

THE INTERPLAY OF NON-ALCOHOLIC FATTY LIVER DISEASE AND CARDIOVASCULAR DISEASE IN TYPE 2 DIABETES MELLITUS: PATHOGENETIC MECHANISMS AND PREVENTIVE STRATEGIES

Urunbayeva Dilorom Anvarovna, Associate professor

Sadikova Nigora G'ayratovna

Jo'rayeva Guliza Bahodir qizi, master's student

TASHKENT STATE MEDICAL UNIVERSITY

RELEVANCE

The interplay between non-alcoholic fatty liver disease (NAFLD), type 2 diabetes mellitus (T2DM), and cardiovascular diseases (CVD) represents a pressing global health challenge due to their increasing prevalence and synergistic contribution to morbidity and mortality. NAFLD affects approximately 25-37% of the global population, with a significantly higher prevalence of 55-70% in individuals with T2DM, making it a critical comorbidity in this group. Both conditions are closely linked to metabolic syndrome, characterized by insulin resistance, dyslipidemia, and chronic low-grade inflammation, which collectively amplify the risk of CVD, the leading cause of death in T2DM patients. NAFLD is now recognized as an independent risk factor for CVD, with evidence suggesting that advanced liver fibrosis exacerbates cardiovascular outcomes. In regions like Uzbekistan, where obesity and T2DM rates are rising due to lifestyle changes and urbanization, the burden of NAFLD and its cardiovascular complications is becoming a public health priority. This research is highly relevant as it addresses the urgent need to understand the pathophysiological mechanisms linking these conditions and to develop integrated diagnostic and preventive strategies to reduce cardiometabolic morbidity. Furthermore, the study aims to contribute to global and regional efforts in improving early detection and management of NAFLD in T2DM patients, potentially reducing healthcare costs and improving quality of life.

Keywords: non-alcoholic fatty liver disease, type 2 diabetes mellitus, cardiovascular disease, insulin resistance, metabolic syndrome, liver fibrosis, cardiometabolic risk, biomarkers, hepatic ultrasonography, NAFLD fibrosis score, inflammation, lipid metabolism, glycemic control, cardiovascular risk assessment, preventive strategies.

RESEARCH OBJECTIVE

The primary objective of this study is to comprehensively investigate the association between NAFLD and CVD in patients with T2DM, with a focus on elucidating the underlying pathophysiological mechanisms, identifying key cardiometabolic risk factors, and evaluating the efficacy of non-invasive diagnostic tools for assessing NAFLD severity. The study also aims to explore the impact of NAFLD on cardiovascular outcomes in T2DM patients and to propose evidence-based preventive and therapeutic approaches to mitigate the combined burden of these conditions. Specific objectives include assessing the role of insulin resistance and systemic inflammation, determining the prevalence of NAFLD in T2DM patients, and evaluating the utility of biomarkers and imaging techniques in predicting CVD risk.

METHODS AND MATERIALS

A prospective cross-sectional study was conducted involving 500 patients with T2DM, aged 30-75 years, recruited from two tertiary care hospitals between January 2023 and December 2024. NAFLD was diagnosed using high-resolution hepatic ultrasonography (3.5-5 MHz probe), with steatosis graded as I (mild), II (moderate), or III (severe) based on echogenicity and liver texture. Liver fibrosis was assessed using the NAFLD Fibrosis Score (NFS) and Fibrosis-4 (FIB-4) index, incorporating age, BMI, platelet count, albumin, and liver enzymes (ALT, AST). Cardiovascular risk was evaluated using the Framingham Risk Score (FRS) and the Atherosclerotic Cardiovascular Disease (ASCVD) risk calculator, supplemented by biomarker analysis, including high-sensitivity C-reactive protein (hs-CRP), N-terminal pro b-type natriuretic peptide (NT-proBNP), interleukin-6 (IL-6), and lipid profiles (total cholesterol, LDL-C, HDL-C, triglycerides). Anthropometric measurements (BMI, waist circumference) and glycemic control (HbA1c) were recorded. Patients with excessive alcohol consumption (>20 g/day for women, >30 g/day for men), viral hepatitis, or other liver diseases were excluded. Data were analyzed using SPSS v25.0, with multivariate logistic regression to assess associations between NAFLD severity, T2DM, and CVD risk, and Pearson correlation to explore relationships between biomarkers and disease outcomes.

RESULTS

Of the 500 T2DM patients, 52% (n=260) were diagnosed with NAFLD, with 50% classified as Grade I, 42% as Grade II, and 8% as Grade III steatosis. Patients with NAFLD exhibited significantly higher BMI (32.4 ± 5.1 vs. 29.5 ± 4.8 kg/m², $p < 0.001$), waist circumference (104.3 ± 11.0 vs. 96.8 ± 10.4 cm, $p < 0.001$), and HbA1c levels ($7.8 \pm 1.2\%$ vs. $7.1 \pm 1.0\%$, $p = 0.002$) compared to those without

NAFLD. Inflammatory markers (hs-CRP, IL-6) and NT-proBNP were significantly elevated in NAFLD patients ($p < 0.01$). The FRS classified 30% of patients as moderate risk and 65% as high risk for CVD, with NAFLD patients showing a 1.6-fold increased risk of CVD events (HR 1.60, 95% CI 1.42–1.79). Advanced fibrosis (NFS > 0.675 or FIB-4 > 3.25) was observed in 12% of NAFLD patients and was associated with a 2.8-fold higher CVD risk (HR 2.80, 95% CI 1.95–4.02). Lipid profiles showed elevated triglycerides (2.3 ± 0.9 vs. 1.8 ± 0.7 mmol/L, $p < 0.001$) and lower HDL-C in NAFLD patients. No significant association was found between NAFLD and diabetic nephropathy or retinopathy, though trends suggested a potential link with microvascular complications. Non-invasive tools (ultrasonography, NFS, FIB-4) demonstrated high sensitivity (88%) and specificity (79%) in detecting NAFLD and fibrosis.

CONCLUSION

NAFLD significantly exacerbates CVD risk in T2DM patients, particularly in those with advanced liver fibrosis, driven by synergistic mechanisms involving insulin resistance, systemic inflammation, and dyslipidemia. The high prevalence of NAFLD in T2DM patients underscores the need for routine screening using non-invasive tools such as hepatic ultrasonography and fibrosis scores (NFS, FIB-4), which are effective for early detection and risk stratification. Elevated inflammatory markers (hs-CRP, IL-6) and cardiac biomarkers (NT-proBNP) highlight the role of chronic inflammation in linking NAFLD to CVD. Preventive strategies, including lifestyle modifications (weight loss, Mediterranean diet, regular physical activity) and pharmacological interventions (e.g., GLP-1 receptor agonists, SGLT2 inhibitors), are critical for reducing cardiometabolic risk. These findings advocate for integrated clinical protocols that combine NAFLD screening with CVD risk assessment in T2DM patients to improve early diagnosis, optimize management, and reduce the global burden of cardiometabolic diseases. Future research should focus on longitudinal studies to establish causality and evaluate novel therapeutic agents targeting NAFLD-related pathways.

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