

ORIGINAL ARTICLE

ASSOCIATION OF NON-ALCOHOLIC FATTY LIVER DISEASE WITH PROLIFERATIVE DIABETIC RETINOPATHY IN TYPE 2 DIABETICS

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ABSTRACT

Background: Diabetes is an emerging disease worldwide, leading to many complications. Non-alcoholic fatty liver disease (NAFLD) being most prevalent condition present in diabetics. Proliferative diabetic retinopathy (PDR) in uncontrolled diabetes is one of major comorbidity. This research investigated association of non-alcoholic fatty liver disease (NAFLD) with proliferative diabetic retinopathy (PDR) among patients diagnosed with type 2 diabetes mellitus (T2DM).

Materials & Methods: This cross-sectional study included 151 type 2 diabetes mellitus patients presented to Endocrinology department of Hayatabad Medical Complex, Peshawar, from August 2024 to February 2025. For NAFLD evaluation hepatic ultrasound provided the classification and fundus photography served to detect diabetic retinopathy. Data was analyzed using descriptive statistics and chi-square test by keeping p value < 0.05 significant.

Results: Out of 151 individuals, NAFLD occurred in 55.6% of patients among which 22% had mild NAFLD, 18% presented with moderate NAFLD and 15.8% had severe NAFLD. 48.3% had diagnosis of diabetic retinopathy. Patients with NAFLD had a PDR rate of 25.0% whereas those without NAFLD demonstrated 10.4%. Results of a chi-square analysis indicated NAFLD and PDR share a strong connection ($\chi^2 = 4.67$, $p = 0.03045$).

Conclusion: This research indicates that non-alcoholic fatty liver disease boosts PDR occurrence among individuals diagnosed with T2DM. NAFLD screenings during routine check-ups can help health providers identify individuals at risk for retinopathy therefore enabling prompt action to enhance diabetic patient care.

KEY WORDS: Alcohol; Complications; Diabetes mellitus; Fatty liver; Fibrosis; Fundus; Retinopathy.

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INTRODUCTION

The health situation due to diabetes mellitus affects millions of individuals across the globe, leading to mortality and morbidity. Type 2 diabetes mellitus stands as the most widespread diabetes form which features insulin resistance plus constant high blood glucose levels that cause multiple damaging effects throughout the body.^{1,2} Diabetes mellitus being a non-communicable public health problem,

is getting serious with the biggest pandemic in the world, which is alarmingly and is of major concern because of high mortality.^{3,4} Diabetic retinopathy and non-alcoholic fatty liver disease have turned into major comorbidities which patients develop from prolonged diabetes management. The mutual occurrence of these metabolic pathways and risk factors between these disorders has elevated scientific interest between them.^{5,6}

The disorder known as non-alcoholic fatty liver disease consists of different liver conditions when liver cells contain too much fat from non-alcoholic sources. The spectrum of NAFLD includes steatosis that gradually develops into non-alcoholic steatohepatitis (NASH), eventually causing fibrosis and cirrhosis before these lead to hepatocellular carcinoma.^{7,8} NAFLD presents as a direct consequence of metabolic syndrome together with obesity and insulin resistance and dyslipidemia thus making these conditions widely prevalent in T2DM patients. The analysis of

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diabetic patients suggests that Non-Alcoholic Liver Disease affects 70% of these patients suggesting an established correlation between diabetic metabolic dysfunction and liver steatosis.^{9,10} Patients of Type 2 Diabetes and NAFLD are more prone to develop steatohepatitis (NASH) and fibrosis with overall increased risk of diabetes related complications and cardiovascular complications.¹¹ Proliferative diabetic retinopathy (PDR) is established complication related to long term un-controlled diabetes, untreated cases lead to blindness and many other ocular complications.^{12,13} Diabetic retinopathies needs special attention especially in diabetes prevalent countries.¹⁴ The recognition of NAFLD links with PDR serves essential purposes for discovering and handling diabetic patients at high risk. Early stage NAFLD exists without symptoms so its detection can serve diagnosis purposes for severe disease progression in patients.^{15,16}

Research investigating the relationship between non-alcoholic fatty liver disease and proliferative diabetic retinopathy shows value in developing better screening and intervention methods because diabetes and its complications continue to increase. Such identification of NAFLD as a PDR severity risk factor allows clinicians to implement special management methods that decrease diabetic vision-related issues.¹⁷ This study showed that diabetes care needs multiple healthcare specialists working together which includes hepatology and endocrinology and ophthalmology professionals to provide the best patient results. The study examined association between NAFLD and PDR in type 2 diabetics and to show clinical implications. Our objective was to search the connection between NAFLD and PDR so healthcare professionals could benefit from our findings and researchers could use them to develop future studies regarding diabetes complications.

MATERIALS AND METHODS

This cross-sectional study was conducted at Endocrinology Department Hayatabad Medical Complex, Peshawar, after taking ethical approval from institutional review and ethic committee dated. 12/8/2024, 1989, from a period between August 2024 and February 2025. A research study aimed to determine the relationship between non-alcoholic fatty liver disease and proliferative diabetic retinopathy in patients who have type 2 diabetes mellitus. The research study included 151 type 2 diabetic patients by purposive sampling, taking 11% prevalence of severe NAFLD in a study¹⁸, with 5 % margin of error and 95% confidence interval, the calculated sample size was 151, by open Epi sample size calculator. Patients with type 2 Diabetes Mellitus with atleast one year of diagnosis, age of 40 years and one willing to participate were included in study. Patients who had a background of heavy alcohol use or viral hepatitis or any other identified persistent liver disease were

excluded.

The study's participants went through ultrasound scans for assessment of liver steatosis. The diagnostic criterion for Grade 0 (No fatty liver) revealed no echogenicity abnormalities in the liver examination. Sample with Grade 1 (Mild NAFLD) displayed slight increased echogenicity pattern in liver tissues with all diaphragm and intrahepatic vessel borders appeared normal. A diagnosis of Grade 2 (Moderate NAFLD) involved a moderate diffuse echogenicity increase of liver parenchyma with slightly impaired intrahepatic vessel border visualizations. Grade 3 (Severe NAFLD) displayed marked steatosis along with the complete disappearance of the posterior part of right lobe liver tissue, an impaired view of intrahepatic vessels, and altered diaphragm visualization.¹⁹

Fundus photography was used as the diagnostic instrument to identify diabetic retinopathy. The condition Proliferative Diabetic Retinopathy included neo-vascularization together with vitreous haemorrhage or tractional retinal detachment.²⁰ Statistical tests were done by SPSS program (version 26). Frequencies and percentages were calculated for categorical variables and means and standard deviations for continuous variables in the analysis. Researchers used cross tabulations to measure associations between NAFLD severity levels and PDR occurrence status. The chi-square test analyzed the relationship between NAFLD and PDR. The analysis found statistical significance at a p-value lower than 0.05.

RESULTS

The research study included 151 patients who carried a T2DM (type 2 diabetes mellitus) diagnosis. The mean age of individuals was 55.3 ± 8.2 years, among them 57% were males and 43% were females. The mean diabetes duration was 12.5 ± 6.7 years. The research participants presented a mean HbA1c level of $10.4 \pm 1.1\%$. (Table 1).

Table 1: Summary Statistics of Study Participants

Variable	Value
Number of Patients	151
Mean Age (years)	55.3 ± 8.2
Duration of Diabetes (years)	12.5 ± 6.7
Mean HbA1c (%)	10.4 ± 1.1

Ultrasound imaging diagnosed 55.6% (n=84) of participants having NAFLD. Of all NAFLD patients, 22% (33 participants) had mild liver damage (grade 1), moderate damage (grade 2) in 18% (27 participants) and severe liver damage (grade 3) in 15.8% (24 participants). NAFLD remained undetected in 44.4% of patients (number=67) based on results from Figure 1.

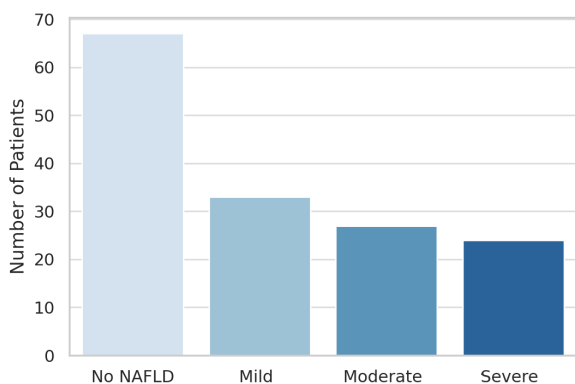


Figure 1: Severity distribution of NAFLD

The research showed that among the study participants 48.3% (n=73) had diagnosis of diabetic retinopathy. Results showed that 29.8% (n=45) of patients had NPDR (non proliferative) diagnosis but PDR (proliferative) was detected in 18.5% (n=28) among the study participants. Among the study subjects PDR developed more frequently in patients who had NAFLD compared to those who did not have NAFLD.

The statistical assessment of NAFLD and PDR relationship depended on a chi-square test. The analysis showed NAFLD is strongly linked to PDR because of the $\chi^2 = 4.67$ p-value of 0.03045. NAFLD patients faced increased probabilities for PDR onset compared to diabetes patients who did not have NAFLD thus demonstrating a possible correlation between liver steatosis and diabetes-associated retinal microvascular damage. This confirms a statistically significant association between NAFLD and PDR ($p < 0.05$). (Table 2).

Table 2: Chi-Square Test Results for NAFLD and PDR

Variable	PDR (n=28)	No PDR (n=123)	Total (n=151)
NAFLD Present (n=84)	21 (25.0%)	63 (75.0%)	84 (100%)
NAFLD Absent (n=67)	7 (10.4%)	60 (89.6%)	67 (100%)
Total	28 (18.5%)	123 (81.5%)	151 (100%)
Chi-Square Test Summary			
Statistic	Value		
Chi-Square (χ^2)	4.67		
Degrees of Freedom (df)	1		
p-value	0.03045		

DISCUSSION

Research evaluated the correlation between non-alcoholic fatty liver disease (NAFLD) with proliferative diabetic retinopathy (PDR) in patients suffering from type 2 diabetes mellitus (T2DM). This research included 151 patients demonstrating that NAFLD affected 54.6% of the group yet diabetic retinopathy occurred in 48.3% of participants. Statistics from a chi-square test show this relationship with statistical significance ($\chi^2 = 4.67, p = 0.03045$) which strengthens the claim that advanced hepatic steatosis causes severe retinal microvascular complications.

In a study done by Mantovani et al. NAFLD appears as a significant parallel risk factor that leads to advanced diabetic retinopathy specifically PDR among T2DM patients in a meta-analysis. This study identified hepatic steatosis as such a clinical marker that helps predict severe retinopathy development based on the reported findings which match our observation about PDR prevalence growth linked to NAFLD severity.²¹ In the research by Targher et al. indicated that metabolic syndrome elements including NAFLD closely correlate with the microvascular diabetes complications. NAFLD patients tend to experience elevated insulin resistance levels and inflammation markers which help advance diabetic retinopathy development according to their research findings.²² Findings of both these researches are in correlation with results of our study.

There was inverse association relationship between diabetic retinopathy and NAFLD in a study done by Afarideh et al.²³ and in a study by Wen et al, prevalence of NAFLD was 61.3% in which the diabetic retinopathy was also inversely associated with NAFLD²⁴, in contrast to our study, further detailed study is needed. A results of the study by Lee et al. showed that NAFLD risk levels were higher among patients who had diabetes. The findings from these studies emphasize that liver fat accumulation functions as a warning sign for microvascular problems including PDR above its role in showing metabolic problems.²⁵

Clinical application of our findings reveals substantial implications that the medical community can use. Routine NAFLD screening of T2DM patients presents dual benefits for prevalent hepatic problems and serves as a surrogate marker for predicting severe diabetic retinopathy onset. Ultrasonic evaluation of non-invasive NAFLD in clinical practice will allow healthcare providers to detect patients whose health status indicates elevated PDR risk. Early ophthalmologic evaluations as well as preventive interventions that aim to prevent vision loss should be provided to these patients.

CONCLUSION

The study confirmed that patients with type 2 diabetes mellitus who had NAFLD demonstrated a notable correlation with PDR. The risk of developing

PDR became significantly higher when patients had NAFLD along with severe liver steatosis. The research findings confirm earlier studies about the pathophysiological links between insulin resistance and inflammation and tissue oxidative stress. Screening patients for NAFLD provides an opportunity for practitioners to detect retinopathy risks early so that proper interventions can start right away. The limitations to the study were single-time data analysis approach used in our study prevents the determination of cause-and-effect relationships. The research performed in one single hospital reduces potential applications of its results toward broader populations. NAFLD diagnosis relied on ultrasound testing although this method shows reduced accuracies compared to doctor biopsy or advanced imaging methods including transient elastography.

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CONFLICT OF INTEREST

Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	MS, S
Acquisition, Analysis or Interpretation of Data:	MS, S
Manuscript Writing & Approval:	MS, S

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.



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