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Original Research

Gender Disparities in Quality of Life Among Chronic Liver Disease Patients: A Meta-Analysis

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Abstract

Introduction: Chronic liver diseases have a high prevalence among males and females in the world. It affects the quality of life of the patients. The chronic liver disease questionnaire is an instrument consisted of 6 domains developed in 1999 to measure the quality of life in chronic liver diseases. Objectives: To compare the quality of life between males and females in chronic liver diseases using the chronic liver disease questionnaire. **Methods:** We searched PubMed, Google Scholar, and Embase through February 2024 for studies that compared the quality of life in chronic liver disease between males and females using the chronic liver disease questionnaire. Effect sizes are reported as the variance of the mean difference and the mean difference values. We used the PRISMA checklist to report our results. Sensitivity analysis was performed to detect any study that had a high impact on our overall results. **Results:** We analyzed data from 8 studies with 6846 total number of patients. Women showed a significant worse quality of life than men in 5 domains of the chronic liver disease questionnaire. These domains are abdominal symptoms, systemic symptoms, activity, emotional functioning, and worry. There was no significant difference in the fatigue measurement between males and females. The overall score shows a significant difference between the two groups with a mean difference of 0.32 (95% confidence interval, 0.14 to 0.49). **Conclusion:** This study reveals that women with chronic liver disease suffer a significantly worse quality of life than men, particularly in areas such as abdominal symptoms, systemic symptoms, activity, emotional functioning, and worry. No significant difference was found in the fatigue domain. These insights underscore the urgent need for gender-specific interventions to enhance the quality of life for women battling chronic liver disease.

INTRODUCTION

Chronic liver disease (CLD) is defined as a continuous process of inflammation that leads to destruction of liver functions, which includes synthesis of clotting factors, other proteins, detoxification of harmful products of metabolism and enzyme excretion. If not controlled, it will lead to fibrosis and cirrhosis. [1] Non- Alcoholic Fatty Liver Disease (NAFLD) is a condition in which excess fat is stored in the liver, which may cause inflammation of cell damage. Non-Alcoholic Steatohepatitis (NASH) is a progressed form of NAFLD when the inflammation increases and causes liver cell damage and liver scarring. NASH is the most leading cause of liver transplantation in the US. [2,3] The burden of liver disease in the United States is substantial and growing. Chronic liver disease (CLD) and cirrhosis were the 12th leading cause of death in the U.S. in 2020, demonstrating the serious public health impact. CLD encompasses a range of conditions, including non-alcoholic fatty liver disease (NAFLD), viral hepatitis, and alcoholic liver disease, all of which can lead to scarring, organ failure, and an increased risk of liver cancer. The economic toll is also significant, with billions of dollars spent annually on liver disease management. Beyond direct medical costs, CLD causes work absenteeism, decreased productivity, and a reduced quality of life, further highlighting the multifaceted ways this disease burdens both individuals and society as a whole.

NAFLD is one of the most growing diseases worldwide with a global prevalence estimated at 24%. In the US, the prevalence is estimated to be more than 31% of the population. [4–6]the burden of the different types of liver diseases in the USA may be changing. Our aim was to assess the shift in the prevalence of different liver disease aetiologies in the USA over the past three decades.\nDesign National Health and Nutrition Examination Surveys (NHANES; cross-sectional 1988–1994 and 1999–2016 Chronic liver disease patients experience different non-specific symptoms including fatigue, abdominal pain, insomnia, depression, distress, and anxiety. These symptoms cause significant impairment in their quality of life and work productivity. [7–9]

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Chronic Liver Disease Questionnaire (CLDQ) is a disease specific instrument. It contained 29 items and it was developed in 1999 for measuring health-related quality of life (HRQL). The domains included in CLDQ are Abdominal symptoms, Fatigue, Systemic symptoms, Activity, Emotional function, and Worry. The response option for each domain consisted of these options: 1 All of the time, 2 Most of the time, 3 A good bit of the time, 4 Some of the time, 5 A little of the time, 6 Hardly any of the time, and 7 None of the time. [10] Based on the response options, less score means worse quality of life

Rationale

With high prevalence and uncertainty of specific symptoms, it is important to measure the quality of life in those patients who experience a disease with many stages and different manifestations. Understanding the difference in quality of life between males and females is a keystone toward enhancing the healthcare.

Objectives

To measure the difference between the quality of life of men and women who are having chronic liver disease using the Chronic Liver Disease Questionnaire (CLDQ).

METHOD

Search strategy

We searched English language publications and abstracts on PubMed, Google Scholar, and EMBASE through February 2024. We also searched the reference list and the citation for each study to identify any additional studies.

Inclusion and exclusion criteria

We included any study that measured the difference between males and females in quality of life by using CLDQ on chronic liver diseases, NAFLD, and NASH. We excluded any studies that did not report the difference between males and females in the CLDQ answers.

Search

We used the following keywords to generate our search: CLDQ AND men vs women, NAFLD AND NASH AND CLDQ, Chronic Liver Disease AND CLDQ, NAFLD AND NASH AND Quality of Life. We did not contact the original authors to obtain extra data parameters.

Data collection process

The following information was extracted from eligible studies: title of the study, author's first and last name, diseases, the total number of patients (males vs females), CLDQ answers (7 domains), and the p values.

Data variables

The variables extracted from the studies are the following: CLDQ scores for males and females for each domain including CLDQ overall, abdominal symptoms, fatigue, systemic symptoms, activity, emotional functioning, and worry.

Statistical analysis

We calculated the variance of the mean difference between males and females for each CLDQ domain. A random-effects model was performed in this meta-analysis to estimate the average mean difference of the studies. Q and I^2 statistics were used to assess heterogeneity among studies. Heterogeneity was considered to be low when I^2 values of 25%, medium heterogeneity when I^2 value of 50%, and high heterogeneity when I^2 value of 75%. [11] We used the metaphor package of R (version 3.6.1) to conduct the analyses and statistical tests. We performed a sensitivity analysis to detect any study that has a high impact on the overall analysis. We performed multiple random-effect models. Every time we run the model; we exclude one study then we run the random-effect model again. We repeated this process 48 times to see if estimates change by excluding some studies.

RESULTS

Study selection

2304 found papers, after removing duplicates and reviewing titles and abstracts, we excluded a total of 2288 papers. We reviewed the remaining 16 papers and we excluded 8 papers, because they did not include a comparison in CLDQ between males and females.

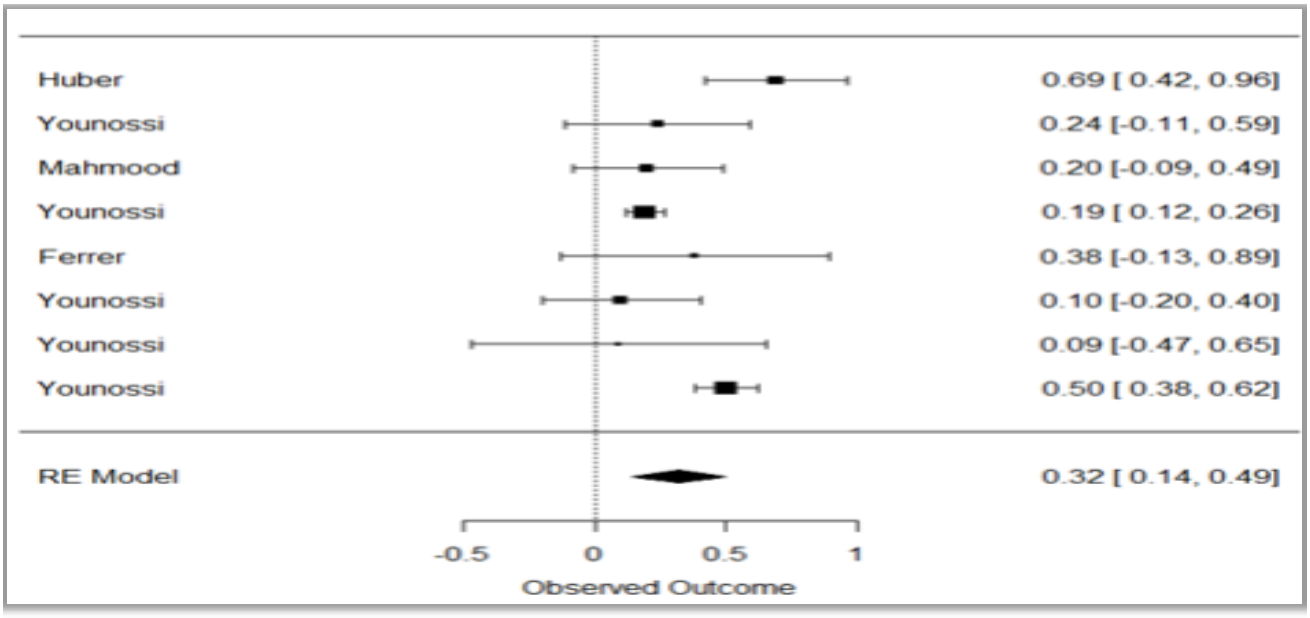
Study characteristics

One study was performed in Germany, United Kingdom, and Spain [12], one study was performed in Japan [13], one study was performed in North America, Europe, Australia, and New Zealand [14], one study was conducted in Spain [15]regardless of underlying etiology. The aim of this study was to develop a Spanish version of the CLDQ, and to assess its acceptability, reliability, validity, and sensitivity to change. The forward and back-translation method by bilingual translators, with expert panel and pilot testing on patients, was used for the adaptation. The final version was self-administered, together with the Short Form-36 Health Survey (SF-36, one study was conducted in 27 countries [16] , and three studies were conducted in the US [17–19]. The sample size between studies varied from 104 patients to 4142 patients. Not all studies reported all the domains of CLDQ; however, we used the information provided by the studies to compare between each domain of quality of life.

Model results

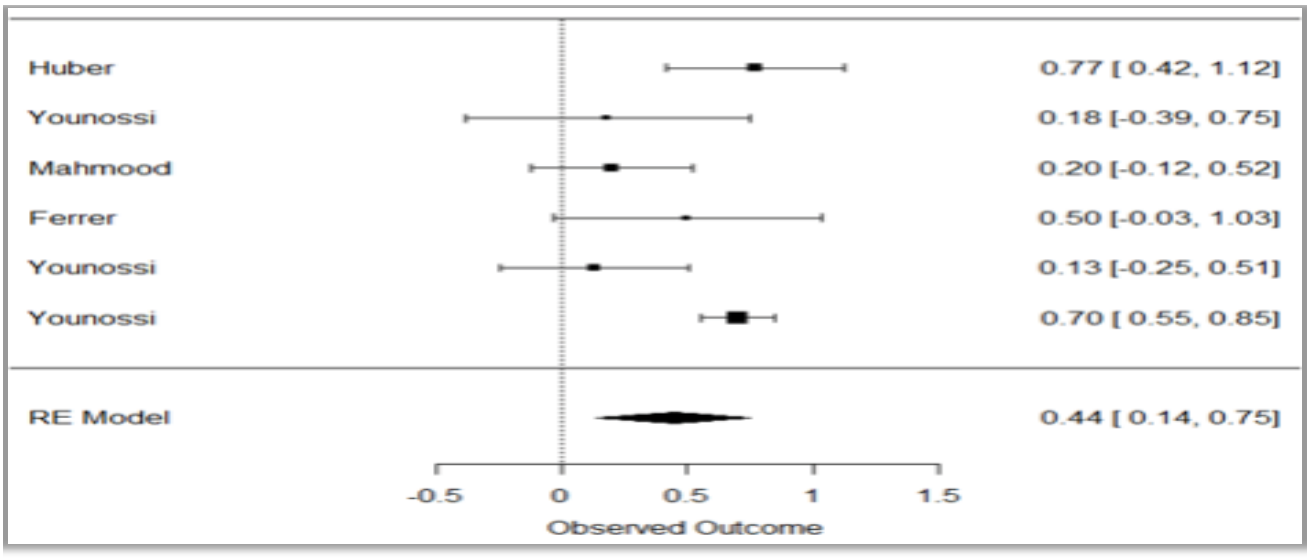
Our results showed that there is a significant difference between the quality of life between males and females in five domains of CLDQ in chronic liver disease including the CLDQ overall score. The results for each domain are: CLDQ overall score (CI = [0.1405 , 0.4938], I^2 = 74.01%), abdominal symptoms (CI = [0.1398 , 0.7483], I^2 = 67.65%), systemic symptoms (CI = [0.2234 , 0.5726], I^2 = 68.56%), activity (CI = [0.1645 , 0.6506], I^2 = 78.09%), emotional functioning (CI = [0.1070 , 0.5497], I^2 = 78.38%), and worry (CI = [0.0416 , 0.4651], I^2 =74.50%). Fatigue domain did not yield a significant result (CI = [-0.05 , 1.04], I^2 = 67.65%).

Figures 1:7 showed the frost plots associated with our result.



I^2 (total heterogeneity / total variability): 74.01%

Figure 1. Forest plot of the difference between male and female quality of life in chronic diseases. Random-Effects Model - CLDQ overall score.



I^2 (total heterogeneity / total variability): 67.65%

Figure 2. Forest plot of the difference between male and female quality of life in chronic diseases. Random-Effects Model - CLDQ abdominal symptoms.

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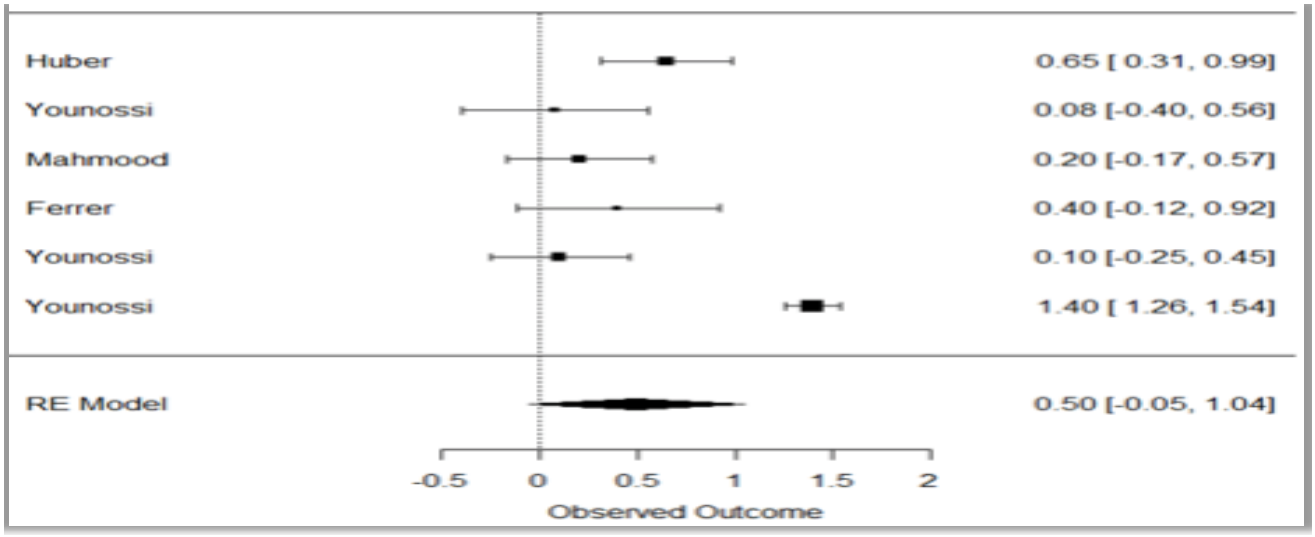
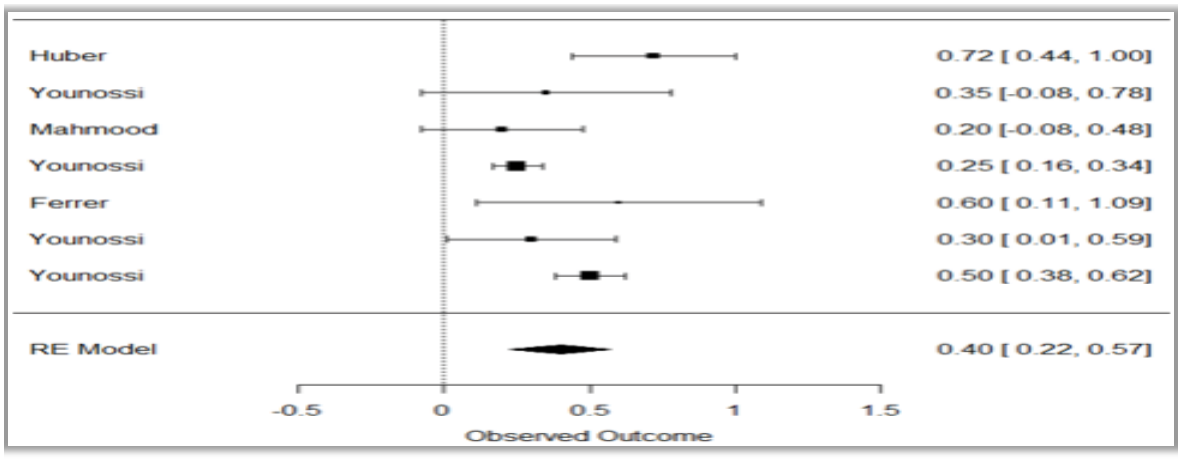


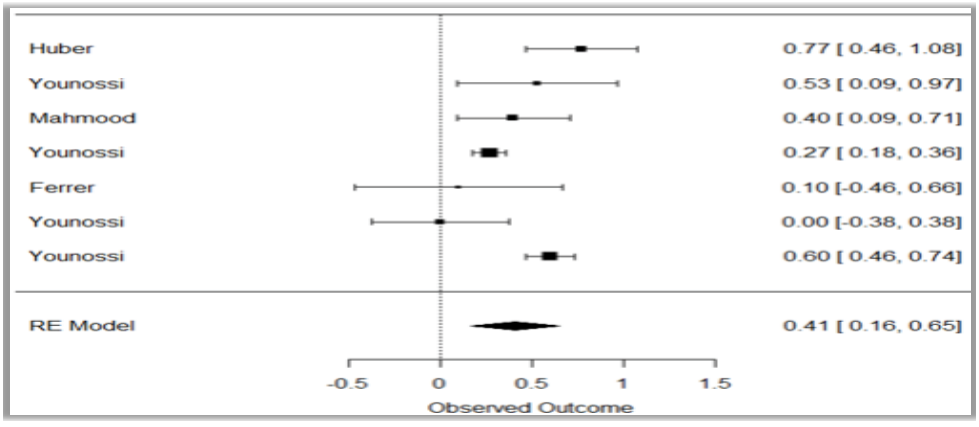
I^2 (total heterogeneity / total variability): 67.65%

Figure 3. Forest plot of the difference between male and female quality of life in chronic diseases. Random-Effects Model - CLDQ fatigue.



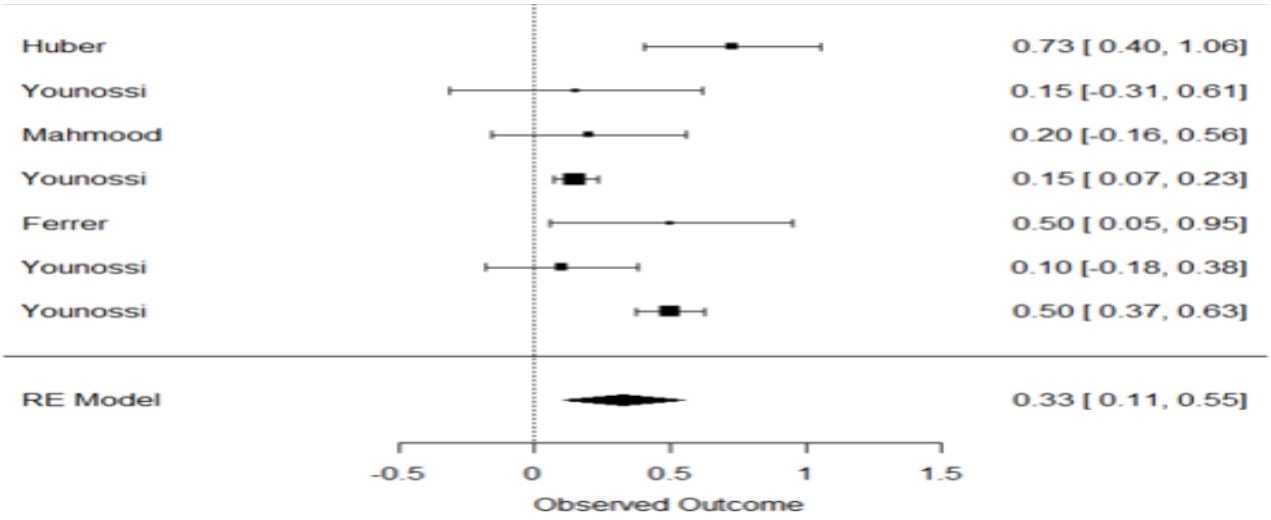
I^2 (total heterogeneity / total variability): 68.56%

Figure 4. Forest plot of the difference between male and female quality of life in chronic diseases. Random-Effects Model - CLDQ Systemic symptoms.



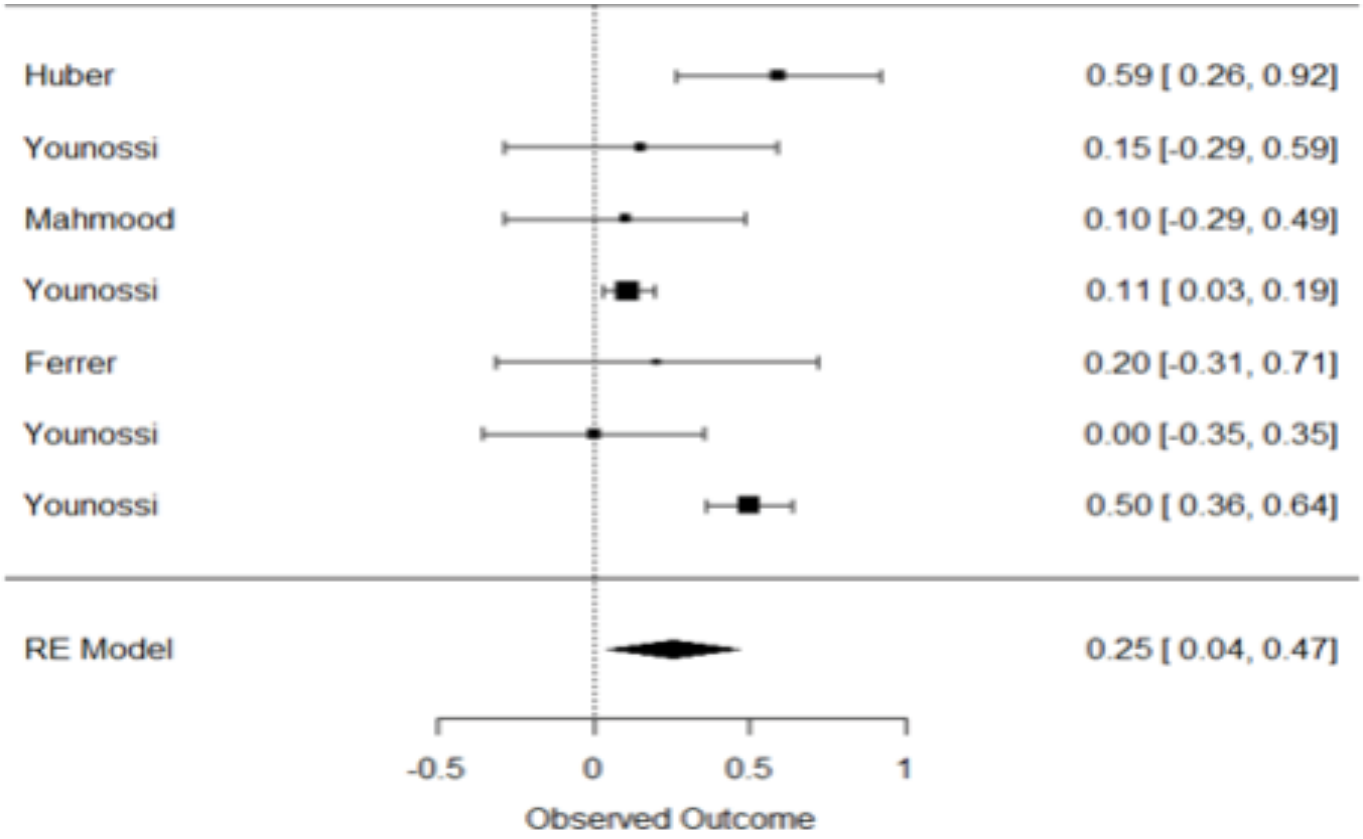
I^2 (total heterogeneity / total variability): 78.09%

Figure 5. Forest plot of the difference between male and female quality of life in chronic diseases. Random-Effects Model - CLDQ activity.



I^2 (total heterogeneity / total variability): 78.38%

Figure 6. Forest plot of the difference between male and female quality of life in chronic diseases. Random-Effects Model - CLDQ emotional functioning.



I^2 (total heterogeneity / total variability): 74.50%

Figure 7. Forest plot of the difference between male and female quality of life in chronic diseases. Random-Effects Model - CLDQ Worry.

Sensitivity analysis

Excluding some studies did not yield any other results. Although when we excluded Younossi et.al (2016) study in the systemic symptom's domain, the heterogeneity reduced significantly (I^2 = 48%). However, the result remains the same with less quality of life for females. Also, the heterogeneity reduced to 44% when we excluded Younossi et.al (2019) study in the worry domain. However, the result of this sensitivity analysis is not significant (CI= 0.18 [-0.03 - 0.39]). Finally, heterogeneity in the fatigue domain is reduced to 41% when we exclude Younossi et.al (2019) study, but the result is still not significant (CI= 0.30 [-0.02 - 0.61]).

DISCUSSION

Our study reveals that women with chronic liver disease experience a significantly lower quality of life than men. This difference was evident across multiple domains of the CLDQ, with the exception of fatigue. Supporting our findings, three independent studies (Huber et al., 2019; Younossi et al., 2016, 2019) also demonstrated a significant disparity in overall CLDQ scores between genders. [12,14,16] While five additional studies showed trends towards lower quality of life in women, these differences did not reach statistical significance. Notably, five studies consistently highlighted significantly worse systemic symptoms and activity limitations in women compared to men.

Our meta-analysis reveals a critical disparity. Women with CLD consistently experience a significantly diminished quality of life compared to men. This finding aligns with existing research emphasizing the detrimental impact of CLD on well-being. Our study uniquely expands the knowledge base by employing the CLDQ to illuminate the gender-specific nuances of this health burden. Women scored notably worse in domains encompassing activity limitations, emotional functioning, worry, systemic symptoms, and abdominal discomfort. These results strongly suggest that the CLD experience for women involves a disproportionate toll on physical and emotional health.

Understanding the root causes of this disparity demands continued investigation into potential biological, psychological, and social factors at play. Acknowledging and addressing these gender-specific challenges within CLD management marks a crucial step towards providing truly equitable and compassionate care. Healthcare professionals hold the key to improving the lives of female CLD patients by not only targeting traditional clinical indicators but also proactively addressing the quality-of-life domains particularly affected in women.

The current study showed that there is no significant difference in the fatigue domain between males and females. One common symptom that people with chronic liver disease describe is fatigue, which is frequently linked to diminished physical and mental functioning. Fatigue may affect men and women with chronic liver disease equally, given there is no significant gender difference in this domain. Recognizing the differences in quality of life across genders among patients with chronic liver disease holds noteworthy consequences for healthcare management and clinical practice. To further combine the biomedical and psychosocial models of health, quality-of-life measurements, such the SF-36 and CLDQ, can complement clinical outcomes, such as Child-Pugh class, liver enzyme indicators, histological stage, and mortality rates. The entire impact of these diseases on patients' health and well-being will be captured by this integrated approach to the study of chronic liver disease. This can help the healthcare professional prioritize decisions to enhance patients' overall wellness and address functional constraints. [20]

When we applied sensitivity analysis to the studies, it did not change any results. However, some sensitivity tests yield a non-significant result for some domains. It is worth mentioning that there are five studies were done by the same first author (Younossi). We acknowledge that having diverse authors may produce different outcomes.

Limitations

One limitation is that one researcher reviewed and searched the literature, we believe that if more than one researcher worked on the searching, reviewing, and finding literature, we might have more studies to include in this meta-analysis. Moreover, we did not contact the authors of the studies that did not provide a direct comparison between males and females. Finally, we believe that measuring and evaluating the quality of life is inherently subjected to some types of biases like "recall bias" and "response shift" along with unclear definitions of the quality of life aspects and standards among participants.

Future research

We recommend to future researchers to compare the quality of life in chronic liver disease using other quality of life measurements like the Short-form 36 questionnaire (SF-36) which is widely used and utilized for routine monitoring and assessment of healthcare outcomes in adult patients. [21]

CONCLUSION

This study underscores the significant gender-specific impact of chronic liver disease on quality of life. Women are disproportionately affected, experiencing greater challenges in areas such as abdominal symptoms, systemic symptoms, activity levels, emotional functioning, and worry. To address this disparity, healthcare providers must prioritize the unique needs of female patients. Utilizing comprehensive quality of life measures can guide the development of personalized interventions, ensuring that care strategies are tailored to enhance the well-being and overall health outcomes for women with chronic liver disease. By acknowledging and addressing these gender-specific differences, we can move towards more equitable and effective healthcare for all patients.

AUTHORS CONTRIBUTION

***** These authors contributed equally to this work

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