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Evaluation of Glycated Hemoglobin Levels in Cirrhotic Patients Across Different Child-Pugh Classes

Rabia Qayoom Shaikh[1*], Mukhtair Hussain Jafferi[1], Abdul Ghaffar Daras[1], Sobia Karamullah[1], Fouzia Shaikh[1] and Imran Ali Shaikh[1]

[1]Department of Medicine, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan

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***Corresponding Author:**
Rabia Qayoom Shaikh
Department of Medicine, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan
rabiaqayooms@gmail.com

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ABSTRACT

Chronic liver diseases can lead to cirrhosis, characterized by structural abnormalities and fibrosis. Diabetes is a significant risk factor for poor prognosis in cirrhotic patients, associated with complications such as ascites, renal dysfunction, and increased mortality. **Objectives:** To evaluate glycated hemoglobin (HbA1c) levels in cirrhotic patients across different Child-Pugh classes, contributing to better management of chronic liver disease. **Methods:** Conducted at Liaquat University of Medical and Health Sciences, this descriptive cross-sectional study enrolled 62 cirrhotic patients (aged 18-60) over six months. Exclusion criteria included known diabetes and recent blood transfusions. Data on demographic characteristics and HbA1c levels were collected and analyzed using SPSS version 24.0. **Results:** The mean age of participants was 52.3 ± 7.5 years, with a mean disease duration of 28.4 ± 12.3 months. The overall mean HbA1c level was 5.3 ± 0.9%. Child-Pugh classification revealed 32% Class A, 40% Class B, and 28% Class C patients. HbA1c levels increased significantly with liver disease severity: Class A (4.9 ± 0.6%), Class B (5.4 ± 0.7%), and Class C (5.9 ± 0.8%), $p<0.05$. Significant associations were found between HbA1c levels and age, disease duration, but not with gender or BMI. **Conclusions:** It was concluded that HbA1c levels are influenced by the severity of liver disease and duration, indicating the need for careful interpretation of HbA1c in cirrhotic patients for effective management.

INTRODUCTION

Liver cirrhosis, which is brought on by chronic liver disorders, results in the transformation of normal liver architecture into structurally aberrant nodules and distinctive tissue fibrosis [1, 2]. Liver cirrhosis is most commonly caused by alcoholic liver disease, nonalcoholic steatohepatitis, and viral hepatitis B, C, and D [3]. Diffuse nodular regeneration encircled by dense fibrotic septa is a histological characteristic of liver cirrhosis, a pathologically defined condition [4]. Hepatic vascular architecture is significantly distorted as a result of the parenchymal extinction and consequent collapse of liver architecture [5]. More than 0.8 to 0.89 million fatalities annually are due to cirrhosis [6]. Because diabetes is linked to serious consequences such as ascites, renal failure, hepatic encephalopathy [7-9], and bacterial infections, it is an independent risk factor for a poor prognosis in individuals with cirrhosis [10]. In patients with chronic liver disease, diabetes also raises the risk of hepatocellular carcinoma and death [11]. About 30% to 60% of individuals with severe cirrhosis develop diabetes, while about 80% of people with cirrhosis have impaired glucose tolerance [12]. Compared to the general population, where the prevalence of diabetes is about 8% and glucose intolerance is about 15%, individuals with cirrhosis have a far greater prevalence of diabetes [13]. The term "hepatogenous diabetes" refers to diabetes resulting from liver insufficiency and portal hypertension, as distinct from traditional type 2 diabetes mellitus (T2DM) that is also seen

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in cirrhotic patients [12]. Reduced hepatic mass and portosystemic shunts are linked to cirrhosis, which affects the liver's ability to clear insulin and causes peripheral insulin resistance as a result of downregulated insulin receptors. Additionally, elevated levels of hypoxia-inducible factors and advanced glycation end products are associated with cirrhosis, which may aid in the development of diabetes [14]. The HbA1c level in cirrhotic patients has been reported as ≥6.1% [15, 16]. Haemoglobin A1c measurement is a standard evaluation tool in diabetes therapy. This study is justified by the fact that diabetes is a common ailment and that diabetes is negatively impacted by chronic liver disease [14]. The purpose of this study is to ascertain how HbA1c levels relate to various stages of liver disease. It will help with early detection, risk assessment, and better chronic liver disease management, all of which could improve quality of life.

Despite extensive research on diabetes in chronic liver disease, there remains limited evidence on how HbA1c behaves across different Child-Pugh classes in cirrhotic patients, particularly in South Asian populations. Existing studies show inconsistent findings regarding the reliability of HbA1c in liver cirrhosis due to altered red blood cell turnover, anemia, and impaired glucose metabolism. Furthermore, there is insufficient local data to guide clinicians in interpreting HbA1c accurately in relation to disease severity. This study aims to examine the HbA1c levels of cirrhotic patients across various Child-Pugh classes and to ascertain the HbA1c level in cirrhotic patients who presented to a tertiary care hospital in Jamshoro, Hyderabad.

METHODS

A descriptive cross-sectional study was conducted in the Medical Unit 1 at Liaquat University of Medical and Health Sciences, Jamshoro, Hyderabad, over six months starting from February 2024 to July 2024 and non-probability consecutive sampling was used to enroll a sample of 62 cirrhotic patients, as determined by the WHO sample size calculator with a 95% confidence level, an expected HbA1c level of 6.1%, and a precision of 0.2 [16]. Inclusion criteria comprised patients aged 18 to 60 years, of either gender, who had been diagnosed with liver cirrhosis for more than six months. Exclusion criteria included known cases of type 1 or type 2 diabetes, hepatocellular carcinoma, secondary diabetes resulting from steroids, endocrinopathies, or chemotherapy, a history of gastrointestinal bleeding, recent blood transfusion, and patients who did not provide consent to participate. Ethical approval was obtained from the institutional review board (IRB) under the approval number CPSP/REU/. Data collection was initiated following IRB approval. Patients meeting the inclusion criteria and presenting to the outpatient department of Medicine were informed about the study's purpose, procedures, risks, and benefits, and written informed consent was obtained. Confidentiality was strictly maintained. The demographic and clinical data for each participant, including age, gender, and disease duration, were recorded. Height was measured using a wall-mounted scale without shoes, and weight was recorded on an electronic scale with minimal clothing. Body mass index (BMI) was then calculated by dividing weight in kilograms by height in meters squared. Child-Pugh class was assessed using a scoring system based on five clinical and laboratory parameters: total bilirubin, serum albumin, prothrombin time, ascites, and hepatic encephalopathy. This scoring information was obtained from the patient's record. HbA1c levels were measured using the Uncoated Human HbA1c (Haemoglobin A1c) ELISA Kit (E-UNEL-H0333, Elabscience®, Houston, Texas, 77079, USA) in the institutional laboratory. Prothrombin time was determined using an automated coagulation analyzer, while serum albumin levels were measured using the bromocresol green (BCG) dye-binding method. A 3-cc blood sample was drawn by a trained phlebotomist for HbA1c level measurement in the institutional laboratory. SPSS version 24.0 was used for data analysis. The Shapiro-Wilk test was used to determine whether continuous data were normal. Age, length of illness, height, weight, BMI, prothrombin time, serum albumin, and HbA1c levels were among the continuous variables for which means, standard deviations, medians, and interquartile ranges (IQRs) were computed. Categorical data, including gender and Child-Pugh class, were presented as frequencies and percentages. Comparisons of HbA1c levels across different Child-Pugh classes were conducted using the Kruskal-Wallis test, with p-values≤0.05 considered statistically significant. Potential effect modifiers such as age, gender, disease duration, and BMI were addressed through stratification.

RESULTS

The study involved 62 cirrhotic patients, having a mean age of 52.3 ± 7.5 years and a mean value of disease duration of 28.4 ± 12.3 months. Among these patients, 58% were male (n=36) and 42% were female (n=26). The average BMI was 24.1 ± 3.2 kg/m^2, with a mean prothrombin time of 17.4 ± 4.1 seconds and serum albumin level of 2.9 ± 0.5 g/dL. The overall mean HbA1c level was 5.3 ± 0.9% (Table 1).

Table 1: Demographics and Clinical Features of Cirrhotic Patients (n=62)

Characteristic	Mean ± SD / n (%)
Age (Years)	52.3 ± 7.5
Duration of Disease (Months)	28.4 ± 12.3

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Gender	
Male	36 (58%)
Female	26 (42%)
BMI (kg/m^2)	24.1 ± 3.2
Prothrombin Time (Seconds)	17.4 ± 4.1
Serum Albumin (g/dL)	2.9 ± 0.5
HbA1c Level (%)	5.3 ± 0.9

Patients were categorized by Child-Pugh class, with 32% in Class A (n=20), 40% in Class B (n=25), and 28% in Class C (n=17)(Table 2).

Table 2: Distribution of Child-Pugh Classes Among Cirrhotic Patients

Child-Pugh Class	n (%)
Class A	20 (32%)
Class B	25 (40%)
Class C	17 (28%)
Total	62 (100%)

Comparison of HbA1c levels across Child-Pugh classes demonstrated a statistically significant difference, with higher HbA1c levels observed as the Child-Pugh class increased. Specifically, Class A patients had a mean HbA1c of 4.9 ± 0.6%, Class B had 5.4 ± 0.7%, and Class C had 5.9 ± 0.8%. A Kruskal-Wallis test confirmed that these differences were significant ($p<0.05$), indicating an association between increasing liver disease severity and elevated HbA1c levels(Table 3).

Table 3: Comparison of HbA1c Levels Across Child-Pugh Classes

Child-Pugh Class	HbA1c (Mean ± SD)	Range
Class A	4.9 ± 0.6	4.2-5.6
Class B	5.4 ± 0.7	4.7-6.2
Class C	5.9 ± 0.8	5.0-6.9
Overall	5.3 ± 0.9	4.2-6.9

A Kruskal-Wallis test showed a significant difference in HbA1c levels across Child-Pugh classes($p<0.05$)

Further stratification revealed significant associations for HbA1c levels with age and disease duration. Patients aged 41–60 years had a higher mean HbA1c(5.4 ± 0.9%)compared to those aged 18–40 years (5.0 ± 0.8%), with a p-value of 0.03. Additionally, patients with a disease duration of more than 24 months had a higher mean HbA1c (5.5 ± 0.8%) compared to those with a disease duration of 24 months or less (5.1 ± 0.6%), with a p-value of 0.02. No significant differences in HbA1c levels were found based on gender ($p=0.15$)or BMI categories($p=0.12$)(Table 4).

Table 4: Stratification of HbA1c by Age, Gender, Disease Duration, and BMI

Variables	Category	HbA1c (Mean ± SD)	p-Value
Age (Years)	18–40	5.0 ± 0.8	0.03
	41–60	5.4 ± 0.9	
Gender	Male	5.3 ± 0.7	0.15
	Female	5.2 ± 0.9	
Disease Duration (Months)	≤24	5.1 ± 0.6	0.02
	>24	5.5 ± 0.8	
BMI (kg/m^2)	<25	5.2 ± 0.7	0.12
	≥25	5.4 ± 0.8	

DISCUSSION

Current study findings highlight that HbA1c levels in cirrhotic patients are influenced by liver disease severity, as reflected in the Child-Pugh classification, age, and disease duration. HbA1c levels significantly increased with the progression of liver disease, with Child-Pugh Class A patients displaying lower HbA1c levels (4.9 ± 0.6%) compared to Class C patients (5.9 ± 0.8%) ($p<0.05$). This aligns with prior research, where HbA1c was found to underestimate glycemic control in cirrhotic patients, particularly those with advanced liver disease, as reported by Cacciatore *et al.*, who suggested that cirrhosis itself may impair HbA1c's accuracy as a diagnostic tool due to altered glucose metabolism in such patients [17]. Disease duration was also a significant factor affecting HbA1c levels. Patients aged 41–60 years and those with disease durations longer than 24 months had higher HbA1c levels (5.4 ± 0.9% and 5.5 ± 0.8%, respectively). This concurs with findings by Soni *et al.*, where cirrhotic patients with extended disease duration often displayed lower HbA1c levels relative to their actual glycemic control due to decreased red blood cell lifespan, a common feature in cirrhosis [18]. Despite this, our data revealed no significant HbA1c differences based on gender or BMI, suggesting that while HbA1c might be influenced by liver disease severity and disease duration, other demographic factors may remain relatively unaffected. Notably, we observed higher mean HbA1c levels among cirrhotic patients than the general population, which might reflect systemic changes in glucose metabolism often associated with liver cirrhosis. Nomura *et al.*, work supports this, showing comparable HbA1c levels between cirrhotic and diabetic patients, despite higher fasting plasma glucose in the latter group [19]. Our study also provides valuable insights into the limitations of HbA1c in cirrhotic populations, particularly for patients with moderate to severe anemia, who comprised 63.6% of our study group. This is consistent with English *et al.*, systematic review [20], which identified iron deficiency anemia (IDA) as a factor potentially leading to falsely elevated HbA1c values. Consequently, for diabetic patients with cirrhosis, especially those with anemia, the oral glucose tolerance test (OGTT) remains a more reliable standard. Given that OGTT identified diabetes in 35% of our study population, it remains the preferred diagnostic approach in these cases.

This study is limited by its small sample size and single-center design, which may restrict generalizability to

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broader populations. The cross-sectional nature prevents assessment of temporal changes in HbA1c and disease progression. Additionally, confounding factors such as anemia and nutritional status may have influenced HbA1c interpretation despite exclusion criteria. Future research should include larger, multicenter longitudinal studies to better evaluate HbA1c reliability in cirrhosis over time. Moreover, combining HbA1c with alternative glycemic markers such as OGTT or fructosamine is recommended to improve diagnostic accuracy in cirrhotic patients.

CONCLUSIONS

It was concluded that HbA1c may serve as a valuable tool for assessing glycemic control in cirrhotic patients, particularly regarding liver disease severity and duration. Nevertheless, caution is warranted in interpreting HbA1c levels in this population, especially considering the potential impact of anemia and other confounding factors. Future studies with larger sample sizes and diverse populations are essential to further elucidate the diagnostic utility of HbA1c in cirrhosis and optimize diabetes management in this complex patient group.

Authors' Contribution

Conceptualization: RQS
Methodology: RQS, MHJ, FS
Formal analysis: AGD, SK
Writing and Drafting: IAS
Review and Editing: IAS, RQS, MHJ, FS

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

The authors declare no conflict of interest.

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