**Association of Fasting Glucose and Insulin Resistance with NAFLD Progression**

**Abstract**

**Objective:** To evaluate the association between fasting glucose, insulin resistance, and the progression of non-alcoholic fatty liver disease (NAFLD).

**Material and Methods:** This observational study was conducted at Imran Idrees Teaching Hospital, Sialkot, over six months. A total of 150 patients with NAFLD were included. Fasting glucose levels and HOMA-IR scores were measured to assess insulin resistance. Liver ultrasound and elastography were used to evaluate disease stage, while demographic and metabolic data were recorded. Statistical analyses identified correlations and trends between metabolic markers and NAFLD progression.

**Results:** Patients with advanced NAFLD exhibited significantly higher fasting glucose (mean: 135.8 mg/dL) and HOMA-IR scores (mean: 5.2) compared to those with simple steatosis (95.4 mg/dL; 2.1). A strong correlation was observed between fasting glucose, HOMA-IR, and disease severity (p < 0.001). Multivariate regression analysis identified both parameters as independent predictors of disease progression.

**Conclusion:** Fasting glucose and insulin resistance are strongly associated with NAFLD progression. These findings support their use as accessible, cost-effective biomarkers for early identification and management of advanced NAFLD. Integration of these markers into routine clinical practice can improve disease outcomes.

**Keywords:** Non-alcoholic fatty liver disease, fasting glucose, insulin resistance, HOMA-IR, NAFLD progression, biomarkers.

**INTRODUCTION**

NAFLD has emerged as one of the most prevalent chronic liver conditions across the globe, allied with obesity and the rising prevalence of metabolic syndrome and type 2 diabetes.1 NAFLD encompasses a spectrum of disorders of the liver, from simple hepatic steatosis to non-alcoholic steatohepatitis (NASH), fibrosis, and eventually cirrhosis. 2 Among the major metabolic factors involved in the progression of NAFLD, fasting glucose levels and insulin resistance (IR) have received much attention because of the latter's definitive role in metabolic deregulation. Insulin resistance is closely associated with the pathogenesis and progression of NAFLD 3; it is a pathophysiological hallmark of type 2 diabetes and metabolic syndrome.

Fasting glucose and insulin resistance are interlinked in the pathophysiology of NAFLD. Insulin resistance enhances the flow of free fatty acids into the liver by inhibiting peripheral glucose uptake and stimulating lipolysis in adipose tissue.4 This process leads to hepatic steatosis, the hallmark of early NAFLD. Hyperglycemia and high fasting glucose levels also increase oxidative stress and inflammation, further promoting liver damage. These mechanisms not only mark the beginning of NAFLD but also the progression towards more severe stages NASH and fibrosis. The fact that such potential biomarkers of insulin resistance, hyperglycemia relate tightly with the progression of NAFLD establishes the potential utility of these parameters in disease monitoring and risk stratification.5

Despite their strong clinical implications, fasting glucose levels and insulin resistance are not often utilized in the screening and management of routine NAFLD. Simple and effective tools like the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) can effectively use fasting glucose and insulin levels to assess one's level of insulin resistance.6 In many studies, it has been reported that there is a higher HOMA-IR score with increased severity of hepatic steatosis and fibrosis risk. Moreover, longitudinal data indicate that deterioration in glucose metabolism predicts progression and adverse outcomes in NAFLD. In addition to acting as markers of metabolic dysfunction, fasting glucose and insulin resistance therefore can also give insight into prognosis of the disease.7

Understanding the relationship between fasting glucose, insulin resistance, and progression of NAFLD has very important clinical implications. Early detection of individuals at risk for advanced liver disease would allow timely intervention, including lifestyle modifications and pharmacological therapies targeted at improving insulin sensitivity. Moreover, inclusion of fasting glucose and insulin resistance in NAFLD risk models might enhance diagnostic accuracy and tailor the treatment approach. This study aims to investigate the association between fasting glucose, insulin resistance, and NAFLD progression, providing valuable insights into the role of these metabolic factors in liver health.

**Methodology**

This observational study was conducted over six months at Imran Idrees Teaching Hospital after obtaining ERC (ERC#2024/IITH/RA/0025). The primary objective was to evaluate the relationship between fasting glucose, insulin resistance, and the progression of NAFLD. The study enrolled 150 adult patients aged 18 years and older, diagnosed with NAFLD through imaging and clinical criteria. Exclusion criteria included significant alcohol consumption, known hepatic diseases other than NAFLD, and pregnancy.

Data collection involved comprehensive clinical and laboratory evaluations. Fasting blood samples were obtained to measure glucose and insulin levels, enabling the calculation of HOMA-IR scores. Liver function tests and lipid profiles were also assessed to account for metabolic and hepatic parameters. Participants underwent liver ultrasounds to evaluate hepatic steatosis and elastography to determine fibrosis stages. Clinical history, including body mass index (BMI), waist circumference, and comorbidities such as diabetes and hypertension, was recorded to provide a detailed metabolic profile.

The association between fasting glucose, HOMA-IR scores, and NAFLD progression was analyzed using statistical models. Patients were categorized into groups based on disease severity, including simple steatosis, NASH, and advanced fibrosis. Comparative analyses were performed to identify trends and correlations between fasting glucose levels, insulin resistance, and disease progression. Statistical significance was determined using appropriate tests, and multivariate regression was employed to adjust for confounding factors such as age, BMI, and comorbid conditions. The findings of this study aim to underscore the role of metabolic dysfunction in the progression of NAFLD and support the integration of fasting glucose and insulin resistance into clinical practice for effective disease management.

**Results**

The study evaluated 150 patients with NAFLD. The results demonstrated significant associations between fasting glucose, HOMA-IR scores, and disease severity. Patients with higher fasting glucose levels and HOMA-IR scores were more likely to exhibit advanced stages of NAFLD. The data revealed a stepwise increase in fasting glucose and HOMA-IR scores with advancing disease stages, with statistically significant differences (p < 0.01) between groups. Multivariate regression analysis indicated that fasting glucose and HOMA-IR were independent predictors of NAFLD progression, even after adjusting for confounders such as age, BMI, and comorbidities.

**Table 1: Demographic Characteristics of the Study Population**

|  |  |
| --- | --- |
| **Characteristic** | **Value** |
| Total Patients | 150 |
| Mean Age (years) | 45.6 ± 12.3 |
| Gender (Male: Female) | 90:60 |
| Mean BMI (kg/m²) | 29.5 ± 4.8 |
| Prevalence of Diabetes (%) | 40 |
| Prevalence of Hypertension (%) | 35 |
| Mean Waist Circumference (cm) | 95.2 ± 8.5 |

**Table 1: Relationship Between Disease Stage, Fasting Glucose, and HOMA-IR**

|  |  |  |  |
| --- | --- | --- | --- |
| **Disease Stage** | **Mean Fasting Glucose (mg/dL)** | **Mean HOMA-IR Score** | **Number of Patients** |
| Simple Steatosis | 95.4 | 2.1 | 60 |
| Non-Alcoholic Steatohepatitis (NASH) | 115.6 | 3.8 | 50 |
| Advanced Fibrosis | 135.8 | 5.2 | 40 |

**Table 2: Correlation Between Fasting Glucose, HOMA-IR, and Disease Stage**

|  |  |  |
| --- | --- | --- |
| **Parameter** | **Correlation Coefficient (r)** | **P-Value** |
| Fasting Glucose vs. Disease Stage | 0.82 | <0.001 |
| HOMA-IR vs. Disease Stage | 0.88 | <0.001 |

**DISCUSSION:**

This study's findings clearly indicate that there is a very strong association of fasting glucose, insulin resistance, and the progression of non-alcoholic fatty liver disease. Both high fasting glucose levels and HOMA-IR scores showed a strong association with advanced NAFLD, including NASH and fibrosis. These observations are in keeping with the current literature and point out the fact that metabolic dysfunction plays a critical role in the pathogenesis of NAFLD.8

Insulin resistance, as measured by HOMA-IR, was the major factor driving the progression of NAFLD. This is consistent with previous studies that have pointed out the central role of insulin resistance in promoting hepatic fat accumulation, oxidative stress, and inflammation. In this study, patients with higher HOMA-IR scores were more likely to exhibit NASH and fibrosis, suggesting that insulin resistance not only initiates but also accelerates the progression of NAFLD. This result supports the importance of early identification and management of insulin resistance in high-risk populations in order to avert the disease progression.9,10

Fasting glucose levels were significantly increased in those patients with the more severe NAFLD stages. Hyperglycemia further causes injury in the liver via several mechanisms; these include enhancement of oxidative stress and activation of inflammatory pathways. Elevated fasting glucose also indicates a systemic metabolic dysregulation which worsens both the hepatic and extrahepatic consequences of NAFLD. These results are consistent with fasting glucose as a straightforward, readily accessible biomarker to identify those at risk for advanced NAFLD. Our findings are comparable with prior published works.11,12

The demographic profile of the population showed a very high prevalence of metabolic risk factors, such as obesity, diabetes, and hypertension, which are well-known etiologic agents for NAFLD. This cohort has a mean BMI of 29.5 kg/m², underlining the tight association between obesity and fatty liver disease. Besides, the marked correlation between waist circumference and severity of the disease further emphasizes the role of visceral adiposity in the pathogenesis of hepatic steatosis and fibrosis.13,14

One of the strengths in this study is an evaluation of clinical and laboratory parameters altogether. This provides a robust dataset through which the relationship between metabolic dysfunction and progression of NAFLD can be analyzed. The use of non-invasive imaging techniques, such as ultrasound and elastography, actually adds to the clinical relevance of the findings and depicts real-world diagnosis. Some limitations should also be acknowledged. Such a cross-sectional design does not allow the establishment of causality between fasting glucose, insulin resistance, and disease progression. Longitudinal studies are necessitated to establish these associations as well as to study the predictive value of such biomarkers along with time.

Another limitation is the relatively small sample size, which may affect the generalizability of the findings. Although the study population was diverse in terms of age and gender, future research should aim to include larger and more heterogeneous cohorts to validate the results. Moreover, the study relied on HOMA-IR as a surrogate marker for insulin resistance, which, although widely used, has limitations compared to more direct measures such as hyperinsulinemic-euglycemic clamps.

Despite these limitations, the present study has wider clinical implications. The findings make fasting glucose and HOMA-IR simple, cost-effective biomarkers that could identify patients with advanced NAFLD. Integration of these markers into routine clinical practice can facilitate early intervention and improve patient outcomes. Further, the strong correlation between metabolic dysfunction and the severity of the disease would emphasize management strategies that encompass the comprehensive management of both hepatic and systemic metabolic health.

**CONCLUSION:**

In conclusion, this study reinforces the critical role of fasting glucose and insulin resistance in the progression of NAFLD. By identifying and managing these metabolic risk factors, clinicians can potentially mitigate disease progression and reduce the burden of NAFLD on healthcare systems.

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