Section: Medicine

Original Research Article

CORRELATION BETWEEN GLYCOSYLATED HEMOGLOBIN LEVELS AND NAFLD SEVERITY: A CROSS-SECTIONAL STUDY

Harmanpal Singh[1], Sahil Gupta[1], Prem Dilip Dhakre[1], Mangat Ram Passi[2]

[1]*Junior Resident, Department of Medicine, Muzaffarnagar Medical College, Muzaffarnagar, Uttar Pradesh, India.*
[2]*Professor, Department of Medicine, Muzaffarnagar Medical College, Muzaffarnagar, Uttar Pradesh, India.*

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Corresponding Author:
Dr. Sahil Gupta,
Junior Resident, Department of Medicine, Muzaffarnagar Medical College, Muzaffarnagar, Uttar Pradesh, India.
Email: guptasahil9728@gmail.com

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ABSTRACT

Background: Non-Alcoholic Fatty Liver Disease (NAFLD) is a leading cause of chronic liver disorders, closely linked with metabolic syndrome and type 2 diabetes mellitus (T2DM). Glycosylated Hemoglobin (HbA1c), a marker of long-term glycaemic control, has emerged as a potential indicator of NAFLD severity. This study investigates the correlation between HbA1c levels and NAFLD severity, aiming to explore its clinical utility as a non-invasive biomarker.

Materials and Methods: This cross-sectional study included 100 NAFLD patients diagnosed through ultrasonography at Muzaffarnagar Medical College from July 2023 to July 2024. Baseline characteristics were documented, including age, BMI, fasting glucose, and liver enzymes. HbA1c levels were measured via high-performance liquid chromatography (HPLC). NAFLD severity was categorized as mild, moderate, or severe. Correlation and regression analyses assessed the relationship between HbA1c and NAFLD severity, adjusting for confounders such as BMI and lipid profiles.

Results: The mean HbA1c was 6.8 ± 1.2%, significantly increasing levels across NAFLD severity groups ($p < 0.001$). Mild, moderate, and severe NAFLD had mean HbA1c levels of 6.1 ± 0.8%, 7.0 ± 1.0%, and 8.3 ± 0.9%, respectively. Positive correlations were observed between HbA1c and metabolic parameters such as fasting glucose ($r = 0.78$, $p < 0.001$), BMI ($r = 0.65$, $p < 0.01$), and ALT ($r = 0.72$, $p < 0.001$). Multivariate regression analysis identified HbA1c as the strongest predictor of NAFLD severity ($\beta = 0.45$, $p < 0.001$).

Conclusion: This study highlights the significant correlation between HbA1c levels and NAFLD severity, emphasizing its potential as a non-invasive risk stratification and management biomarker. Further research is warranted to validate these findings and explore their utility in predicting long-term outcomes.

Keywords: NAFLD, HbA1c, glycaemic control.

INTRODUCTION

Non-alcoholic fatty Liver Disease (NAFLD) has emerged as one of the most prevalent chronic liver disorders worldwide, affecting nearly a quarter of the global population.[1] As a condition characterized by excessive fat accumulation in the liver without significant alcohol consumption, NAFLD poses a major health burden due to its association with metabolic syndrome, type 2 diabetes mellitus (T2DM), and cardiovascular disease.[2,3] NAFLD's silent and progressive nature often makes it challenging to detect early, highlighting the need for accessible and reliable biomarkers to aid in its diagnosis and management.[4]

Glycosylated Hemoglobin (HbA1c) is a well-established marker for long-term blood glucose control and a cornerstone in diagnosing and managing diabetes.[5] Recent research suggests that HbA1c may have a broader utility beyond glycaemic assessment, potentially as a marker for metabolic disturbances associated with NAFLD.[6] This is of particular importance as NAFLD and diabetes frequently coexist, creating a bidirectional

relationship that accelerates disease progression and worsens outcomes for affected individuals.

Understanding the correlation between HbA1c levels and NAFLD could provide crucial insights into the shared metabolic pathways linking these conditions.[7] Such a correlation may also enable the development of cost-effective screening strategies, particularly in high-risk populations, and inform targeted interventions to mitigate liver and systemic complications. Despite the growing interest in this area, the evidence remains mixed, necessitating further investigation.

This study explores the potential relationship between HbA1c levels and the severity of NAFLD, analyzing how glycaemic control may reflect or influence liver health. By addressing this gap, the research seeks to enhance our understanding of the metabolic interplay between diabetes and NAFLD, ultimately contributing to improved patient care and disease management strategies.

MATERIALS AND METHODS

The study was conducted at Muzaffarnagar Medical College, Muzaffarnagar, Uttar Pradesh, over one year from July 2023 to July 2024. A total of 100 participants were recruited for the study, comprising individuals diagnosed with Non-Alcoholic Fatty Liver Disease (NAFLD) through ultrasonographic imaging. The inclusion criteria required participants to be aged 18 years or older, have no significant history of alcohol consumption, and exhibit no secondary causes of hepatic steatosis. Participants with chronic liver diseases, active infections, or malignancies were excluded to ensure the focus remained solely on NAFLD and its metabolic correlations.

Data collection involved detailed medical histories, anthropometric measurements, and laboratory investigations. Fasting blood samples were obtained from all participants to measure glycosylated Hemoglobin (HbA1c) levels using standardized high-performance liquid chromatography (HPLC) techniques. Additional parameters, including fasting blood glucose, liver enzymes (alanine transaminase and aspartate transaminase), lipid profiles, and markers of metabolic syndrome, were also evaluated to provide a comprehensive metabolic assessment. Experienced radiologists performed ultrasonographic grading of hepatic steatosis, and the severity of NAFLD was categorized as mild, moderate, or severe based on echogenicity patterns.

Statistical analyses were conducted to explore the relationship between HbA1c levels and the severity of NAFLD. Correlation coefficients and regression models were utilized to assess the strength and significance of associations. At the same time, adjustments were made for potential confounders such as age, body mass index (BMI), and lipid levels. Ethical clearance for the study was obtained from the institutional ethics committee of Muzaffarnagar Medical College, and written informed consent was secured from all participants before enrolment. Data confidentiality and participant anonymity were maintained throughout the study.

RESULTS

The study population consisted of 100 participants with a mean age of 42.81 ± 10.52 years (range: 20–65 years). The gender distribution was 58% male and 42% female, as shown in [Figure 1]. The participants' mean body mass index (BMI) was 28.56 ± 3.83 kg/m², with values ranging from 22.3 to 36.1 kg/m². Fasting blood glucose levels averaged 112.52 ± 24.38 mg/dL, while the mean glycosylated Hemoglobin (HbA1c) was 6.8 ± 1.2% (range: 5.5–9.5%). Based on ultrasonographic findings, 50% of participants had mild NAFLD, 30% had moderate NAFLD, and 20% had severe NAFLD, as depicted in [Figure 2].

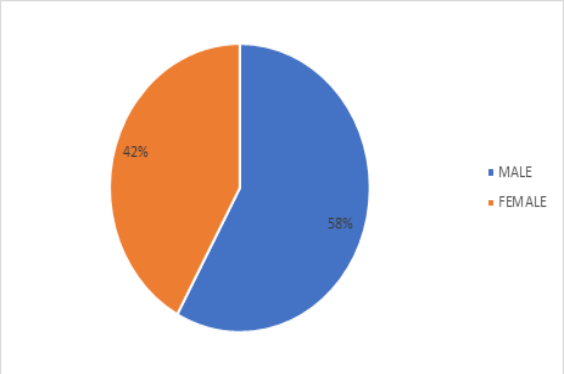

Figure 1: Pie chart showing gender distribution

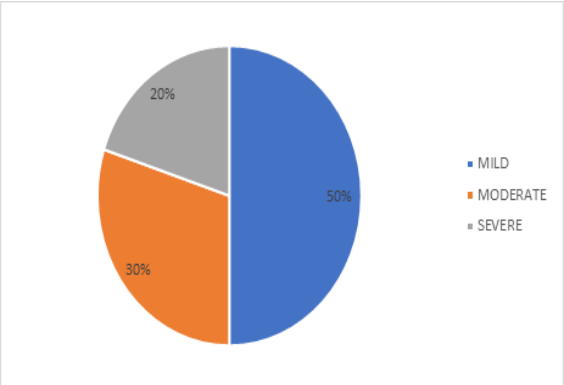

Figure 2: Pie chart showing NAFLD severity

Analysis of HbA1c levels across different NAFLD severity groups revealed a statistically significant trend of increasing HbA1c with worsening NAFLD severity ($p < 0.001$). Participants with mild NAFLD had a mean HbA1c of 6.1 ± 0.8%, while those with moderate and severe NAFLD exhibited mean HbA1c levels of 7.0 ± 1.0% and 8.3 ± 0.9%, respectively [Table 2]. This clear gradient underscores the potential link between poor glycaemic control and the progression of NAFLD.

Table 1: Baseline Characteristics of the Study Population.

Parameter	Mean ± SD	Range
Age (years)	42.81 ± 10.52	20–65
Body Mass Index (BMI, kg/m²)	28.56 ± 3.83	22.3–36.1
Fasting Blood Glucose (mg/dL)	112.52 ± 24.38	85–165
HbA1c (%)	6.8 ± 1.2	5.5–9.5

Table 2: HbA1c Levels Across NAFLD Severity Groups

NAFLD Severity	HbA1c (%) [Mean ± SD]	Range	P-Value
Mild	6.1 ± 0.8	5.5–7.2	<0.001
Moderate	7.0 ± 1.0	6.0–8.4	
Severe	8.3 ± 0.9	7.1–9.5	

Correlation analysis demonstrated significant positive relationships between HbA1c and various metabolic parameters [Table 3]. Fasting blood glucose showed the strongest correlation ($r = 0.78$, $p < 0.001$), followed by alanine transaminase (ALT) levels ($r = 0.72$, $p < 0.001$). BMI ($r = 0.65$, $p < 0.01$), triglycerides ($r = 0.67$, $p < 0.01$), and total cholesterol ($r = 0.59$, $p < 0.05$) also exhibited notable associations with HbA1c. These findings highlight the interplay between glycaemic control and metabolic dysfunction in patients with NAFLD.

Table 3: Correlation Between HbA1c Levels and Metabolic Parameters

Parameter	Correlation Coefficient (r)	P-Value
Fasting Blood Glucose	0.78	<0.001
BMI	0.65	<0.01
Total Cholesterol	0.59	<0.05
ALT (Alanine Transaminase)	0.72	<0.001
Triglycerides	0.67	<0.01

Multivariate regression analysis identified HbA1c as the strongest independent predictor of NAFLD severity ($\beta = 0.45$, $p < 0.001$), followed by BMI ($\beta = 0.35$, $p < 0.01$), ALT levels ($\beta = 0.41$, $p < 0.01$), and fasting blood glucose ($\beta = 0.25$, $p < 0.05$) [Table 4]. The adjusted R^2 value of 0.68 indicated a robust model explaining the variance in NAFLD severity. These results suggest that HbA1c levels, alongside other metabolic markers, could serve as reliable indicators of disease severity, potentially aiding in the clinical management of NAFLD.

Table 4: Multivariate Regression Analysis of Predictors of NAFLD Severity

Variable	Beta Coefficient	P-Value
HbA1c (%)	0.45	<0.001
BMI (kg/m²)	0.35	<0.01
Fasting Blood Glucose (mg/dL)	0.25	<0.05
ALT (U/L)	0.41	<0.01

DISCUSSION

The findings of this study highlight a significant correlation between glycosylated Hemoglobin (HbA1c) levels and the severity of Non-Alcoholic Fatty Liver Disease (NAFLD), reinforcing the metabolic interplay between glycaemic control and liver health. Participants with more severe NAFLD exhibited higher HbA1c levels, suggesting that poor glycaemic control contributes to the progression of hepatic steatosis. This aligns with previous studies, such as those conducted by Masroor M et al,[7] and Bae JC et al,[8] which demonstrated that elevated HbA1c is associated with increased liver fat content and inflammation, emphasizing its role as a marker for metabolic dysfunction in NAFLD patients.

The significant positive correlation observed between HbA1c and other metabolic parameters, such as fasting blood glucose, BMI, triglycerides, and alanine transaminase (ALT), further supports the association between hyperglycemia and metabolic disturbances in NAFLD. Similar findings were reported by Fabbrini E et al,[9] who identified hyperglycemia and obesity as critical drivers of NAFLD progression. The robust relationship between ALT and HbA1c in this study also highlights liver enzyme elevation as a key feature of metabolic stress, consistent with the results of a large cohort study by Nguyen QM et al.[10]

The multivariate regression analysis revealed HbA1c as the strongest independent predictor of NAFLD severity, even after adjusting for confounders like BMI and fasting glucose. This is consistent with the work of Chen C et al,[11] who demonstrated that HbA1c reflects glycaemic control and systemic insulin resistance and chronic inflammation, both of which are pivotal in NAFLD pathogenesis. The present study underscores the utility of HbA1c as a non-invasive biomarker that could potentially guide risk stratification and early intervention in NAFLD, as advocated by recent clinical guidelines.

While this study provides valuable insights, its findings should be interpreted within the context of its limitations, including the relatively small sample

size and single-center design. Nevertheless, the results are consistent with the growing body of evidence linking hyperglycemia and NAFLD, suggesting a need for integrated metabolic management in affected individuals. Future longitudinal studies with larger cohorts are warranted to validate these findings and explore the utility of HbA1c in predicting long-term outcomes, including fibrosis progression and cardiovascular complications, in NAFLD patients.

CONCLUSION

This study demonstrates a strong correlation between glycosylated hemoglobin (HbA1c) levels and the severity of Non-Alcoholic Fatty Liver Disease (NAFLD), underscoring the role of glycaemic control as a critical factor in disease progression. The findings highlight that higher HbA1c levels are associated with worsening NAFLD severity, alongside significant correlations with metabolic parameters like BMI, fasting glucose, and ALT levels. These results align with previous research and reinforce the potential of HbA1c as a non-invasive marker for risk stratification and management of NAFLD. Further studies are warranted to validate these observations and explore HbA1c's role in predicting long-term outcomes in NAFLD patients.

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