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Unveiling the Link: Exploring the Impact of Anaemia on the Severity of Chronic Liver Disease in Patients at A Tertiary Care Hospital

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ABSTRACT

Introduction: Despite the clinical relevance and potential implications of anaemia in CLD, the available evidence regarding the association between anaemia and the severity of liver disease remains inconsistent and limited.

Method: A cross sectional study was done among 116 CLD patients to address this research gap by investigating the prevalence, Etiology, and clinical implications of anemia among patients with CLD.

Result: Out of total 116 patients, 57.8% had anemia. Among patients with anaemia, there were 56 males and 11 females. 71.2% (48) had mild anaemia, compared to 20.1% (14) and 20.1% (14) who had moderate and severe anaemia, respectively. 31 out of 67 (46.3%) were classified as CPS A and CPS B, and only 5 (7.4%) were classified as CPS C. When comparing patients with and without anaemia, the mean MELD points were 12.1 and 9.5, respectively.

Conclusion: there was association found between anaemia and the severity of chronic liver disease, as indicated by higher MELD, and a higher proportion of patients in the more severe Child-Pugh scores categories with anaemia.

INTRODUCTION

Chronic liver disease (CLD) is a significant global health burden affecting millions of individuals worldwide.[1] It encompasses various etiologies, such as viral hepatitis, alcoholic liver disease, non-alcoholic fatty liver disease, and autoimmune liver diseases. CLD progression is associated with substantial morbidity and mortality, often leading to liver failure and the need for liver transplantation. One common complication of CLD is the development of anaemia, which can further complicate the clinical course of these patients.[2]

Prevalence of Anemia in CLD: Multiple studies have reported a high prevalence of anemia among patients with CLD. A study by Scheiner et al. (2020) found that anemia affected approximately 2/3 (66%) of patients with advanced chronic liver disease.[3]

Anaemia is a condition characterized by a decrease in the number of circulating red blood cells or a decrease in the concentration of hemoglobin, resulting in reduced oxygen-carrying capacity.[4] It is a prevalent comorbidity in patients with CLD, with reported prevalence rates ranging from 20% to 90%, depending on the underlying liver disease etiology

and severity.[5–7] However, the association between anaemia and the severity of CLD remains an area of ongoing research and debate.

The etiology of anemia in CLD is multifactorial. Chronic blood loss from gastrointestinal bleeding, impaired bone marrow function, nutritional deficiencies, and renal dysfunction are common contributing factors. Inflammation and the release of pro-inflammatory cytokines in CLD also play a significant role in the development of anemia.[8]

Anemia has been associated with an increased risk of mortality, reduced exercise capacity, and impaired quality of life among patients with CLD. [9] In a study by Møller et al. (2014), anemia was an independent predictor of mortality in patients with cirrhosis.[10] Additionally, anemia has been linked to an increased risk of hepatic decompensation, portal hypertension, and hepatic encephalopathy.

Understanding the relationship between anaemia and the severity of CLD is of utmost importance for several reasons. Firstly, anaemia can significantly impact the quality of life of CLD patients, leading to symptoms such as fatigue, weakness, and impaired exercise tolerance. Secondly, anaemia may further worsen liver function and exacerbate the underlying liver disease, potentially accelerating disease progression and increasing the risk of complications. Lastly, the presence and severity of anaemia in CLD patients may have implications for treatment decisions, such as the initiation of erythropoietin-stimulating agents or blood transfusions, which can carry their own risks and benefits.

Despite the clinical relevance and potential implications of anaemia in CLD, the available evidence regarding the association between anaemia and the severity of liver disease remains inconsistent and limited. While some studies have suggested a direct correlation between anaemia and disease severity, others have failed to establish a significant relationship. This discrepancy in findings may be attributed to variations in study populations, sample sizes, disease etiologies, and the definition of anaemia and disease severity used across studies.

This study aims to address this research gap by investigating the prevalence, Etiology, and clinical implications of anemia among patients with CLD. By doing this study, we can enhance our understanding of the clinical implications of anaemia in CLD patients and pave the way for more targeted interventions to optimize patient outcomes. The findings from this study will contribute to the existing body of knowledge and inform healthcare professionals involved in the care of patients with CLD, ultimately aiming to reduce the burden of liver disease and improve patient outcomes.

METHODOLOGY

This study utilized a cross-sectional design to assess the association between anemia and the severity of chronic liver disease among patients admitted to a tertiary care hospital. Study was conducted in Saraswathi institute of medical sciences after getting approval of protocol from the Ethical committee.

According to a study done by Scheiner et al. (2020)[3] prevalence of anemia among patients with advanced chronic liver disease was 66%. Calculated sample sized based on prevalence of 66% with absolute error 10% was 116 based on formula $4pq/L^2$. Where, p=66%, q= (100-p)=44%, L=allowable error=10%.

Patients with a confirmed diagnosis of chronic liver disease, based on clinical, radiological, and/or histopathological criteria and were hospitalized or attended outpatient department of general medicine and fit to the inclusion and exclusion criteria were included for the study till the calculated sample size achieved. Patients age more than 18 years and willing to give informed written consent to participate in the study were included.

Patients with acute liver disease or acute-on-chronic liver failure, Patients with a known history of hematological disorders, such as sickle cell disease or thalassemia, history of recent blood transfusion within the past three months, active bleeding or recent gastrointestinal bleeding, recent erythropoietin therapy or iron supplementation, pregnant or lactating women, Patients with comorbid conditions that can independently influence anemia, such as chronic kidney disease or hematological malignancies and who were unable to provide informed consent or cooperate with the study procedures were excluded from the study.

Relevant clinical and demographic information was collected from the participants' medical records, including age, gender, etiology of chronic liver disease, duration of liver disease, presence of comorbidities, and medication history.

Laboratory data was collected, including complete blood count (CBC), liver function tests (e.g., serum albumin, bilirubin, prothrombin time), and relevant markers of liver disease severity (e.g., Model for End-Stage Liver Disease [MELD] score, Child-Pugh

score). MELD score was calculated using the formula 9.57 × $\log_e$ (creatinine mg/dL) + 3.78 × $\log_e$ (bilirubin mg/dL) + 11.2 × $\log_e$ (INR) + 6.43, where 6.43 is the constant for liver disease etiology.

Hemoglobin levels was used to assess anemia status. The criteria for mild anemia were hemoglobin levels <13 g/dL for men and <12 g/dL for non-pregnant women. 7-11.9 for moderate and <7 was considering as severe anaemia. [11]

Descriptive statistics will be used to summarize the demographic, clinical, and laboratory characteristics of the study participants. The association between anemia and the severity of chronic liver disease will be analyzed using appropriate statistical methods, such as chi-square test, t-test, or logistic regression analysis. Multivariate analysis may be performed to control for potential confounding factors. 95% confidence interval with p value less than 0.05 was considered for the statistically significance.

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the institutional review board of the tertiary care hospital. Informed consent was obtained from all study participants before enrollment, ensuring confidentiality, voluntary participation, and the right to withdraw at any time.

Potential limitations of this study may include its cross-sectional design, which limits the ability to establish causal relationships. The study's generalizability may be limited to the specific population and setting of a tertiary care hospital.

RESULT

Out of total 116 patients, there were 88 males and 28 females, resulting in a male percentage of 75.7%. Among patients with anaemia, there were 56 males and 11 females, with a higher male percentage of 83.6%. In the group without anaemia, there were 32 males and 17 females, resulting in a male percentage of 65.3%. The p-value associated with this comparison is 0.121, indicating that the difference in sex distribution between patients with and without anaemia is not statistically significant.

Overall mean age of patients was 58.3±8.2 years. Patients with anaemia had a slightly lower mean age of 56.5±7.8 years. Among patients without anaemia, the mean age was 57.4±1.9 years. The p-value associated with this comparison is 0.536, indicating that there is no statistically significant difference in the mean age between patients with and without anaemia in this sample.

Out of 116 chronic liver disease patients, among the anaemic individuals, 71.2% (48) had mild anaemia, compared to 20.1% and 20.1% who had moderate and severe anaemia, respectively.

Table 1: Chronic liver disease patients with and without anaemia

Variables	All patients (n = 116)	Any anaemia (n = 67)	Without Anaemia (n = 49)	*P*-value
Sex, male/female (% male)	88/28 (75.7%)	56/11 (83.6%)	32/17 (65.3%)	**0.121**
Age, years	58.3 ± 8.2	56.5 ± 7.8	57.4 ± 1.9	0.536

Table 2: Proportion of chronic liver disease patients of different etiology with and without anaemia.

Aetiology	All patients (n = 116)	Any anaemia (n = 67)	Without Anaemia (n = 49)	*P*-value
Alcohol, n (%)	53 (45.7%)	31 (46.3%)	9 (18.4%)	**0.012**
Viral hepatitis, n (%)	51 (44%)	23 (34.3%)	31 (46.3%)	
Cryptogenic, n (%)	12 (10.3%)	13 (19.4%)	9 (18.4%)	

Table 3: Patients with and without anaemia in relation to their Child-Pugh scores.

Child-Pugh score	All patients (n = 116)	Any anaemia (n = 67)	Without Anaemia (n = 49)	*P*-value
Child-Pugh score (points)	6.8 ± 2.1	7.4 ± 1.7	6.1 ± 0.9	**0.022**
CPS A	67 (57.8%)	31 (46.3%)	41 (83.7%)	**<.001**
CPS B	42 (36.2%)	31 (46.3%)	7 (14.3%)	
CPS C	7 (6%)	5 (7.4%)	1 (2%)	

Table 4:Patients with and without anaemia in relation to their MELD scores.

MELD	All patients (n = 116)	Any anaemia (n = 67)	Without Anaemia (n = 49)	*P*-value
MELD points	11.3 ± 3.8	12.1 ± 4.9	9.5 ± 1.9	**0.017**

"MELD points" refers to the mean MELD (Model for End-Stage Liver Disease) points, which is a scoring system used to assess the severity of chronic liver disease.

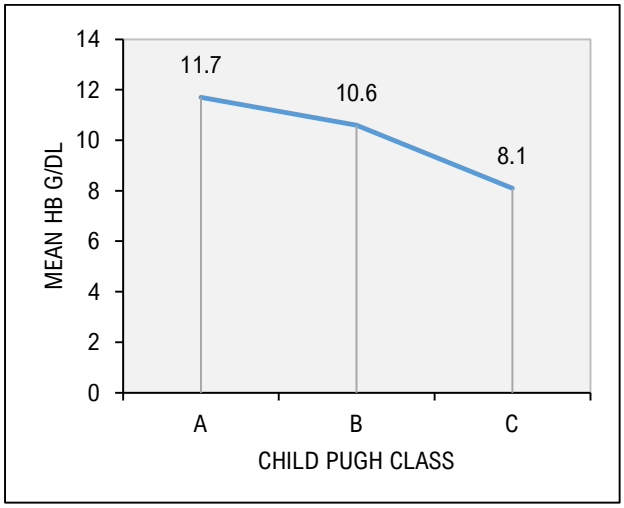

Figure 1: Mean plot of haemoglobin in correlation with child pugh class

Out of 116, there were 53 patients (45.7%) with alcohol-related etiology. Among patients with any anaemia, 31 patients (46.3%) had alcohol-related etiology. In the group without anaemia, only 9 patients (18.4%) had alcohol-related etiology. There were 51 patients (44%) with viral hepatitis. Among patients with any anaemia, 23 patients (34.3%) and in the group without anaemia, 31 patients (46.3%) had viral hepatitis. Out of 116,12 patients (10.3%) had cryptogenic etiology. Among patients with any anaemia, 13 patients (19.4%) and from group without anaemia, 9 patients (18.4%) had cryptogenic etiology.

Performing a chi-square test with these values, the p-value was calculated as 0.012, there was a significant difference in the distribution of aetiologies between patients with and without anaemia in this sample.

The Child-Pugh score is a measure of the severity of chronic liver disease, with higher scores indicating more severe disease. the mean Child-Pugh score for each group: 7.4 ± 1.7 for patients with anaemia and 6.1 ± 0.9 for patients without anaemia. The p-value associated with this comparison is 0.022, indicating a statistically significant difference in the mean Child-Pugh scores between the two groups.

Among patients with anaemia, 31 out of 67 (46.3%) were classified as CPS A, compared to 41 out of 49 (83.7%) patients without anaemia. Among patients with anaemia, 31 out of 67 (46.3%) were classified as CPS B, compared to 7 out of 49 (14.3%) patients without anaemia. Among patients with anaemia, 5 out of 67 (7.4%) were classified as CPS C compared to 1 out of 49 (2%) patients without anaemia.

Overall, the table suggests that patients with anaemia have higher mean Child-Pugh scores and a higher proportion of patients in the more severe CPS categories (CPS B and CPS C) compared to those without anaemia. These differences are statistically significant, indicating a potential association between anaemia and the severity of chronic liver disease as measured by the Child-Pugh score.

The mean MELD points for all patients were 11.3±3.8. When comparing patients with and without anaemia, the mean MELD points were 12.1 and 9.5, respectively. This indicates that patients with anaemia had higher mean MELD points, suggesting a potentially greater severity of chronic liver disease in this group. The p-value of 0.017 indicates a statistically significant difference in mean MELD points between patients with and without anaemia. These findings suggest that the presence of anaemia may be associated with increased severity of chronic liver disease, as measured by MELD points.

DISCUSSION

The present study aimed to assess the association of anaemia with the severity of chronic liver disease among patients admitted to a tertiary care hospital.

With regards to the distribution of sex among chronic liver disease patients, our study's observation of a higher proportion of males aligns with previous studies.[12] This male predominance is a well-documented characteristic of chronic liver disease populations, likely attributed to factors such as higher rates of alcohol consumption and viral hepatitis infections among males.[13]

Regarding age, our study found no statistically significant difference in mean age between patients

with and without anaemia, in line with the findings of Rai et al study.[14] This suggests that age may not be a determining factor for the development of anaemia in chronic liver disease patients, and other factors such as liver dysfunction and comorbidities may play a more prominent role in anaemia pathogenesis.

Regarding the severity of anaemia, our study's observation of a higher proportion of patients with mild anaemia is consistent with the findings reported by Chalasani et al.[15] This highlights the predominance of mild anaemia in chronic liver disease patients and underscores the need for appropriate management and monitoring of anaemia in this population.

The study results indicate that alcohol-related etiology is a prominent factor in chronic liver disease, with 45.7% of the patients in the study having alcohol-related liver disease. This finding is consistent with Scheiner et al research that has identified alcohol consumption as a leading cause of liver disease.[3] It suggests that alcohol-related liver disease continues to be a significant public health concern.

Furthermore, the study highlights an interesting association between alcohol-related liver disease and the presence of anemia. Among patients with any anemia, 46.3% had alcohol-related etiology, while in the group without anemia, only 18.4% had alcohol-related etiology. This suggests that anemia may be more prevalent in individuals with alcohol-related liver disease. However, it is essential to note that the study does not establish a causal relationship between alcohol-related liver disease and anemia. Further investigations are needed to understand the underlying mechanisms and the direction of this association.

The study also reveals that viral hepatitis is another significant etiology of chronic liver disease, with 44% of the patients having this cause. Among patients with any anemia, 34.3% had viral hepatitis, while in the group without anemia, 46.3% had viral hepatitis. These findings suggest that anemia may not be strongly associated with viral hepatitis compared to alcohol-related liver disease. However, it is important to consider that the prevalence of viral hepatitis in this study is relatively high, emphasizing the importance of addressing viral hepatitis as a critical factor in chronic liver disease.[16]

In our study there was a significant correlation be-

tween the MELD score and Hb levels. Lower Hb levels were associated with a higher MELD score. Similar findings were seen in a study conducted by Scheiner *et al*, where anemic patients showed a higher MELD (12±4 vs. 9±3; P<0.001).[3]

The present study investigated the association between anaemia and the severity of chronic liver disease using the Child-Pugh score. The results revealed that patients with anaemia had significantly higher mean Child-Pugh scores compared to those without anaemia. This indicates that the presence of anaemia is associated with more severe liver disease. The statistical analysis further supported this finding, with a significant p-value of 0.022.

Among patients with anaemia, a lower proportion (46.3%) were classified as CPS A, indicating milder disease, compared to the group without anaemia, where a higher proportion (83.7%) fell into CPS A. Conversely, a higher percentage of patients with anaemia (46.3%) were classified as CPS B, representing moderate disease severity, compared to those without anaemia (14.3%). Furthermore, a small percentage of patients with anaemia (7.4%) were classified as CPS C, the most severe category, while only 2% of patients without anaemia fell into this category.

The findings from this study suggest that anaemia is associated with increased disease severity in chronic liver disease, as reflected by the higher mean Child-Pugh scores and a higher proportion of patients in the more severe CPS categories. These results align with Singh et al research indicating that anaemia can be a significant clinical marker of liver disease progression and worse outcomes.[17]

It is important to acknowledge some limitations of the study. Firstly, the cross-sectional nature of the study design prevents establishing a causal relationship between anaemia and liver disease severity. Longitudinal studies would be valuable in investigating the temporal relationship between anaemia and disease progression. Secondly, the sample size and population characteristics should be considered when generalizing these findings to broader populations. It would be beneficial to replicate this study with larger cohorts and diverse patient populations to validate the observed associations.

CONCLUSION

In conclusion, this study provides evidence for an association between anaemia and the severity of chronic liver disease, as indicated by higher MELD, and a higher proportion of patients in the more severe Child-Pugh scores categories among those

with anaemia. These findings highlight the clinical significance of anaemia as a potential marker for disease severity in chronic liver disease. Further research is warranted to elucidate the underlying mechanisms and explore the implications of managing anaemia in the context of liver disease.

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