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Association of Insulin Resistance and Ectopic Fat Accumulation with HOMA Indices: A Single-Centre Observational Study

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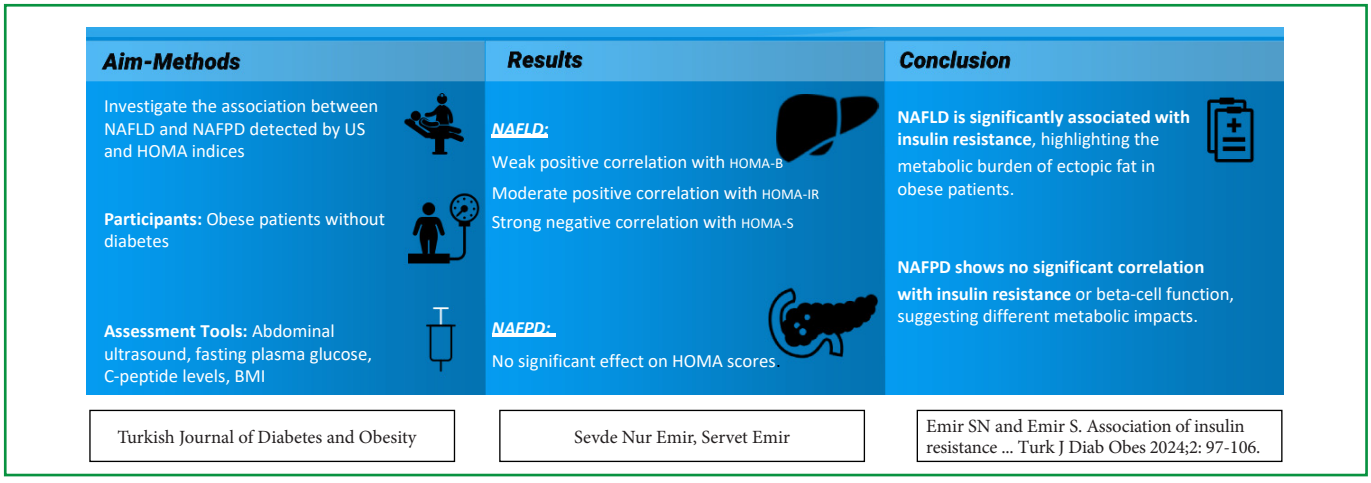
GRAPHICAL ABSTRACT



ABSTRACT

Aim: The aim of this study was to investigate the relationship between non-alcoholic fatty liver disease (NAFLD), non-alcoholic fatty pancreas disease (NAFPD) and HOMA indices in obese patients without a diagnosis of diabetes mellitus, using ultrasound (US) as a common non-invasive diagnostic tool during routine examinations.

Material and Methods: In this single-centre, retrospective study, the records of patients who applied to the obesity outpatient clinic in 2023 were reviewed. Digital records were scanned and patients with abdominal ultrasound reports indicating age, gender, body mass index (BMI), fasting plasma glucose, C-peptide level and degree of pancreatic and hepatic steatosis were included in the study. Patients with known chronic disease or diabetes mellitus and patients with specific drug use were excluded from the study. HOMA indices were calculated using fasting plasma glucose and C-peptide levels. Descriptive statistics were calculated. Spearman's rho coefficient assessed correlations between NAFLD, NAFPD, and HOMA indices and the Kruskal-Wallis and Mann-Whitney U tests evaluated the effect of NAFLD and NAFPD on HOMA indices. ROC analysis predicted NAFLD presence using HOMA-IR and HOMA-S values, showing high model accuracy. Statistical analyses were performed with IBM SPSS v28.0, with significance set at $p<0.05$.

Results: A total of 62 patients were included. Body mass index was 39.1; 91% had NAFLD and 82% had NAFPD. There was a significant positive correlation between BMI and NAFLD and NAFPD. In our study, NAFLD showed a weak positive correlation with beta-cell function (HOMA-B) (Spearman's rho = 0.277, $p=0.029$), a moderate positive correlation with insulin resistance (HOMA-IR) (Spearman's rho = 0.555, $p<0.00001$), and a strong negative correlation with insulin sensitivity (HOMA-S) (Spearman's rho = -0.555, $p<0.001$). No significant effect of NAFPD on HOMA scores was observed.

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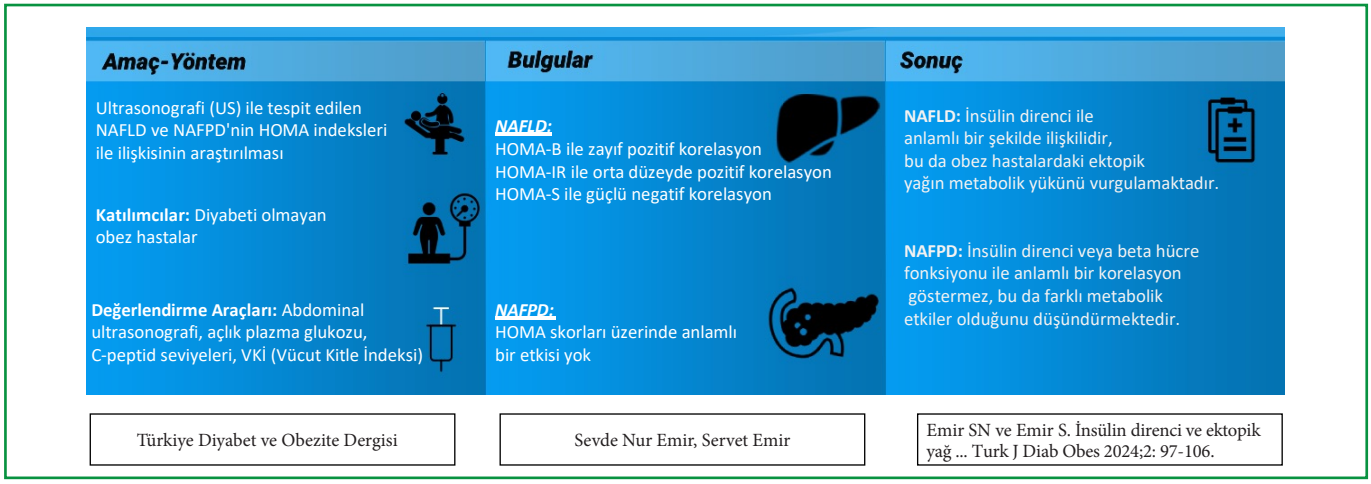
Conclusion: The findings underline the association between NAFLD and insulin resistance and highlight the metabolic burden of ectopic fat deposition in obese patients. In contrast, there was no significant correlation between NAFPD and either insulin resistance or beta-cell function, suggesting that the metabolic impact of pancreatic steatosis might be different. These findings may help to guide clinical strategies for detecting and treating metabolic disorders in obesity.

Keywords: *Non-alcoholic fatty liver disease, Non-alcoholic fatty pancreas disease, Insulin resistance, Obesity, HOMA index, Ultrasound imaging*

İnsülin Direnci ve Ektopik Yağ Birikiminin HOMA İndeksleri ile İlişkisi: Tek Merkezli Bir Gözlem Çalışması

GRAFİKSEL ÖZET



ÖZ

Amaç: Bu çalışmanın amacı, diyabetes mellitus tanısı olmayan obez hastalarda, rutin muayeneler sırasında yaygın bir non-invaziv tanı aracı olan ultrason (US) kullanılarak, non alkolik yağlı karaciğer hastalığı (NAFLD), non alkolik yağlı pankreas hastalığı (NAFPD) ve HOMA indeksleri arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntemler: Bu tek merkezli, retrospektif çalışmada, 2023 yılında obezite polikliniğine başvuran hastaların kayıtları gözden geçirilmiştir. Dijital kayıtlar taranmış ve yaş, cinsiyet, vücut kütle indeksi (VKİ), açlık plazma glikozu, açlık plazma glikozu, C-peptid seviyesi ve pankreatik ve hepatik steatoz derecesini belirten abdominal ultrason raporlarına sahip hastalar çalışmaya dahil edilmiştir. Bilinen kronik hastalığı veya diyabetes mellitusu olan ve belirli ilaçları kullanan hastalar çalışma dışı bırakılmıştır. HOMA indeksleri, açlık plazma glikozu ve C-peptid seviyeleri kullanılarak hesaplanmıştır. Tanımlayıcı istatistikler hesaplandı. NAFLD, NAFPD ve HOMA indeksleri arasındaki korelasyonlar Spearman'ın rho katsayısı ile değerlendirildi ve Kruskal-Wallis ve Mann-Whitney U testleri, NAFLD ve NAFPD'nin HOMA indeksleri üzerindeki etkisini değerlendirdi. ROC analizi, HOMA-IR ve HOMA-S değerlerini kullanarak NAFLD varlığını öngördü ve modelin yüksek doğruluğa sahip olduğunu gösterdi. İstatistiksel analizler IBM SPSS v28.0 ile gerçekleştirildi ve anlamlılık düzeyi $p<0,05$ olarak kabul edildi.

Bulgular: Toplam 62 hasta dahil edildi. Vücut kütle indeksi 39,1; %91'inde NAFLD ve %82'sinde NAFPD vardı. VKİ ile NAFLD ve NAFPD arasında anlamlı pozitif bir korelasyon vardı. Çalışmamızda, NAFLD ile beta hücre fonksiyonu (HOMA-B) arasında zayıf bir pozitif korelasyon (Spearman's rho = 0,277, p=0,029), insülin direnci (HOMA-IR) arasında orta derecede pozitif bir korelasyon (Spearman's rho = 0,555, $p<0,00001$) ve insülin duyarlılığı (HOMA-S) arasında güçlü bir negatif korelasyon (Spearman's rho = -0,555, $p<0,001$) gözlendi. NAFPD' nin HOMA skorları üzerinde anlamlı bir etkisi gözlenmedi.

Sonuç: Bulgular, NAFLD ile insülin direnci arasındaki ilişkiyi vurgulamakta ve obez hastalarda ektopik yağ birikiminin metabolik yükünü ön plana çıkarmaktadır. Buna karşın, NAFPD ile insülin direnci veya beta hücre fonksiyonu arasında anlamlı bir korelasyon bulunmamıştır, bu da pankreatik steatozun metabolik etkisinin farklı olabileceğini öne sürmektedir. Bu bulgular, obezitede metabolik bozuklukların tespiti ve tedavisi için klinik stratejileri yönlendirmede yardımcı olabilir.

Anahtar Sözcükler: *Non alkolik yağlı karaciğer hastalığı, Non alkolik yağlı pankreas hastalığı, İnsülin direnci, Obezite, HOMA indeksi, Ultrason görüntüleme*

INTRODUCTION

Obesity, with changing lifestyle, has become one of the leading factors increasing the risk of cardiovascular disease,metabolic syndrome and type 2 diabetes mellitus (T2DM) (1). These results are associated with hypertrophy and hyperplasia of adipocytes and the accumulation of ectopic adipose tissue in non adipose organs such as liver, pancreas, heart and muscle tissue due to increased energy (2,3).

The best known organ localisation of fatty tissue accumulation is the liver, formerly known as non-alcoholic fatty liver disease, now known as metabolic associated fatty liver disease (MAFLD). Recently, fat accumulation in pancreatic cells has also been described and is known by various terms such as non-alcoholic fatty pancreas disease (NAFPD), fatty pancreas, pancreatic steatosis, pancreatic lipomatosis, fatty replacement of pancreas, and fatty infltration of pancreas (4,5).

In the literature, there are many studies indicating that NAFLD and NAFPD are associated with insulin resistance, T2DM, hyperlipidemia, metabolic syndrome and obesity (6-8).

The diagnosis of NAFLD and NAFPD can be evaluated by non-invasive imaging techniques such as abdominal ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI). Although MRI is the best imaging method, abdominal US is the first and most preferred method because it is easily accessible and inexpensive (9,10).

NAFPD is often detected using ultrasound in epidemiological studies and is characterized by increased echogenicity of the pancreatic parenchyma compared to the kidneys (11,12). The prevalence of NAFPD has been found to be 16-35% in adults and its frequency is progressively increasing (13). In addition, 67% of NAFLD patients are also associated with NAFPD (14).

Pancreatic beta cell dysfunction and decreased insulin sensitivity predispose to the development of T2DM. Insulin resistance (IR) is another important pathophysiological factor in the development and progression of T2DM (15).

Known methods for the assessment of insulin resistance include dynamic tests (hyperinsulinemic euglycemic clamp, known as the reference technique), simple indices that do not require external administration of insulin or glucose (e.g. HOMA-IR, a homeostasis model assessment) and biochemical markers (e.g. insulin-like growth factor binding protein-1). In particular, simple indices such as HOMA-IR are often used to estimate IR (16-18).

The Homeostasis Model Assessment (HOMA) calculates pancreatic beta cell dysfunction (%β) as a percentage of a reference population with normal body insulin sensitivity (%S). HOMA-%B is used to estimate beta cell function in most studies (19,20).

HOMA-IR is an index calculated from fasting plasma insulin and glucose values. As stated in diabetes guidelines, evaluation with HOMA-IR can be performed in patients in the early stages of DM (21,22).

The objective of this study was to investigate the potential association between NAFLD and NAFPD, which are commonly detected by ultrasonography in non-diabetic obese patients and HOMA indices.

MATERIAL and METHODS

The Health Sciences University Umraniye Training and Research Hospital Clinical Research Ethics Committee approved the study protocol. Informed consent was not required due to the retrospective design and nature of the study.

The records of patients admitted to our hospital's obesity outpatient clinic in 2023 with follow-up by a single team were retrospectively reviewed.

Patients were included in the study based on age, BMI, fasting plasma glucose and fasting plasma C-peptide levels, and those with evidence of fatty liver and pancreas on abdominal ultrasound. Patients with known chronic liver or pancreatic disease, patients with any other chronic disease, patients with DM, metformin, pioglitazone, statin and fenofibrate users and patients with a BMI below 27 were excluded from the study. After being evaluated based on these criterias, the number of patients included in the study was determined as 62.

Abdominal ultrasonography examinations of all patients in the study were performed by a single radiologist using high resolution ultrasonography. Patients were evaluated with the standart approach after 8-12 hours of fasting.

Assessment of Hepatic and Pancreatic Steatosis

Fatty liver was assessed on a qualitative scale ranging from normal to severe (grades 0-3). Grade 1 (mild) is defined by a slight increase in parenchymal echogenicity, with normal visualization of intrahepatic vascular structures and the diaphragm. Grade 2 (moderate) reflects a moderate increase in parenchymal echogenicity, accompanied by partial visualization of the vascular structures and diaphragm. Grade 3 (severe) is characterized by a marked increase in echogenicity, with indistinct or poorly defined borders of the vascular structures, diaphragm, and posterior lobe (10,23).

Pancreatic steatosis is usually diagnosed by comparing the echogenicity of the pancreas with that of the kidneys. The

condition is qualitatively graded on a scale from normal to severe (grades 0-3). In grade 0, the pancreatic echogenicity is similar to that of the kidneys. Grade 1 indicates that the pancreatic echogenicity is slightly higher than that of the kidneys. Grade 2 is defined by a significant increase in pancreatic echogenicity relative to the kidneys, though it remains lower than the echogenicity of retroperitoneal fat. In grade 3, the pancreatic echogenicity matches or exceeds that of retroperitoneal fat (24,25).

Assessment of HOMA indexes

HOMA is used to assess insulin resistance and beta cell function (26).

Levy et al. (2004) introduced an updated version of the HOMA model, known as HOMA2, which accounts for variations in hepatic and peripheral glucose resistance, adjustments in the insulin secretion curve at elevated plasma glucose levels, and the impact of circulating proinsulin (18,19,27).

In this model, C-peptide concentration is utilized to evaluate beta cell function (HOMA2-%B), while specific insulin levels are used to determine insulin sensitivity (HOMA2-%S). Insulin clearance, however, varies significantly between individuals as it is dependent on liver function. C-peptide, which is secreted in equal amounts with insulin, is cleared by the kidneys. Hence, it is regarded as a more reliable marker for assessing beta cell response (28).

This model gives HOMA2-%B and HOMA2-%S values of 100% and HOMA2-IR = 1 in normal adult individuals (IR index simply represents the reciprocal of %S) (18).

In 2004, the HOMA2 Calculator was published to provide researchers with fast and easy access to the HOMA2 model. In our study, we calculated HOMA2 values by using this web based calculator (29).

Statistical Analyses

The power analysis of the study was conducted using the G*Power 3.1 software package. During the analysis, Cohen's d value was used for the calculation of effect size. Spearman's rho coefficient was used to evaluate the correlations between NAFLD, NAFPD, and HOMA indices. According to the power analysis results, with a sample size of 62, an 80% power and a 5% error rate were achieved. This indicates that our study has sufficient power to assess the results of the specified statistical tests.

In this study, various tests were employed during the statistical analyses. To evaluate the effect of NAFLD and NAFPD on HOMA indices, Kruskal-Wallis and Mann-Whitney U tests were used. ROC analysis was conducted to predict the presence of NAFLD using HOMA-IR and HOMA-S values. The AUC values in the ROC analysis indicated that the model had a high level of accuracy. IBM SPSS v28.0 (IBM SPSS Inc., Chicago, IL, USA) was used for statistical analyses. The level of signifcance was set at $p<0.05$.

RESULTS

In our study, there were 62 patients, 48 females and 14 males. The mean age was 37.9 (SD:11.5). The mean body mass index of the patients was 39.2 (SD:6.1). NAFLD was present in 91% and NAFPD in 82% of the patients. The demographic data and metabolic characteristics in the sudy subjects are shown in Table 1.

Firstly, there was no significant association between age and NAFLD (p=0.298), whereas there was a significant and moderately positive association between age and NAFPD (p=0.005).

There is a moderate positive correlation between BMI and NAFLD (Spearman's rho = 0.428, p=0.469) and a moderate positive correlation between BMI and NAFPD (Spearman's rho = 0.481, p=0.146), These results suggest that the risk of NAFLD and NAFPD may increase with increasing BMI values (Table 2).

Table 1: The demographic data and metabolic characteristics in the sudy subjects.

Characteristics*	Findings (n=62)	
Age (year)	39.5±11.5	37.9 (19-69)
BMI (kg/m^2)	38.2±6.1	39.2 (28.2-55.2)
Fasting Glucose (mg/dL)	93.0±15.8	95.9 (86-174)
Fasting C-peptide (ng/mL)	3.2±1.6	3.6 (1.1-7.2)
HOMA-B	169.1±61.6	171.4 (44.9-343.4)
HOMA-S	42.3±22.8	45.6 (21.4-124.3)
HOMA-IR	2.4±1.2	2.7 (1.57-6.1)

Age (year), BMI (kg/m^2), Fasting Glucose (mg/dL), Fasting C-peptide (ng/mL), HOMA-B, HOMA-S, HOMA-IR values are presented as "mean±-Standart Deviation, median (minimum – maximum)"

Table 2: Moderate positive correlations were found between BMI, HOMA scores, NAFLD and NAFPD.

Correlations	NAFLD	p	NAFPD	p
	Correlation coefficient		Correlation coefficient	
BMI	0.428	0.469	0.481	0.146
HOMA-B	0.277	0.029	-0.164	0.202
HOMA-S	-0.555	<0.00001	-0.041	0.753
HOMA-IR	0.555	<0.00001	0.042	0.747

Spearman's rho was used for correlation coefficients.

Relationships Between NAFLD and HOMA Scores

In our study, a weak positive correlation was found between NAFLD and HOMA-B (Spearman's rho = 0.277, p=0.029) and a moderate positive correlation was found between HOMA-IR (Spearman's rho = 0.555, p<0.00001). A strong negative correlation was found between NAFLD and HOMA-S (Spearman's rho = -0.555, p<0.001) (Table 2).

The negative correlation with HOMA-S indicates that NAFLD reduces insulin sensitivity, while the positive correlations with HOMA-B and HOMA-IR indicate increased insulin resistance and pancreatic beta-cell burden.

Relationships Between NAFPD and HOMA Scores

In our study, the relationship between NAFPD and HOMA-B (p=0.202), HOMA-IR (p=0.747), and HOMA-S (p=0.753) scores was not statistically significant (Table 2).

When the presence and absence of NAFLD was binary coded (present = 1, 2, 3 and absent = 0), the accuracy of the model was calculated to be 84.62%. This shows that the model is a strong indicator for predicting the presence of NAFLD based on the HOMA-S score.

In our study, post-hoc analyses performed to evaluate differences between NAFPD groups using Mann-Whitney U tests for HOMA-S (p=0.753) and HOMA-IR (p=0.747) scores did not show statistically significant differences.

Conversely, the analyses performed to assess differences between the NAFLD groups showed statistically significant results between Grade 1 and Grade 3 groups for both HOMA-S and HOMA-IR scores, with a p= 0.001.

The area under the curve (AUC) value was calculated as 0.79 in ROC curve analysis to predict the presence of NAFLD using HOMA-S scores in logistic regression analysis (Figure 3).

The AUC value was calculated as 0.71 in ROC curve analysis to predict the presence of NAFLD using HOMA-IR scores in logistic regression analysis.The optimum HOMA-IR cut-off value for differentiating patients with and without NAFLD was determined as 2.76 (Figure 4).

DISCUSSION

Insulin resistance refers to a condition where the biological response of tissues to insulin is diminished. Although this impairment can occur in all tissues with insulin receptors, the most clinically relevant tissues are the liver, skeletal muscles, and adipose tissue. Reduced insulin sensitivity and insulin resistance hinder glucose uptake into cells, prompting increased insulin production by pancreatic beta cells, leading to hyperinsulinemia. The metabolic effects of insulin resistance include hyperglycemia, hypertension, dyslipidemia, and elevated inflammatory markers. As insulin

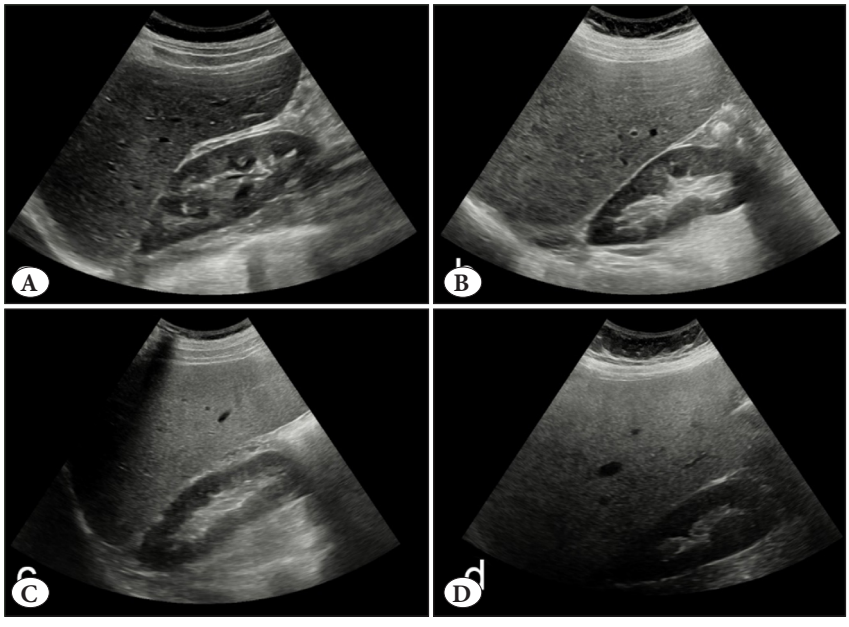


Figure 1: Ultrasonographic findings of NAFLD.

Grade 0 (Normal liver): the liver and the kidney have the same echogenicity.
Grade 1 (Mild fatty liver): slight increase in the liver echogenicity, with echogenic discrepancy between the liver and the kidney.
Grade 2 (Moderate fatty liver): increased liver echogenicity, with echogenic discrepancy between the liver and the kidney.
Grade 3 (Severe fatty liver): marked increase in the hepatic echogenicity, with echogenic discrepancy between the liver and the, and poor visualization of the diaphragm.

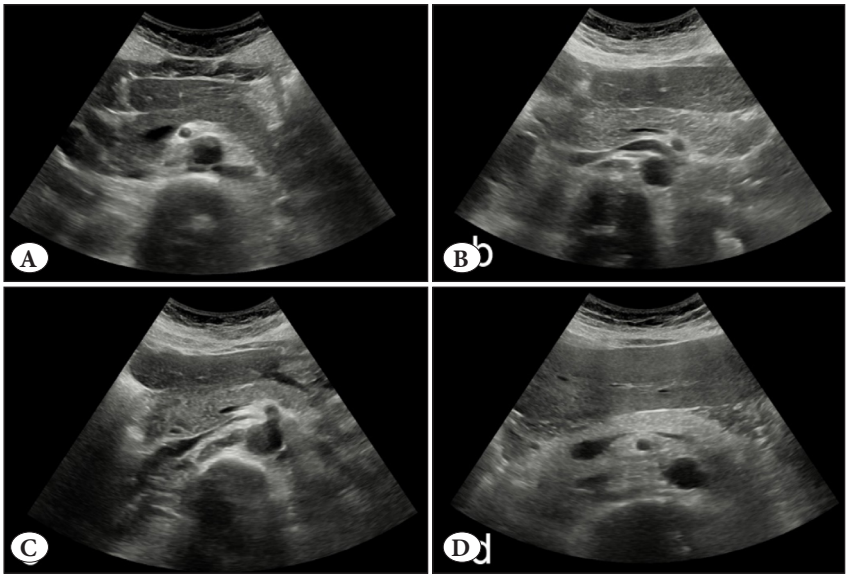


Figure 2: Ultrasonographic findings of NAFPD

Grade 0 (Non-fatty pancreas): normal pancreas parenchyma.
Grade 1 (Mild fatty pancreas): pancreas echogenicity is increased and is slightly higher than the kidney however.
Grade 2 (Moderate fatty pancreas): substantial increase in pancreas echogenicity than renal echogenicity but the retroperitoneal fat echogenicity is more than pancreatic echogen).
Grade 3 (Severe fatty pancreas): the pancreas echogenicity is ≥ retroperitoneal fat echogenicity.

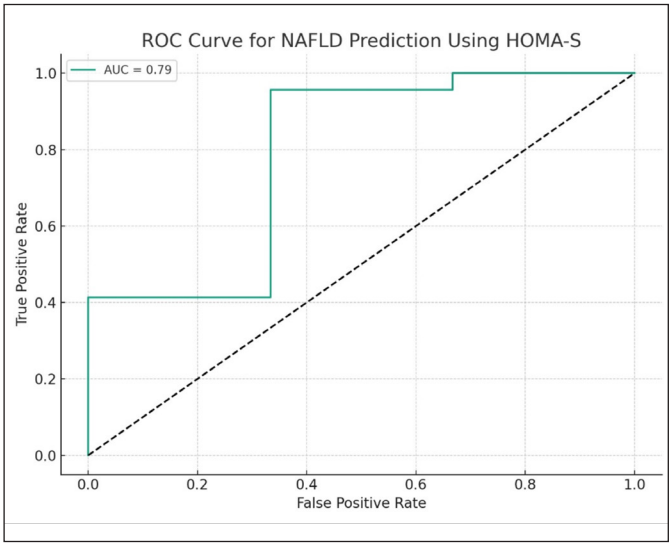


Figure 3: ROC curve showing the performance of predicting the presence of NAFLD using HOMA-S scores. The AUC of the model is 0.79, indicating a high level of accuracy in predicting NAFLD.

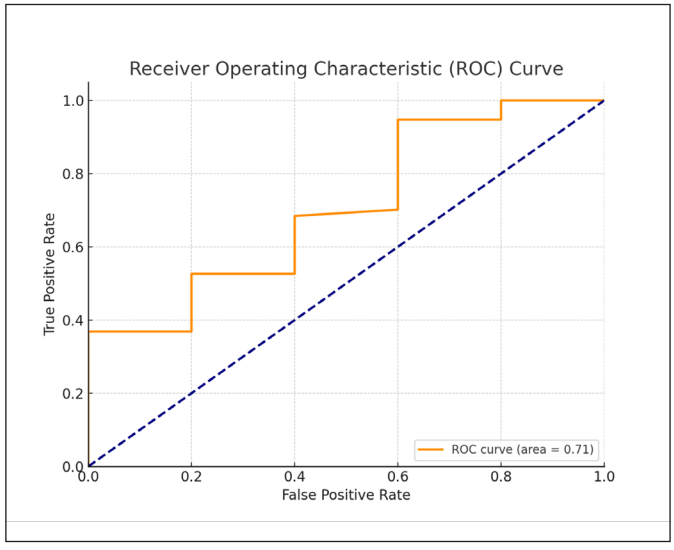


Figure 4: The ROC curve below demonstrates the performance of HOMA-IR values in distinguishing between patients with and without NAFLD. The AUC of the model is 0.71, indicating a high level of accuracy in predicting NAFLD.

resistance continues, it contributes to the development of metabolic syndrome and its components, such as NAFLD and T2DM (30,31).

Insulin increases glycogen synthesis and lipogenesis in the liver. When insulin resistance increases, these processes are impaired, which can lead to fat accumulation in the liver and the development of NAFLD. In addition, hyperinsulinemia caused by insulin resistance can increase adiposity by stimulating fatty acid synthesis in the liver (32).

HOMA-IR is a widely used index in the assessment of insulin resistance and is known to play an important role especially in individuals with NAFLD. In many studies, HO-

MA-IR values have been found to have a high diagnostic value in differentiating NAFLD patients from healthy individuals (33-37).

In our study, we found that HOMA-S score decreased and HOMA-IR score increased with increasing fatty liver disease. In other words, insulin sensitivity decreased and insulin resistance increased with increasing fatty liver disease. We did not find any other study directly comparing HOMA-S score with NAFLD in the literature. These results suggest that NAFLD is closely associated with metabolic syndrome and insulin resistance.

In a study, they evaluated the applicability of the HOMA-IR index for the diagnosis of NAFLD and reported that the cut-off values of HOMA-IR values between patients with NAFLD and patients without NAFLD were 1.65 in men and 1.90 in women (38).

In another population-based study between patients with NAFLD and healthy controls, the optimal cut off values were 1.79 (39). Salgado et al, performed measurements between patients with NAFLD and a healthy control group and stated the cut-off value as HOMA-IR index ≥2 or 2.5 (33).

Guttirez-Buey et al, found 4,5 as the best cut off value between NAFLD and non-NAFLD patient groups in patients with type 2 DM (40).

Isokuortti et al, compared individuals with NAFLD selected from the general population and healthy control subjects without NAFLD and found a cut-off value of 1.9 (41).

In our study, we determined the cut-off value as 2.76. Unlike the studies conducted with the general population, our patient group was a group with a BMI above 26. This may explain the high HOMA-IR cut-off value.

The clinical consequences of pancreatic steatosis are still poorly understood (42).

Considering the similar embryological origins of the liver and pancreas, it can be understood that steatosis in the pancreas, much like in the liver, describes a spectrum ranging from fat accumulation to pancreatitis and subsequent fibrosis (43).

Pancreatic steatosis is closely associated with increased BMI, insulin resistance, and metabolic issues. Individuals with a fatty pancreas have a higher risk of developing diabetes compared to those without. Wang et al. have shown that fatty infiltration of the pancreas can lead to a loss of beta cell mass and function, ultimately resulting in the development of diabetes (14).

Due to the anatomical and embryological similarity of the liver and pancreas, many studies have investigated the pathophysiology and clinical effects of adiposity with US, CT and MR. As in other organs, NAFPD shows a significant and reproducible association with obesity (4,7,44).

While obesity is strongly linked to pancreatic steatosis, the precise mechanisms behind this association are not well understood. Unlike liver tissue, where fat accumulates intracellularly, in pancreatic tissue, fat deposits intercellularly through adipocyte infiltration in the intralobular regions of both acinar and islet cells (7,44).

NAFPD is connected with various common clinical conditions, such as metabolic syndrome, type 2 diabetes mellitus (T2DM), cardiovascular risk, and both acute and chronic pancreatitis, pancreatic fibrosis, and pancreatic cancer. Although the exact causal links between NAFPD and these conditions are not yet fully clarified, their frequent association with obesity implies the potential for shared etiological pathways. Over the past decade, increasing evidence has supported the link between NAFPD and metabolic syndrome. Consequently, NAFPD has been recognized as one of the conditions associated with metabolic syndrome, alongside NAFLD, T2DM, and cardiovascular and cerebrovascular diseases (11,44-46).

The nature of the relationship between pancreatic adiposity and general obesity—whether it is causal or merely correlational—remains unresolved and is a focus of ongoing research. Current studies involving T2DM patients do not establish a definitive link between pancreatic fat and diabetes. One theory suggests that impaired glucose metabolism may result from lipotoxicity due to triglyceride accumulation in beta cells, which leads to cell apoptosis and subsequent fat replacement. Another theory proposes that adipocytes in the pancreas might negatively affect beta cells through paracrine signaling. Nonetheless, existing evidence suggests that both NAFPD and T2DM are associated with obesity and may not have a direct causal relationship with each other (44,47).

In our study, we found no significant statistical correlation between pancreatic stetaosis and HOMA indices. Although adiposity and HOMA indices are associated with metabolic syndrome and DM, it suggests that there are other accompanying factors related to beta cell dysfunction, insulin sensitivity and resistance.

In one of the largest studies to date, Ou et al. examined 7464 people with US and found that pancreatic steatosis was more common in people with T2DM (12).

In some studies, no relationship was found between pancreatic adiposity and T2DM and beta cell function (48-50).

In a study, pancreatic adiposity was visually evaluated on CT and it was observed that mild and moderate pancreatic adiposity correlated with BMI and T2DM, whereas severe adiposity did not correlate. This suggests that other factors are also effective in the advanced stage of pancreatic adiposity and its relation with the development of DM (51).

Our study has some limitations. Firstly, the small number of patients in our study may limit the applicability of the results to the general population. Our study was designed as a single-centre-retrospective study. Finally, the patients included in the study were restricted to those with certain laboratory parameters and ultrasound scans, so selection bias may occur. Therefore, the results obtained may vary in regions with different demographic and socio-economic characteristics. Multicentre studies with a larger number of patients will allow a more detailed examination of this issue.

In conclusion, in obese but non-diabetic individuals, pancreatic steatosis appears to be associated with increased insulin levels. However, the relationship between pancreatic steatosis and insulin sensitivity is still poorly understood. Our study was conducted in a single centre with a limited group of patients and cannot be applied to the whole population. However, the results of the analyses give us an idea about the relationship between NAFLD and NAFPD and HOMA indices. In our study, no statistically significant association was found between NAFPD and HOMA scores. This indicates that NAFPD may not be directly associated with insulin resistance and beta cell function (measured by HOMA scores).These findings suggest that the assessment of NAFPD, compared with NAFLD, may indicate different mechanisms of insulin resistance and pancreatic beta cell function. Further research and multicentre studies are needed to extrapolate the findings to the general Turkish population.

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Author's Contributions
Conceptualization, methodology, investigation, resources data curation, writing - original draft, visualization: **Sevde Nur Emir**, Conceptualization, methodology, resources software, validation, formal analysis, writing - review & editing: **Servet Emir**.

Conflict of Interest
The authors declare that there are no conflicts of interest regarding the publication of this paper.

Financial Disclosure
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Ethical Approve and Informed Consent
The study protocol received approval from the Clinical Research Ethics Committee at the Health Sciences University Umraniye Training and Research Hospital. Due to the retrospective nature of the study, the requirement for informed consent was waived.

Peer Review Process
Extremely and externally peer-reviewed.

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