reports (p=0.001) and their parent proxy-reports (p=0.002). Furthermore, there was a statistically significant correlation between the severity and physical functioning as reported by the Child-Pugh score (p=0.03, r= -0.31) and the MELD/PELD scores (p=0.01, r= -0.35), based on child self-reports. Gender, age of onset, CLD types, duration of the disease, and treatment showed no significant differences with total HRQOL. **Conclusion:** HRQOL is significantly lower in children with CLD in comparison to the normal population. We

strongly recommend considering different aspects of quality of life, especially emotional functioning concomitant to the therapy programs.

Keywords: chronic disease, liver disease, quality of life, children, questionnaire

1. Introduction

Health-related quality of life (HRQOL) is a concept that involves an individual's perception of her or his health status in relation to the culture and value systems in which they live. In addition to their expectations, goals, concerns, and living standards, HRQOL takes into account the presence of physical, mental, and social well-being. This notion is influenced by the patients' healthcare systems. Chronic liver disease (CLD) includes a broad spectrum of diseases, including viral and alcoholic hepatitis, and autoimmune and metabolic diseases, all of which may result

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Received: June 07, 2015, Accepted: July 29, 2015, Published: August 10, 2015

iThenticate screening: July 29, 2015, English editing: August 06, 2015, Quality control: August 08, 2015

© 2015 The Authors. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made. in cirrhosis and hepatocellular carcinomas. Patients may suffer from different types of CLDs and concomitant symptoms, including fatigue, anorexia, pruritus, and depression. The long recrudescent course of the disease exerts considerable negative impact on patients' health and lifestyle. Therefore, several arrangements and validated questionnaires have been designed to measure the HRQOL in CLD patients. In patients with CLDs, the severity of disease, as determined by stage of fibrosis or Child-Pugh scores, appears to have a considerable relationship with HRQOL.

Considering the percentage of the general population affected by CLDs and the severity and chronic nature of the symptoms, a need emerges for evaluating the quality of life using standard protocol questionnaires in different agegroups. The aim of this study is to assess the HRQOL in children with CLD using the PedsQLTM 4.0 questionnaire based on child self-report and parent proxy-report forms. We assumed that CLD in children would exert a significant negative effect on their quality of life and the severity of the disease would also be a matter of importance.

2. Material and Methods

This was a prospective case-control study approved by the ethics committee of Islamic Azad University. Patients and their parents were informed of the purpose of the current trial and they signed informed consent forms before their enrollment. A total of 164 children (55 CLD and 109 healthy children) were recruited from the Pediatric Department at Ghaem Hospital in Mashhad from 2010 to 2014. Inclusion criteria included children and adolescents (aged 2 to 18 years old) affected by chronic liver disease without considering its etiology. Chronic disease was defined as a disease that lasted for 6 months or more for which there is no cure. Parents of patients did not suffered from any type of liver dysfunction.

The current HRQOL questionnaire in pediatrics was designed by the World Health Organization (WHO) and consisted of the 23-item HRQOL generic core scales for children and teens aged 2 to 18 years old. We used the PedsQL[™] 4.0 questionnaire Farsi version that evaluated the reliability, validity, and feasibility of the questioner in healthy Iranian children of the same age group. The PedsQL[™] 4.0 generic core scale is a 23-item questionnaire of self and proxy reports consisting of 4 scales to evaluate physical, emotional, social, and academic functioning. A 5-point response scale ranges from 0 (never a problem) to 4 (almost always a problem). Each item is reverse-scored and linearly transformed to a 0-100 scale, with higher agreement placed at the top of the scale. Our participants were aged between 6 and 17 years and if the child or teen was unable to complete the self-report forms, the study administrator read a questionnaire aloud for them and avoided suggesting a specific answer by avoiding intonation change. Parents self-administered the PedsQLTM 4.0 after a brief instruction from the administrator. Upon entry, we also gathered the required demographic data and laboratory tests related to CLD to calculate Child–Pugh and MELD/PELD scores in the case group. The mean score of each scale was calculated for further statistical analysis.

In order to measure the magnitude of the differences between two groups, we calculated the effect size defined as the difference between the means of the case and control groups, divided by the pooled standard deviation (SD). The most well-known benchmarks have been presented by Cohen, whereby 0.2 equates to a small effect, 0.5 equates to a medium effect, and effects larger than 0.8 equate are considered large (14). A negative effect size means that, on average, the control group performed better than case group. SPSS version 11.5 (SPSS Inc., Chicago, IL, USA) was used for all statistical procedures. Data were expressed as mean \pm SD. Statistical analysis was performed with the Wilcoxon rank-sum test, Chi-square analysis, Fisher's exact test, and Spearman's rank correlation coefficient. P-values less than 0.05 was deemed to imply a statistically significant difference.

3. Results

Among the 164 participants, 55 CLD cases (27 boys and 28 girls) and 109 healthy individuals (52 boys and 56 girls) were enrolled and completed the questionnaire. We matched the two groups based on their ages (case= 8.91 ± 4.73 vs. control= 8.97 ± 4.54 years old), sex, and ethnicity. The demographic characteristics of our patients (Table 1) showed that the most common etiology of chronic liver disease was autoimmune hepatitis and metabolic diseases were the most common cause of cirrhosis (25.5%). Children and their parents completed the PedsQLTM 4.0 questionnaire independently and the final results are presented in Tables 2 and 3. According to the results, the total HRQOL of child self-report scores in the case group (89.93 ± 9.63) was significantly lower (p=0.006) than CLD control group (93.05 ± 9.28). While based on parent proxy-reports, total HRQOL was slightly higher in control group, but not statistically significantly different. The effective size for both reports were in the small range (Tables 2 and 3).

| <u> </u> | 1 |
|---|---------------|
| Female, n ¹ (%) | 27 (49.1) |
| Male, n (%) | 28 (50.9) |
| Age of onset (months), mean (SD^2) | 59.31 (59.36) |
| Duration of treatment (months), mean (SD) | 45.43 (25.8) |
| Course of disease (months), mean (SD) | 51.96 (29.67) |
| CHILD ³ , mean (SD) | 5.78 (1.15) |
| MELD/PELD ⁴ , mean (SD) | 9.67 (3.74) |
| Metabolic disease, n | 14 |
| Cryptogenic cirrhosis, n | 11 |
| Autoimmune hepatitis, n | 11 |
| Wilson, n | 10 |
| Chronic hepatitis B, n | 6 |
| Cholestatic diseases, n | 3 |

Table 1. Demographic and clinical characteristics of patients with chronic liver disease

¹*n*: Number; ²*SD*: Standard deviation; ³*CHILD*: Child-Pugh score; ⁴*MELD*/*PELD*: Model for end-stage of Liver Disease/Pediatric end-stage liver disease

| Scale | Case | | Control | | | |
|-----------------------|-------|--------|---------|-------|---------|-------------|
| | Mean | SD^1 | Mean | SD | P-value | Effect size |
| Physical functioning | 88.78 | 17.55 | 93.11 | 10.63 | 0.176 | -0.14 |
| Emotional functioning | 85.25 | 12.62 | 92.87 | 12.24 | 0.001 | -0.29 |
| Social functioning | 93.15 | 18.91 | 92.74 | 12.65 | 0.326 | 0.01 |
| School functioning | 92.59 | 15.51 | 93.72 | 12.98 | 0.993 | -0.03 |
| Total mean score | 89.93 | 9.63 | 93.05 | 9.28 | 0.006 | -0.16 |

Table 2. Child-self reports of the PedsQL 4.0 Generic Core Scale scores in case and control groups

¹SD: Standard deviation

| Table 3. Parent-proxy rep | oorts of the PedsQL 4.0 Gener | ric Core Scale scores in case | and control groups |
|---------------------------|-------------------------------|-------------------------------|--------------------|
|---------------------------|-------------------------------|-------------------------------|--------------------|

| Scale | Case | | Control | | | |
|-----------------------|-------|-------|---------|-------|---------|-------------|
| | Mean | SD | Mean | SD | P-value | Effect size |
| Physical functioning | 84.00 | 20.69 | 87.54 | 14.05 | 0.551 | -0.09 |
| Emotional functioning | 78.40 | 17.50 | 85.99 | 16.34 | 0.002 | -0.21 |
| Social functioning | 88.48 | 20.50 | 87.65 | 16.20 | 0.344 | 0.02 |
| School functioning | 87.72 | 22.04 | 89.75 | 16.22 | 0.898 | -0.05 |
| Total mean score | 86.72 | 15.42 | 87.80 | 11.49 | 0.119 | -0.39 |

¹SD: Standard deviation

Comparing each scale in both groups, there was only a significant difference in emotional functioning based on the child self-reports (p=0.001) and total HRQOL score (p=0.006), with the majority of effect sizes in the small range (>0.2). According to the parent proxy-reports, HRQOL scores in children with CLD were statistically significant with regards to emotional functioning in comparison to the control group (p=0.002), with small effect sizes across all domains. The greatest negative effect size (-0.29) occurred in emotional functioning based on child self- and parent proxy reports. Moreover, the analysis showed significant correlation between CLD children and their parents` scores (p=0.001) on all four PedsQLTM 4.0 Generic scales (physical (r=0.723), emotional (r=0.726), social (r=0.528), and school (r=0.740) functions), with the greatest level of agreement with the PedsQLTM 4.0 school scale. There were no significant differences in total HRQOL scores between girls (88.66±12.16) and boys (91.27±5.986) in the children self-reports (p=0.865) and the parent proxy-reports (p=0.533). Our results found no correlation between age and total HRQOL considering child self-reports (r=0.133, p=0.227) and parent proxy-reports (r=0.554, p=0.082). We also evaluated the severity of CLD disease based on Child-Pugh and MELD/PELD scores in the case group (Table 4). Based on child self-reports, there was no statistically significant correlation between severity and HRQOL score scales, except that physical functioning was statistically related to the Child-Pugh score (p=0.03, r=-0.31) and MELD/PELD scores (p=0.01, r=-0.35). There was no significant relation between Child-Pugh and MELD/PELD scores and parent proxy-reports in case group (p < 0.05, Table 4). Finally, based on child self- and parent proxy-reports, we found no significant relation between the onset age of CLD, types of CLD, duration of the disease, and treatment type.

| | CLD ¹ cł | nild self-repo | ort | | Parent proxy-report | | | | |
|-----------------------|---------------------|----------------|-----------------------------------|-------------|---------------------|---------|-----------------|---------|--|
| Scale | CHILD ² | score | core MELD/PELD ³ score | | CHILD s | score | MELD/PELD score | | |
| | r ⁴ | P-value | r | r P-value r | | P-value | r | P-value | |
| Physical functioning | -0.310 | 0.038 | -0.359 | 0.016 | -0.208 | 0.127 | -0.009 | 0.946 | |
| Emotional functioning | 0.112 | 0.466 | 0.063 | 0.679 | -0.011 | 0.938 | 0.129 | 0.346 | |
| Social functioning | 0.289 | 0.054 | 0.154 | 0.311 | -0.200 | 0.143 | -0.182 | 0.184 | |
| School functioning | 0.043 | 0.777 | 0.059 | 0.703 | 0.021 | 0.879 | 0.045 | 0.744 | |
| Total mean score | 0.084 | 0.585 | 0.098 | 0.522 | 0.095 | 0.489 | 0.025 | 0.858 | |

| Table 4. Comp | arison of | CHILD | and MELD/ | PELD sco | es based | on | child-self | and | parent-proxy | reports | of the |
|----------------|-----------|-----------|----------------|----------|----------|----|------------|-----|--------------|---------|--------|
| PedsQL 4.0 Gen | eric Core | Scale sco | ores in case g | roup | | | | | | | |

¹*CLD*: Chronic liver disease; ²*CHILD*: Child-Pugh score; ³*MELD/PELD*: Model for End stage of Liver Disease/Pediatric end-stage liver disease; ⁴*r*: Correlation coefficient

4. Discussion

In recent decades, there has been a rise in concern regarding HRQOL for different diseases. To our knowledge, this is the first study to evaluate the HROOL of CLD children in Iran. In the current study, we assessed the HROOL of children with CLD using the PedsQLTM 4.0 questionnaire, which is based on child self-report and parent proxyreports. Our finding suggested a significantly lower emotional functioning and total HRQOL in CLD children, based on self-reports. Nydeggar et al. showed lower physical functioning in children with chronic hepatitis C virus (HCV) relative to non-HCV children. In Alonso et al.'s study, pediatric liver transplant recipients also scored significantly lower in physical and general health compared to the normative sample. In agreement with our results, several studies have reported that HRQOL in children with chronic diseases is lower than in the healthy population. These results can be explained by the fact that illness places a heavy burden on different aspects of their health, which changes their attitude towards life. As far as children are concerned, parents' judgment is of great value. To help define this relationship, our investigation revealed a correlation between CLD child self- and parent proxy-reports in all five scales. This result is in concordance with Alonso et al., which studied liver transplant in children and Gulati et al., where children with autoimmune disease were studied. A recent cross-sectional study by Sundaram (2013) showed moderate agreement across all scales, except social functioning in children with biliary atresia with their native livers. In our study, the strongest agreement was in school functioning that may represent parents' higher ability to judge the observable health status in their children. According to a systematic review by Upton (2008), parents of affected children exhibit a tendency to underestimate child HROOL. We also found a negative correlation between severity (Child-Pugh and MELD/PELD scores) and physical functioning based on child self-reporting. This result is supported by Younossi and Gutteling, who showed that disease severity was related to lower HRQOL scores in patients with CLD. These results differ from Häuser et al., which determined severity of disease had no effect on HRQOL. Parent-proxy reports showed no significant correlation with severity on any scale. Gender assessment in Afendy et al.'s study showed more HRQOL impairment in female patients with CLD. In contrast to their result, we found no differences between males and females in both child and parent reports, similar to the Zuberi and Häuser studies. Some studies have previously reported no relation between age and HRQOL in CLD patients. This result is in concordance with our own and in contrast to Younossi et al. who stated that more advanced age is associated with poorer HRQOL. Our results may originate in the negative health perceptions and emotional statuses that occur during chronic diseases that influence different aspects of life in every age group. Although the results of this study report lower HRQOL in children with CLD, a chronic liver disease-specific questionnaire accompanied with the PedsQLTM 4.0 questionnaire can shed light on other particular and negative effects CLD has on patients' health. A validated CLD-specific questionnaire in Farsi may be more helpful to reach the desirable goal.

5. Conclusions

In summary, these findings have various implications for future practice. Clinicians, healthcare, and policy makers should be more concerned with the practical value of measuring HRQOL. Furthermore, this study highlights the

importance of parents being well acquainted with their child perception of quality of life and illness to help the children consciously adapt to the situation.

Acknowledgments:

We would like to express our appreciation to the Clinical Research Development Center at Ghaem Hospital in Mashhad, Iran for their valuable assistance with this manuscript.

Conflict of Interest:

There is no conflict of interest to be declared.

Authors' contributions:

All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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