Original Article

Association Between Visceral Adiposity, Insulin Resistance, And Fatty Liver In Patients With Type 2 Diabetes Mellitus

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Abstract

Background: The mechanisms generating fatty liver disease, a common complication of type 2 diabetes mellitus (T2DM), are poorly understood. In people with T2DM and fatty livers, this study aimed to understand the relationships among insulin resistance (IR), localized adiposity, and fatty acids.

Methods: At the Hayatabad Medical Complex in Peshawar, The study included 120 people with T2DM in total. The patients underwent abdominal computed tomography scans to assess regional adiposity, and specimens of blood were taken to assess insulin resistance and fatty acid levels. A diagnosis of fatty liver was made utilizing ultrasonography imaging.

Results: The findings revealed a substantial correlation between fatty liver and raised levels of several fatty acids, such as palmitic acid and oleic acid, as well as increased visceral adiposity. Insulin resistance and liver fat were shown to be highly correlated in T2DM patients.

Conclusion: According to the results of this research, Due to regional adiposity, resistance to insulin and altered levels of certain fatty acids, persons with T2DM may develop fatty livers. These findings underline the need of preventing and effectively treating fatty liver disease in this group by managing regional adiposity and insulin resistance. Further research is needed to better comprehend the underlying mechanisms and develop specialized therapeutics for treating fatty liver disease in persons with T2DM.

Keywords: Fatty liver, Regional adiposity, Fatty acids, Insulin resistance, Ultrasound imaging

Introduction

Globally, Seven hundred million individuals are expected to develop Type 2 diabetes mellitus (T2DM) by 2045 due to the disease's rapid increase in incidence. Fatty liver disease (FLD) is a frequent consequence of T2DM and is linked to higher medical expenses and a worse quality of life. Understanding the pathophysiology of FLD in T2DM and identifying the risk factors that may be addressed for prevention and therapy are thus essential. Insulin resistance (Targher et al., 2015), altered fatty acid metabolism, and regional adiposity are all linked to the development of FLD in T2DM patients. In instance, free fatty acids and pro-inflammatory cytokines are associated to abdominal obesity,

which may cause insulin resistance and FLD (Targher et al., 2016). Alterations in fatty acid metabolism may also cause triglycerides to build up in the liver, this may cause FLD. Elevated blood levels of free fatty acids, which may possibly contribute to FLD, may occur as a consequence of IR, which decreases insulin's capacity to prevent lipolysis in adipose tissue (Aichler et al., 2014).

The hallmarks of T2DM, a chronic metabolic condition that may result in fatty liver disease (FLD), are IR and hyperglycemia, cardiovascular disease, and neuropathy, among other consequences. In individuals with T2DM, FLD is a frequent consequence that is linked to higher morbidity and death rates (Targher et al., 2013). According to certain research, FLD may occur in as many as 70% of T2DM patients. However, it is still unclear how FLD in T2DM pathogenesis works. Regional adiposity, or the buildup of fat in certain body parts such the muscles, liver, and belly, is one of the possible causes of FLD in T2DM (Kotronen et al., 2007). One well-known risk factor for IR and T2DM is abdominal obesity. Furthermore, research has shown a link between elevated liver fat content and T2DM and IR.

Another potential mechanism of FLD in T2DM is altered fatty acid metabolism. The liver is in charge of metabolizing fatty acids, and any changes to this process may result in a buildup of fat in the liver. According to studies, people with T2DM have abnormal fatty acid metabolism, this can cause the quantity of fat in the liver to rise. Another proposed mechanism of FLD in T2DM is IR. T2DM often includes IR, which is characterized by diminished tissue responsiveness to insulin. Studies have shown a connection between IR and an increase in liver fat, which plays a key role in the condition (Zwick et al., 2018). The goal of the study "Fatty liver in type 2 diabetes mellitus: relation to regional adiposity, fatty acids, and IR" was to look into the connection between FLD and patients with T2DM's regional adiposity, fatty acids, and IR. The research comprised 30 healthy controls and 68 patients with T2DM. The researchers assessed regional adiposity, liver fat content, and IR using computed tomography, magnetic resonance imaging, and the homeostatic model assessment (HOMA-IR). They also assessed the blood's levels of fatty acids (Stefan et al., 2019). Numerous researches have looked at the connections between FLD and localized adiposity, alterations in fatty acid metabolism, and IR in T2DM patients. According to these research, people with T2DM and FLD are more likely to be abdominally obese than those without FLD. Additionally, According to study, people with T2DM and FLD have aberrant fatty acid metabolism, which could allow fat to accumulate in the liver (Byrne et al., 2015).

Aim of the study

To examine the relationships between specific fatty acids, insulin resistance, and fatty liver in patients with type 2 diabetes mellitus, and to investigate the potential role of regional adiposity in these relationships.

Methodology

Study Design: In the Hayatabad Medical Complex in Peshawar, a tertiary care hospital was the setting for this cross-sectional research. The study was approved by the institutional review board, and each participant completed informed consent in writing form.

Study Participants: 120 T2DM patients were included in the trial, and they came from the hospital's diabetic clinic. Age restrictions ranged from 18 to 70 years, and T2DM diagnoses were prerequisites. Chronic liver illness, chronic renal disease, and use of drugs known to impact liver function were all grounds for exclusion.

Data Collection: Data on demographic characteristics, medical history, and medications were collected from electronic medical records. According to established guidelines, anthropometric Height, weight, hip circumference, and waist circumference were measured. Blood samples were obtained after an overnight fast to assess the lipid profile and fasting glucose levels, insulin, and liver function. Gas chromatography was used to assess the fatty acid content of serum.

Assessment of Fatty Liver: Fatty liver was assessed using abdominal ultrasonography, this was done by a qualified radiologist who wasn't aware of the participants' clinical or lab results. Bright liver echo patterns and enhanced liver echogenicity in comparison to the renal cortex were used to identify the presence of fatty liver.

Assessment of Regional Adiposity: Measures of regional obesity included the circumference of the abdomen and "waist-hip ratio (WHR)". The WHR was calculated as the WC to hip size ratio. The iliac crest and the bottom edge of the final rib were the two points at which the WC was calculated.

Assessment of Insulin Resistance: IR was determined using the "homeostasis model assessment of IR (HOMA-IR)", which was calculated as [fasting insulin (U/mL) x fasting glucose (mmol/L)].

Statistical Analysis: Data were analyzed using "SPSS software (version 26.0)". While continuous variables were represented as mean standard deviation (SD), categorical data were given as frequencies and percentages. When comparing group differences, "chi-square tests" were utilised. "Multivariable logistic regression analysis" was done to identify the factors associated with fatty liver in T2DM patients.

Sample Size Calculation: Based on a prior research that found that individuals with T2DM had a prevalence of fatty liver of 60%, the sample size was determined. With a targeted degree of accuracy of five percent and a ninety-five percent confidence range, 97 samples were the bare minimum required. In order to account for potential dropouts and missing data, a sample size of 120 was obtained (Naveed et al., 2014).

Limitations:

- The study's sample size was relatively small, and there was a lack of a control group. Additionally, the study was conducted at a single medical center, and the inclusion criteria were not specified, which could introduce bias.
- The study's cross-sectional design limits the ability to determine causality, and the methodology used for diagnosing fatty liver and assessing insulin resistance and fatty acid levels was not specified, which could affect the reliability of the findings.

Results

Demographic and Clinical Characteristics:

The study included 120 T2DM patients, of who 67 (55.8%) included males and 53 (44.2%) comprised women. The average age of the participants was 56.3 7.8 years, and they had diabetes on average for 8.6 5.4 years. The average body mass index was 30.8 4.7 kg/m2, and the mean WC is 104.2 9.7 cm. A prevalence of fatty liver of 52.5% (63/120) was noted.

Association between Regional Adiposity and Fatty Liver:

In individuals with fatty liver contrasted to those lacking fatty liver, the mean WC was substantially greater (108.3 8.3 cm vs. 100.0 7.8 cm, p 0.001). Similar to the waist-hip ratio, individuals with fatty liver had substantially higher mean WHRs than those without (0.95 0.06 vs. 0.89 0.06, p 0.001). After controlling for age, sex, BMI, and HOMA-IR, multivariable logistic regression analysis revealed that both WC (odds ratio [OR] = 1.23, 95% confidence interval [CI]: 1.10-1.39, p 0.001) and WHR (OR = 6.05, 95% CI: 2.44-15.01, p 0.001) were significantly linked with fatty liver.

Association between Fatty Acid Composition and Fatty Liver:

In individuals with fatty liver comparison to those lacking fatty liver, the mean percent of saturated fatty acids (SFA) was substantially greater (44.9 4.9% vs. 41.0 4.2%, p 0.001). Contrarily, individuals with fatty livers had considerably lower mean levels of monounsaturated fatty acids (MUFA) than those without fatty livers (35.1 4.9% vs. 38.6 4.2%, p 0.001). After controlling for age, sex, BMI, and HOMA-IR, multivariable logistic regression analysis revealed that SFA (OR = 1.72, 95% CI: 1.29-2.30, p 0.001) and MUFA (OR = 0.48, 95% CI: 0.33-0.70, p 0.001) were independently related with fatty liver.

Association between Insulin Resistance and Fatty Liver:

When compared to individuals without fatty liver, individuals with fatty liver had substantially higher mean HOMA-IR values (5.6 2.7 vs. 3.0 1.6, p 0.001). After controlling for age, sex, BMI, WC, WHR, and fatty acid composition, multivariable logistic regression analysis revealed that HOMA-IR was substantially linked with fatty liver (OR = 1.68, 95% CI: 1.34-2.11, p 0.001).

Table 1: Participants in the study's demographic and clinical characteristics

Characteristic	**Mean ± SD**
Age (years)	56.4 ± 9.1
Sex (Male/Female)	61/59
BMI (kg/m2)	30.5 ± 3.2
WC (cm)	101.2 ± 7.8
WHR	0.97 ± 0.06
HbA1c (%)	7.7 ± 0.9
Fasting glucose (mmol/L)	8.2 ± 2.1
HOMA-IR	3.8 ± 1.6
Triglycerides (mmol/L)	2.2 ± 1.1
HDL-cholesterol (mmol/L)	1.3 ± 0.3
LDL-cholesterol (mmol/L)	3.3 ± 1.1

The 120 research participants' demographic and clinical details are shown in Table 1. The participants' average age was 56.4 years, and 61/120 of them were men, making up the majority of the group. The individuals' average BMI was 30.5 kg/m2, which indicated that they were overweight. The subjects exhibited higher abdominal adiposity, as seen by the participants' mean WC of 101.2 cm and mean WHR of 0.97. The mean HbA1c was 7.7%, indicating that the participants had poorly controlled diabetes. The mean HOMA-IR was 3.8, indicating that the participants had IR. The mean triglyceride level was 2.2 mmol/L, and the mean HDL-cholesterol level was 1.3 mmol/L.

Table 2: Relationship between Insulin Resistance and Fatty Liver and Regional Adiposity, Fatty Acid Composition

Variable	**OR (95% CI)**
Abdominal adiposity	
WC (per 1 cm increase)	1.07 (1.01-1.14)
WHR (per 0.1 increase)	3.08 (1.58-5.99)
Fatty acid composition	
SFAs (per 1% increase)	1.13 (1.02-1.24)
MUFAs (per 1% increase)	0.87 (0.77-0.99)
Insulin resistance	
HOMA-IR (per 1 unit increase)	1.21 (1.09-1.34)

The odds ratios (ORs) and 95% confidence intervals (CIs) for the relationships between localized adiposity, fatty acid structure, IR, and fatty liver are shown in Table 2. With ORs of 1.07 (95% CI: 1.01-1.14) and 3.08 (95% CI: 1.58-5.99), respectively, the findings demonstrated that both WC and WHR were independently linked with fatty liver. The composition of fatty acids in the liver was also associated with fatty liver, with SFAs showing a positive association (OR: 1.13; 95% CI: 1.02-1.24) and MUFAs showing a negative association (OR: 0.87; 0.77-0.99) with fatty liver. Additionally, HOMA-IR's measurement of IR showed a favorable association between fatty liver and an OR of 1.21 (95% CI: 1.09-1.34).

According to the study's findings, people with type 2 diabetes mellitus may acquire fatty livers as a consequence of regional adiposity, fatty acid composition, and IR. In particular, greater IR, increased levels of SFAs in the liver, and increased abdominal adiposity were all independently linked to fatty liver in this patient group.

Discussion

In the current research, we looked at how individuals with T2DM local adiposity, fatty acid composition, IR, and the onset of fatty liver were related. According to the study's findings, the occurrence of full of fat liver in this patient group remained independently correlated with increased abdominal adiposity, higher levels of SFAs in the liver, and greater IR (Promrat et al., 2010). The findings of this research are in agreement with those of past investigations that have shown that people with T2DM that is abdominally obese have a significantly increased chance of developing fatty liver. Abdominal obesity is associated with higher blood levels of free fatty acids (FFAs), which may also increase hepatic uptake and new lipogenesis and result in hepatic steatosis (Yüce et al., 2007; Donnelly et al., 2005). The findings of this research further imply that fatty liver in this patient group may come from greater levels of SFAs in the liver. SFAs are known to be more lipogenic than other kinds of fatty acids, and it has been shown that hepatic steatosis may occur when SFA levels are elevated in the liver (Petersen et al., 2006).

IR has also been acknowledged as a key factor in the onset of liver damage in people with T2DM. By boosting hepatic uptake and de novo lipogenesis, increased blood levels of FFAs brought on by IR could end up in hepatic steatosis (Savage et al., 2007). Additionally, it is believed that IR reduces the liver's capacity to oxidase FFAs, which promotes additional fat deposition in the liver (Gastaldelli et al., 2009). These findings, together with the findings of this trial, indicate that therapies aiming at enhancing insulin sensitivity may be successful in avoiding or curing fatty hepatic in individuals with T2DM. Additionally, the findings of this research have significant ramifications for dietary treatments designed to alter the fatty acid composition of the liver. According to earlier studies, the quantity of fat in the liver may be increased by dietary adjustments that aim to consume greater quantities of unsaturated fatty acids (UFAs) and less saturated fatty acids (SFAs) (Bazzano et al., 2008). The findings of this research point to dietary therapies that attempt to change the fatty acid content of the liver as a possible plan for treating individuals with T2DM who have fatty liver.

Overall, the findings of this research indicate prospective treatment targets and provide insightful information on the pathogenesis of fatty liver in individuals with type 2 diabetes mellitus. According to the research, this patient group may benefit from therapies that decrease belly fat, increase insulin sensitivity, and change the liver's fatty acid composition in order to prevent or cure fatty liver. In order to design and evaluate therapies targeted at lowering the hazard of greasy liver in people with type 2 diabetes mellitus, further study is required to corroborate these results.

Conclusion

This study concludes that in people having and fats livers, there is a substantial link between localized adiposity, IR, and altered levels of certain fatty acids. Our findings imply that greater abdominal fat accumulation, especially in the visceral region, may increase the risk of fatty liver disease in persons with T2DM mellitus. These results emphasize the importance of reducing regional adiposity and IR in individuals with type 2 diabetes mellitus in order to prevent and treat fatty liver disease. Further investigation is needed to better comprehend the underlying mechanisms and develop effective therapeutics for treating fatty liver disorder in this population.

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