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Insulin Resistance and Glycaemic Markers in a Sample of Non-Alcoholic Fatty Liver Disease Libyan Patients

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A B S T R A C T

Background: Non-alcoholic fatty liver disease (NAFLD) is a common chronic liver disorder worldwide, mainly associated with obesity and insulin resistance. Aims: This study aimed to evaluate the association between NAFLD and insulin resistance . Methods: A comparative cross-sectional study was conducted at Zliten Medical Centre (ZMC) from February to August 2025. It included 85 participants (55 with NAFLD and 30 healthy controls). Age, gender, Body mass index (BMI), fasting blood glucose (FBG), HbA1c (glycated heamoglobin), and serum insulin were measured. Insulin resistance was assessed using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) index. Results: Patients with NAFLD had significantly higher BMI, FBG, HbA1c, serum insulin, and HOMA-IR compared to controls. Mann–Whitney U tests showed significant differences in HOMA-IR, HbA1c. Receiver Operator curve (ROC) analysis indicated excellent diagnostic accuracy for insulin and HOMA-IR (AUC) (Area under curve) ` ≈ 0.88). Regression analysis revealed that insulin and HOMA-IR were positively associated with NAFLD risk. The linear regression analysis revealed that among metabolic parameters in NAFLD group, HbA1c had a significant association with HOMA-IR, while BMI showed weak or non-significant relationships; the logistic regression model showed an excellent accuracy (AUC = 0.998), indicating strong prediction ability for NAFLD compared to previous studies. Conclusion: Insulin resistance plays a pivotal role in fatty liver development ,that could be concluded from elevated insulin, HOMA-IR, and impaired glycaemic control. higher BMI, further highlighting the underlying metabolic abnormalities. Insulin and HOMA-IR may be used as clinical markers for identifying high-risk individuals. Early diagnosis and lifestyle modification targeting insulin resistance are recommended.

Key words: NAFLD, insulin resistance, HOMA-IR, Libya

1. Introduction

Non-alcoholic fatty liver disease (NAFLD), also known as hepatic steatosis, is a common chronic liver disease characterized by fat deposition with in the liver, which may lead to insulin resistance and other metabolic disturbances (1). Understanding this relationship between NAFLD and insulin resistance is important for early diagnosis, prevention, and management of related metabolic disorders.

NAFLD can progress to non-alcoholic steatohepatitis (NASH), which may advance to cirrhosis and hepatocellular carcinoma (2). Metabolic syndrome—comprising obesity, insulin resistance, dyslipidaemia, and hypertension—is closely associated with NAFLD pathogenesis (3).

The hyperinsulinemic-euglycemic clamp is the gold standard for measuring of insulin resistance (4), but, surrogate indices such as Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) and Quantitative Insulin Sensitivity Check Index (QUICKI) are widely

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used in large-scale studies due to their practicality (5). Insulin resistance impairs hepatic glucose suppression and peripheral glucose uptake, leading to hyperglycaemia and hyperinsulinaemia.

Hepatic steatosis is defined by triglyceride accumulation in more than 5% of hepatocytes or >55 mg/g of liver tissue (6). Progression to NASH involves inflammation, hepatocyte injury, and fibrosis, which may result in cirrhosis and increased hepatocellular carcinoma risk (7). Although liver biopsy still considered as confirmed diagnostic tool for the disease, its invasiveness makes it undesirable. Histological examination can provide additional insight into the degree of steatosis and its correlation with insulin resistance markers (8).

Due to the increasing prevalence of NAFLD and its correlation with insulin resistance, investigations and understanding of this relationship is required for early diagnosis and guiding effective preventive and therapeutic strategies.

1.1. Aims:

The aim of this comparative cross-sectional study was to evaluate the prevalence of insulin resistance in patients diagnosed with NAFLD. The research focused on identifying glycemic alterations in patients with NAFLD compared to healthy individuals, aiming to understand the potential role of insulin resistance and glycemic parameters in disease progression.

2. Methods

2.1 Study Participants

The study was carried out at Zliten Medical Hospital and included 55 patients with NAFLD who attended the hospital in the period from February to June 2025. All cases underwent a comprehensive assessment which included clinical history taking, physical examination, and liver ultrasonography to evaluate age, gender, and disease status

The control group of 30 healthy individuals, free from liver disease based on physical examination, was recruited and followed the same study protocol.

2.2.1 Inclusion Criteria

The study enrolled adults aged 18 to 65 years with a confirmed diagnosis of hepatic steatosis via abdominal ultrasonography. Participants were required to have no prior history of chronic liver diseases other than NAFLD to ensure the specificity of the metabolic findings. Finally, all subjects provided verbal informed consent prior to their participation in the clinical evaluation

2.2.2 Exclusion Criteria

Participants were excluded if they have other chronic liver conditions, such as viral hepatitis, autoimmune hepatitis, or cirrhosis. Individuals currently using medications that alter lipid metabolism or insulin level, such as statins, metformin, antidiabetic agents, or hydrocortisone therapy, were also excluded. Moreover, the study excluded any case with pregnancy, lactation, and the presence of severe comorbidities, such as malignancy or chronic kidney disease.

3. Materials

3.1 Equipment and Apparatus

The equipment used in this study are listed in Table1.

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Table 1. Equipment and Apparatus

Equipment	Company (origin)
Cobas c 311 (biochemical analysis & HbA1C)	Roche - Switzerland
Labofuge-400	Roche - Switzerland
Pipette-200-500 µL	Heraeus - Germany
InBody 770	Eppendorf - Germany
Digital height and weight scale	Asmid - Turkey
Tubes, EDTA tubes, cotton, alcohol	

3.2 Criteria for NAFLD Diagnosis

The cases with hepatic steatosis were identified using abdominal ultrasound reports provided by the attending physicians. Participants were referred to the outpatient department (OPD) after consultation with either a surgical or internal medicine specialist. Cases were defined as individuals with ultrasonographic evidence of steatosis consistent with NAFLD. To ensure the diagnosis of disease, patients with secondary causes of liver disease—including significant alcohol consumption, viral hepatitis, or drug-induced steatosis—were excluded from the study.

3.3 Determination of BMI

Weight and height were measured by a digital InBody device or a physical scale during blood sample collection.

3.4 Specimen collection

Specimen were collected from all participants using standardized techniques appropriate for each biochemical analysis.

3.5 Insulin Testing and Analysis

Serum insulin was quantified using ECLIA on the Cobas e 411 analyzer following the manufacturer's protocol.

3.6 Glycemic Analysis

Fasting blood glucose, and HbA1C were measured using the Cobas c311 analyzer according to manufacturer instructions.

3.7 Statistical Analysis

The data collected for this study was analysed using SPSS software (version 21). Statistical analysis is imperative for the summarisation and interpretation of data, the evaluation of differences between groups, and the examination of potential correlations among study variables.

A descriptive statistical analysis was conducted for the purpose of obtaining a general description of the study population. The mean, median, and standard deviation of the continuous variables, such as clinical and biochemical measures, were computed for each of the study groups and of the total study cohort. The utilisation of this approach facilitates the estimation of both the central tendency and the variability of the data.

The frequency distributions and percentages were utilised to ascertain the representation of male and female participants in the study, given that categorical variables, such as gender, were employed. These descriptive statistics formed the foundation for the subsequent application of comparative and inferential statistics.

The Shapiro test was employed to evaluate the normality of data distribution, given that the total number of participants was less than 100 (n

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= 85). The subsequent analyses employed non-parametric tests due to the indication that the data were not normally distributed.

To compare continuous variables between groups, the Mann-Whitney U test was employed. The comparison of means was evaluated using the chi-squared test, and the coefficient of rank correlation between variables was calculated using Spearman's method. For all statistical tests, a p-value of < 0.05 was considered statistically significant.

The utilisation of inferential statistics has been employed in the context of diagnostic checks, encompassing the evaluation of receiver operating characteristic (ROC) curves.

Furthermore, regression evaluation determined the strength and path of the relationship between observed variables. Predictive linear regression was applied to assess the accuracy of the data in predicting future cases. P-value of equal or less than 0.05 was deemed to be significant

4.Results

4.1 Descriptive Analysis of Data

The study sample was predominantly female, with females making up 88.2% of the total population. In terms of health status; females were over -represented in the healthy category (83.3 %).

4.1.1 Healthy Participants

The descriptive statistics of the healthy participants are summarized as follows.

Table 2. statistical description of healthy participants

Parameter	**Mean**	**Median**	**Standard deviation**
Age	34.13	34.13	9.85
BMI	25.50	25.30	3.49
FBG	98.36	98.65	8.99
HbA1C	5.08	5.09	0.25
HOMA_IR	2.53	2.30	1.27

4.1.2 NAFLD Participants

The descriptive statistics of NAFLD participants are summarized as follows.

Table 3 statistical description of NAFLD participants

Parameter	Mean	Median	SD
Age	35.56	35.00	11.94
BMI	43.39	43.98	9.66
FBG	104.61	97.0	24.98
HbA1C	5.67	5.50	0.71
HOMA_IR	5.95	5.51	6.06

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4.1.3 All Participants

For overall study population, the descriptive statistics are summarized as follows.

Table 4 statistical description of all cases

Parameter	Mean	Median	Standard deviation
Age	35.05	35.00	11.21
BMI	37.08	36.58	11.75
FBG	102.40	97.40	20.93
HbA1C	5.46	5.30	0.65
HOMA_IR	5.39	4.06	5.36

4.2 Relationship Between Age and Disease Status

Chi-square test of independence was conducted. The distribution of cases within the three age groups revealed that the youngest group had a higher proportion of healthy individuals, whereas the oldest group had more diseased cases. The middle-aged group showed a nearly balanced distribution. Chi-square test gave a non-significant association between age group and disease status (P = 0.230).

4.3 Correlation of HOMA-IR with BMI

The statistics indicate a moderate positive correlation between BMI (mean = 37.08 ± 11.75 kg/m²) and HOMA-IR, suggesting that greater obesity is associated with higher insulin resistance. As shown in Table 5.

Table 5. Correlation of HOMA-IR with BMI.

Parameter	Sig (2-tailed)	Correlation coefficient
BMI	<0.001*	0.510

*Correlation is significant at the 0.01 level (2-tailed)

4.4 Comparison Between NAFLD and Control Groups

Significant differences between NAFLD and control groups were observed for HOMA-IR, Insulin, HbA1c and BMI, whereas FBG expressed non-significant difference between the two groups. As show in Table 6.

Table 6. Comparison Between NAFLD and Control Groups.

Parameter	Sig (*P*)
BMI	<0.001
HOMA-IR	<0.001
Insulin	<0.001
HbA1C	<0.001
FBG	0.46

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4.5 Receiver-Operating Characteristic (ROC) Analysis

One of the most well-known applications of ROC curve analysis is its use as a simple graphical tool for displaying the accuracy of a medical NAFLD. In this study, the predictive power of insulin, biochemical, demographic and anthropometric parameters in diagnosis of disease was evaluated. The sample included 85 cases, 55 were classified as positive cases and 30 as negative cases.

4.5.1 HOMA-IR and Insulin

HOMA-IR and insulin demonstrated high diagnostic performance with AUC values of 0.87 and 0.89, respectively. Both showed 80.0% sensitivity and specificity above 83.2%, indicating strong discriminative ability between NAFLD and healthy participants.

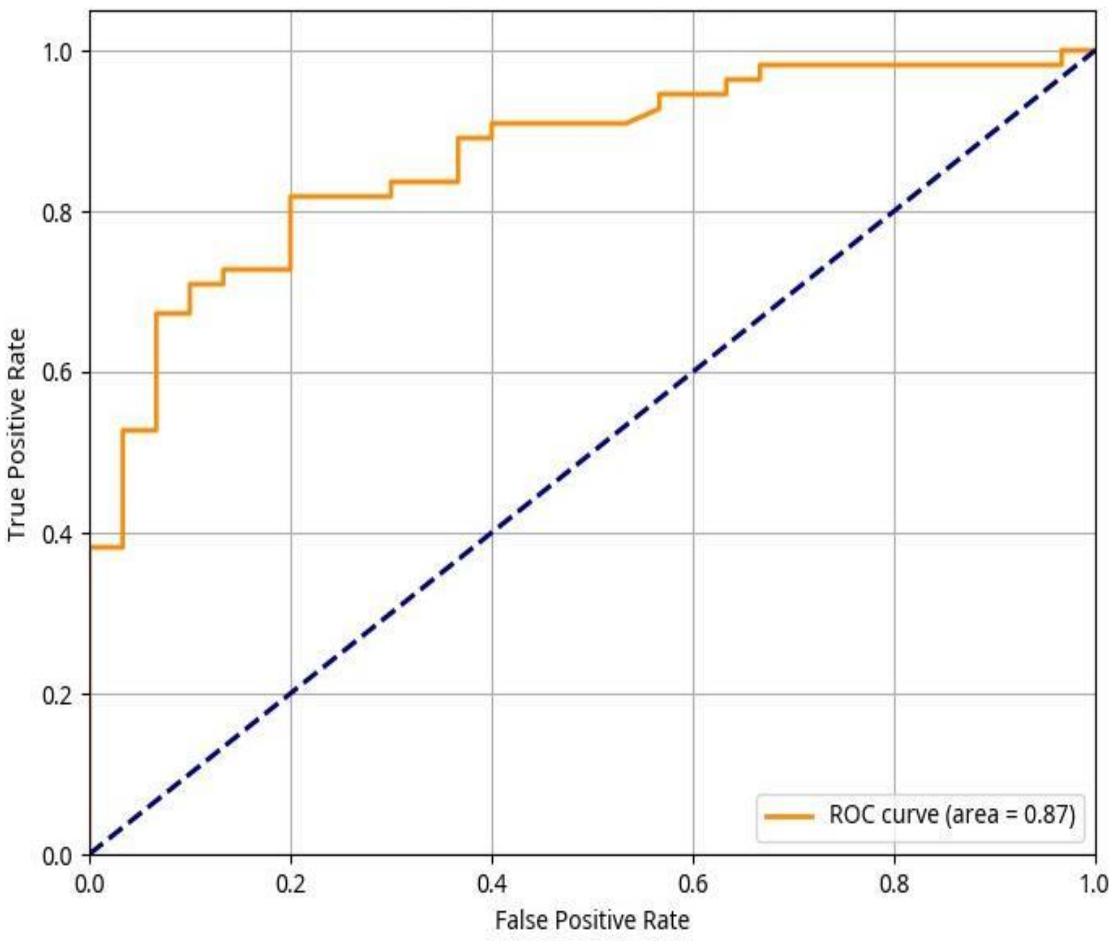

Figure 1. Receiver Operating characteristic (ROC) curve for HOMA-IR

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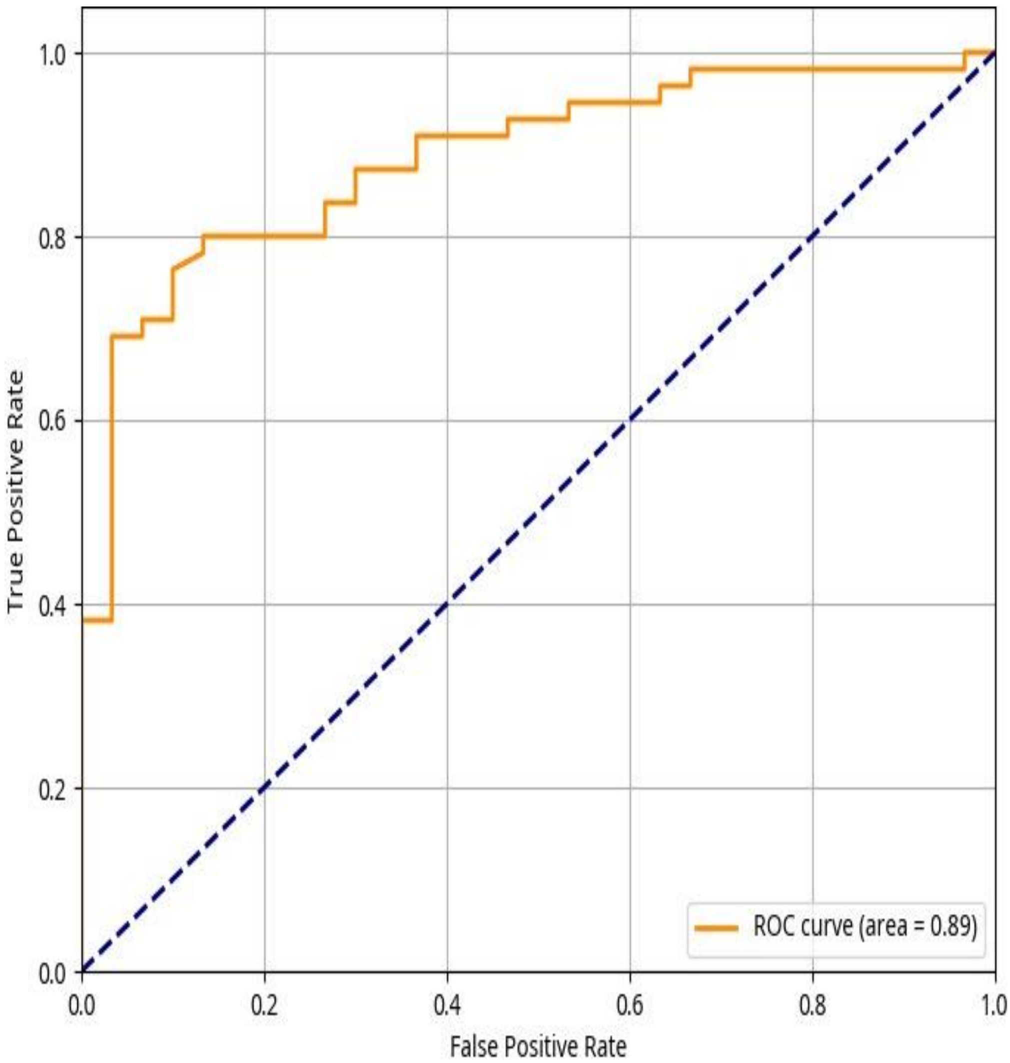

Figure 2. Receiver Operating characteristic (ROC) curve for Insulin

4.5.2 The predictive value of anthropometric parameters and age

The ROC analysis revealed that BMI (AUC = 0.97) and weight (AUC = 0.96) had an excellent ability to discriminate between outcomes, showing high sensitivity and specificity. On other hand, height (AUC = 0.54) and age (AUC = 0.51) showed poor predictive performance, suggesting that they are unreliable markers when considered in differentiation. These results suggest that, in this population, anthropometric measures reflecting body mass and adiposity, particularly BMI and weight, are strong predictors, whereas age and height have low predictive value. As shown in figures (3.-6) below.

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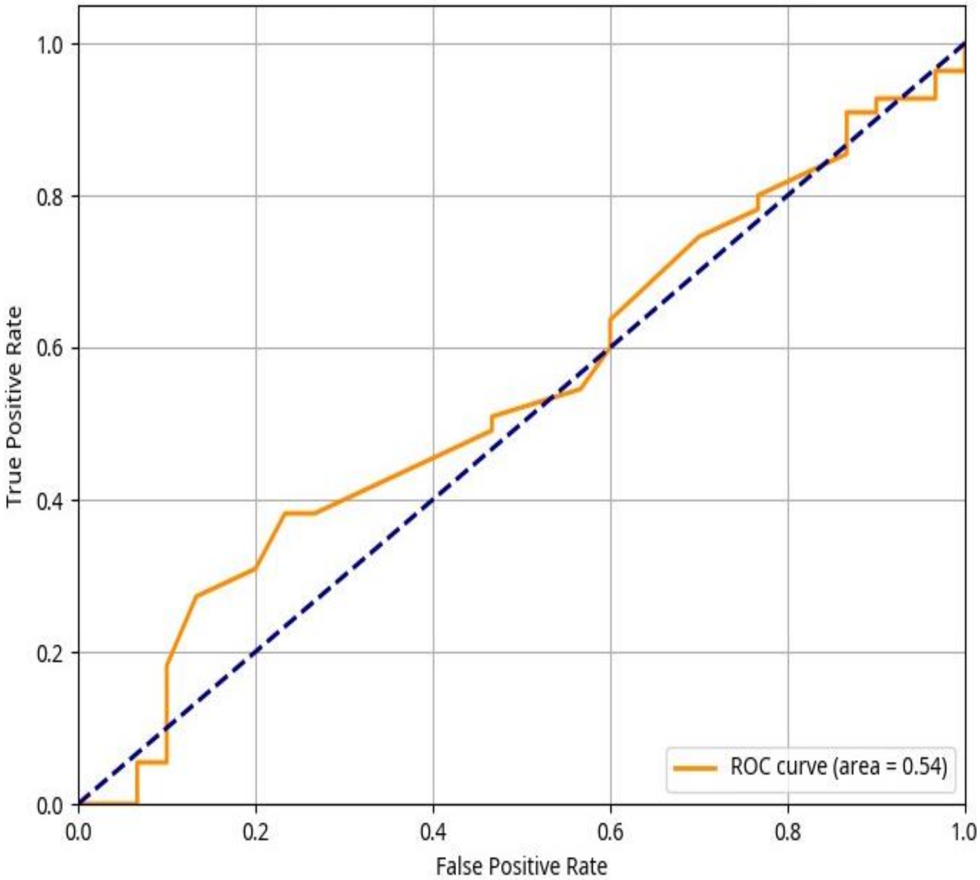

Figure 3. Receiver Operating characteristic (ROC) curve for height

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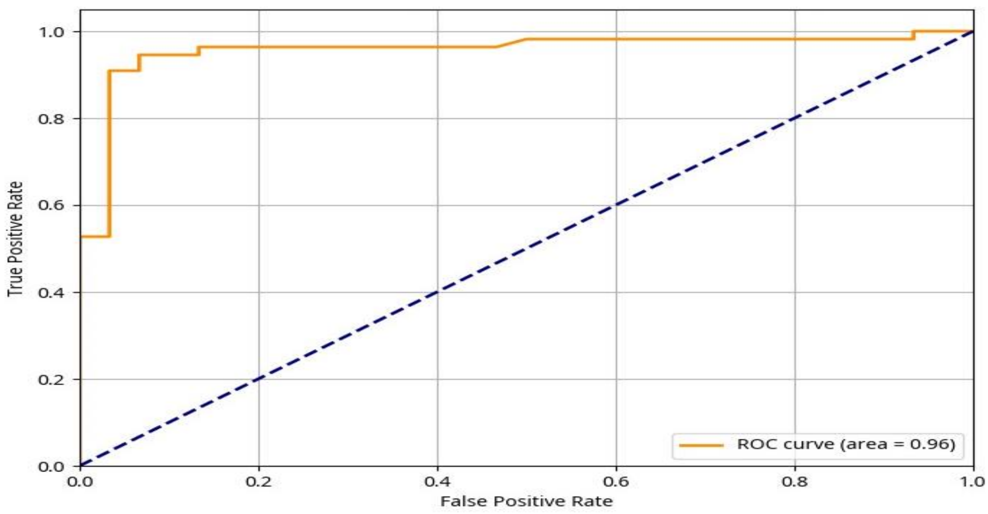

Figure 4. Receiver Operating characteristic (ROC) curve for Weight

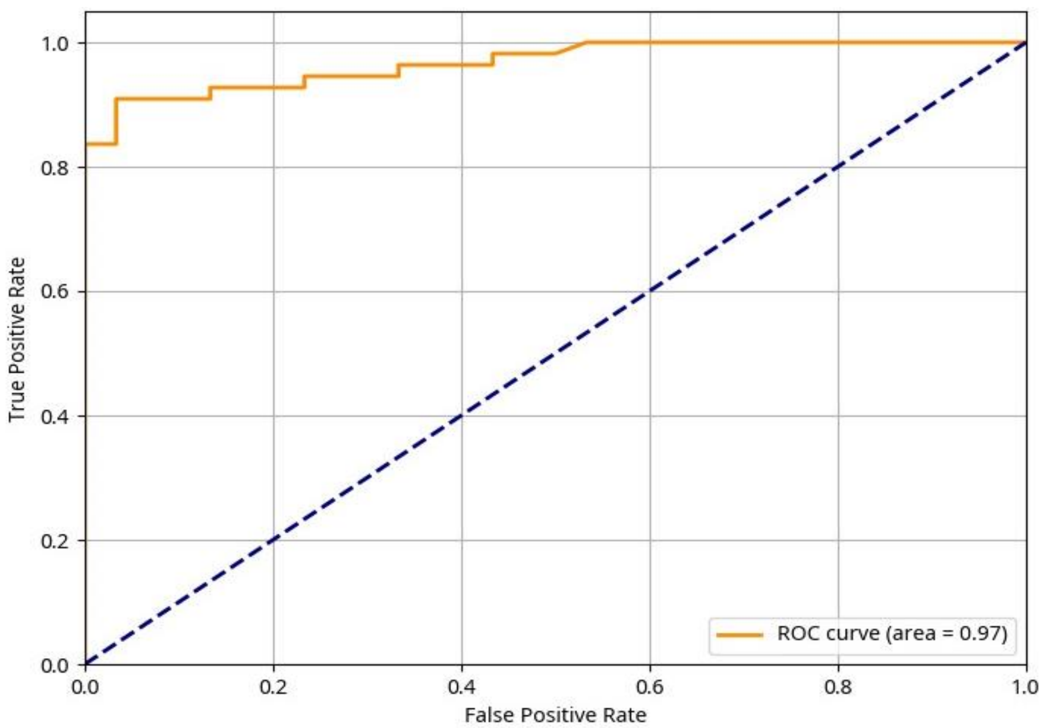

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Figure 5. Receiver Operating characteristic (ROC) curve for BMI

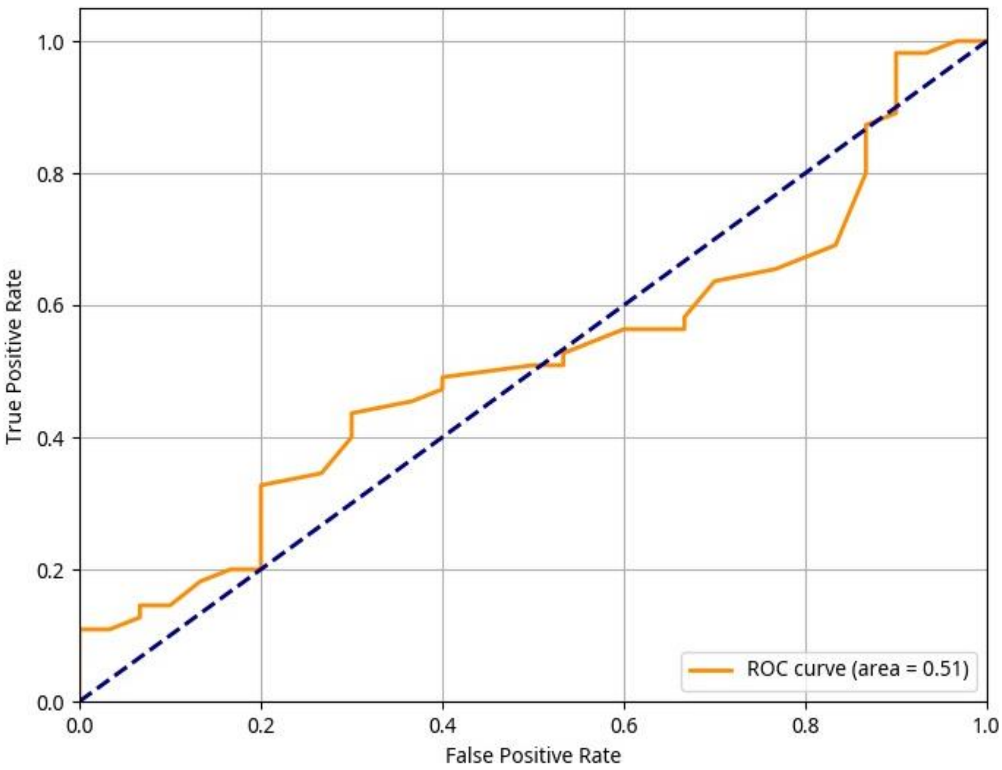

Figure 6. Receiver Operating characteristic (ROC) curve for age

4.5.3 Glycemic Parameters

HbA1c demonstrated good diagnostic ability (AUC = 0.82, sensitivity 63.6%, specificity 90.0%), whereas FBG showed poor discriminative ability (AUC = 0.55, sensitivity 34.6%, specificity 86.7%). This indicates that HbA1c was more reliable than FBG in identifying true positive and true negative cases. As shown in figures 7 & 8.

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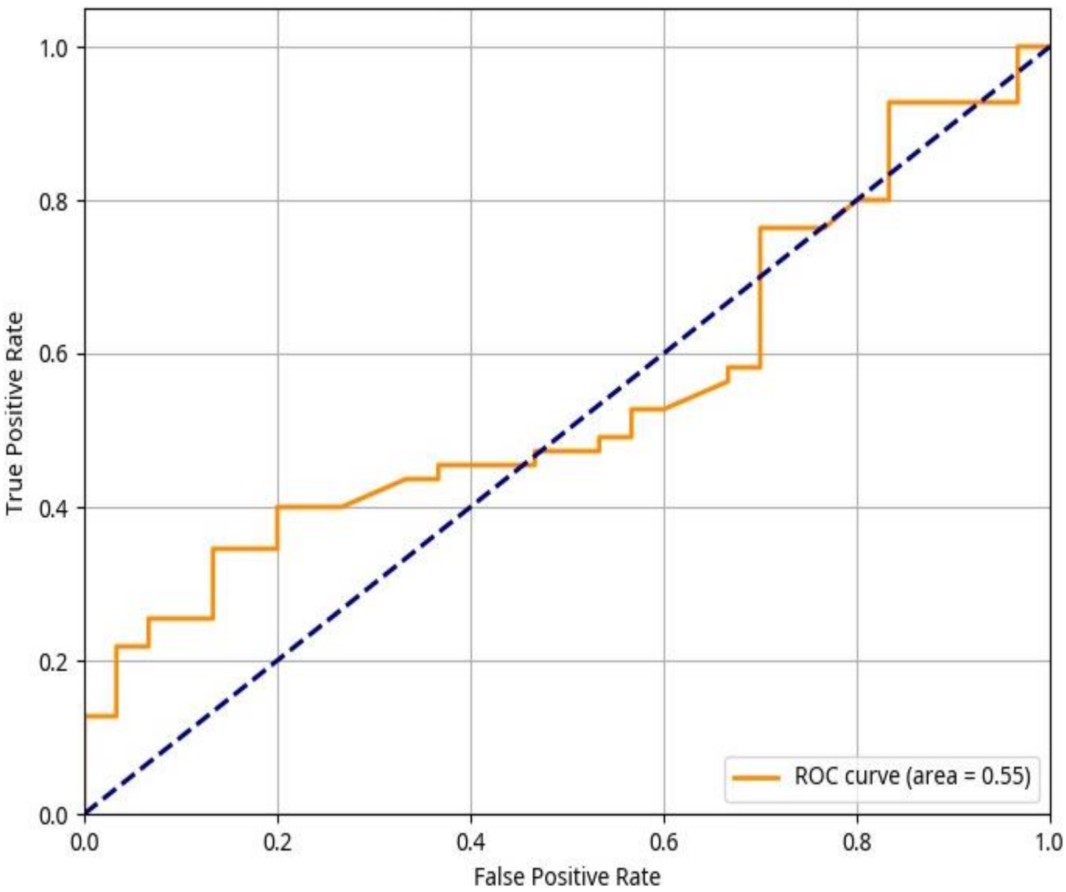

Figure 7. Receiver Operating characteristic (ROC) curve for FBG

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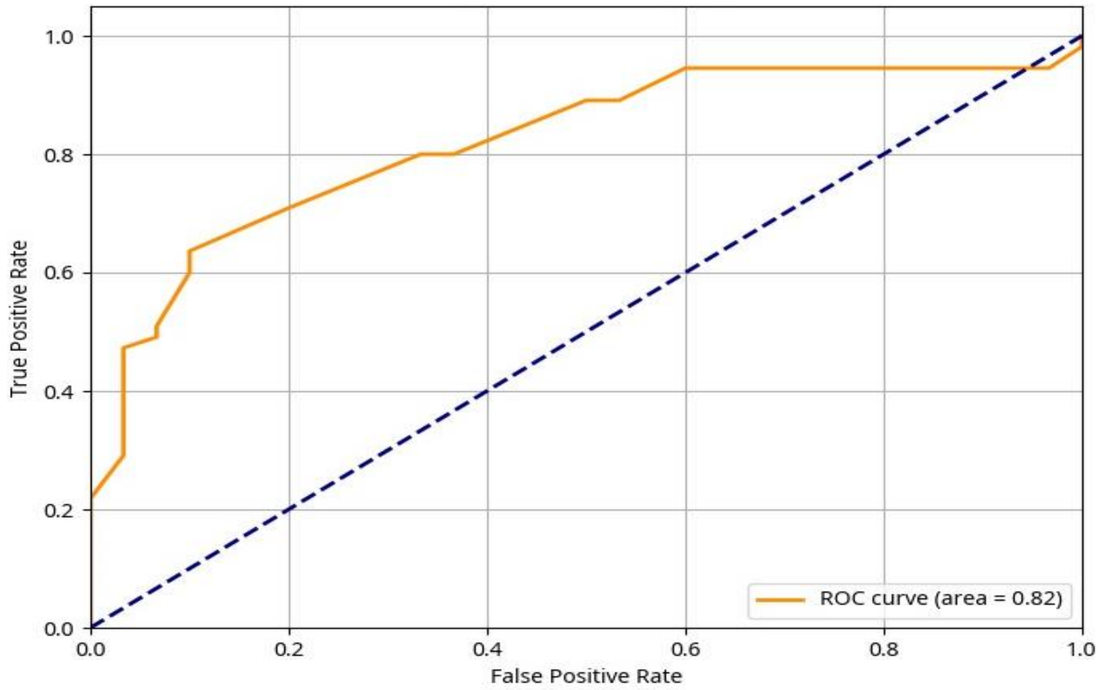

Figure 8. Receiver Operating characteristic (ROC) curve for HbA1c.

4.6 Simple Linear Regression

Linear regression analyses indicated that HbA1c was positively associated with HOMA-IR ($R^2 = 0.078$, $P = 0.039$).

In the present study, no significant correlation was found between body mass index (BMI) and insulin resistance (HOMA-IR) ($R = 0.021$, $p = 0.881$). The correlation coefficient was very close to zero, indicating the absence of a linear relationship between these two variables. Furthermore, the P-value was well above the conventional threshold for statistical significance ($p < 0.05$), suggesting that BMI did not significantly predict HOMA-IR levels in this study population.

This result indicates that, within our data, variations in BMI were not associated with reliable alterations in insulin resistance. The regression line ($y = 6.39 + 0.01x$) gave a nearly flat slope (0.01), further emphasizing the lack of a clear effect. See figure 9.

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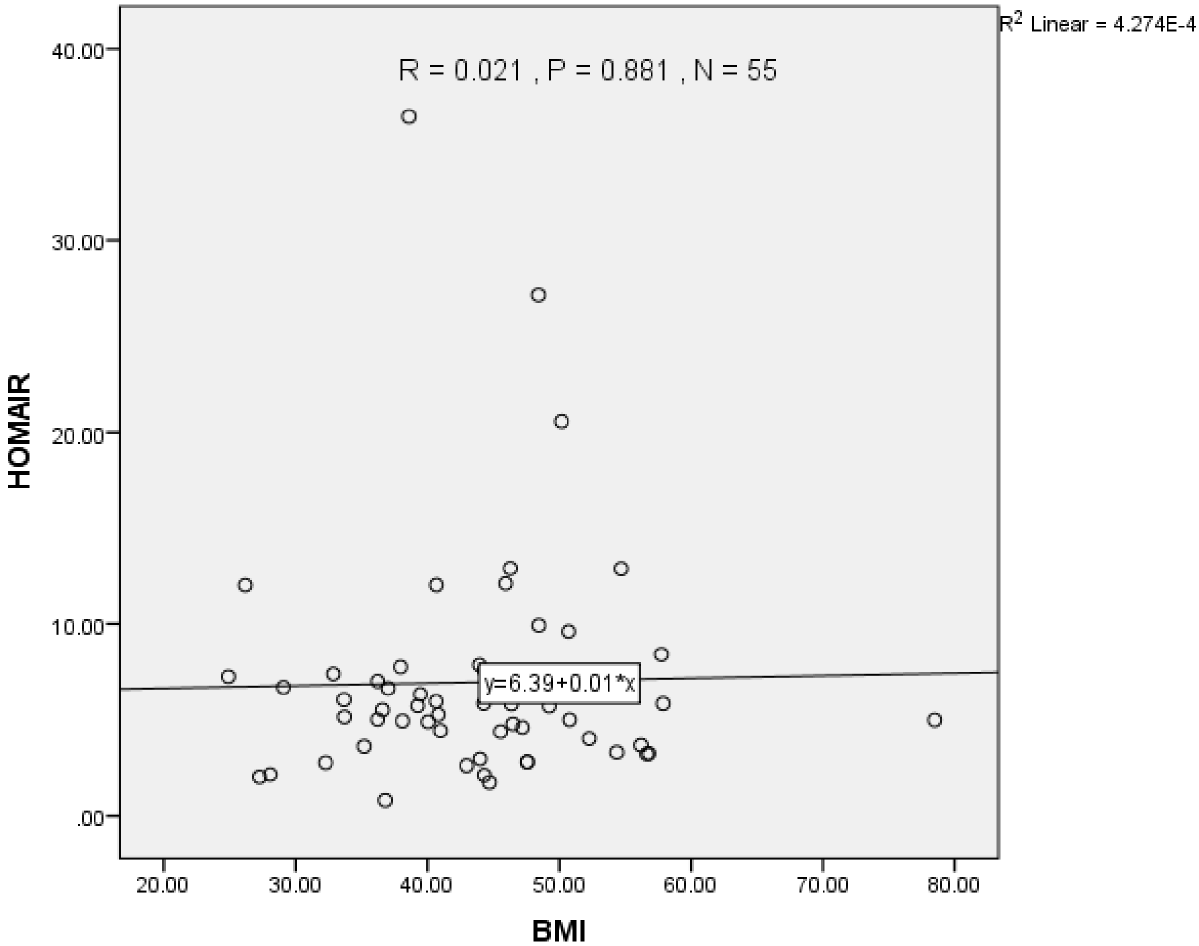

Figure 9. Linear regression between insulin and BMI.

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Linear regression analysis demonstrated a statistically significant positive association between HbA1c and insulin resistance (HOMA-IR) (R^2 = 0.078, P = 0.039) (Figure 10). This indicates that higher HbA1c levels are associated with a slight increase in HOMA-IR, with HbA1c explaining approximately 7.8% of the variance in insulin resistance.

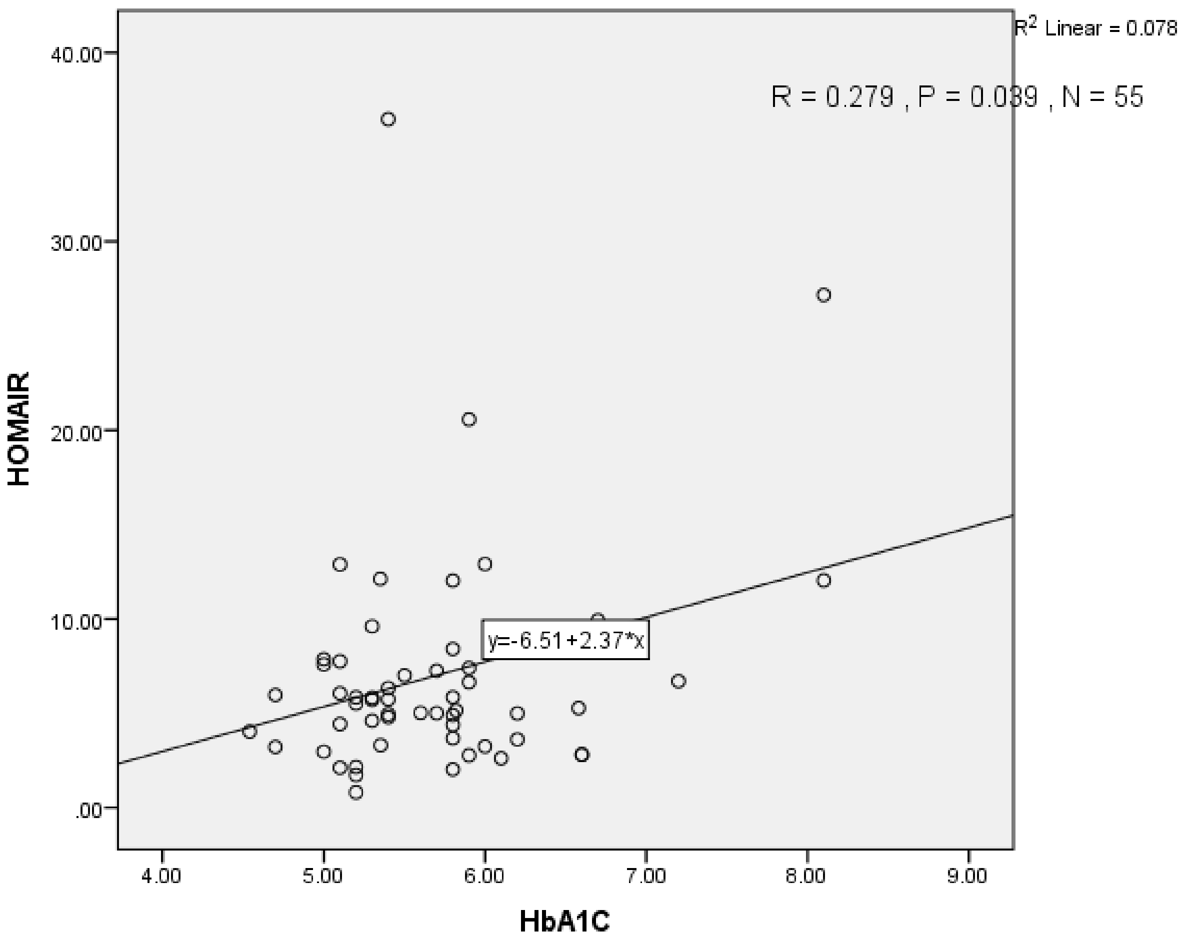

Figure 10. Linear regression between insulin and HbA1c.

4.7 Binary Logistic Regression Analysis

Binary logistic regression indicated that insulin and HOMA-IR were strong predictors for NAFLD (AUC > 0.8). Insulin had the strongest positive association with NAFLD (B = 0.389), while HbA1c also had positive coefficients. HOMA-IR had a negative coefficient (B = -0.600), potentially due to collinearity.

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In the multivariate logistic regression analysis, BMI was considered one of the predictor variables that demonstrated a statistically significant relationship with NAFLD prior to adjustment but its significance reduced when adjusted for insulin-related measures.

The model showed 97.6% of cases, with 96.7% accuracy for controls and 98.2% for NAFLD cases. ROC analysis of the predictive power showed an AUC of 0.998, indicating near-perfect discriminating ability.

5. Discussion

This study analyzed the metabolic and demographic parameters of NAFLD patients compared to healthy controls, spotting on insulin resistance, lipid parameters, and demographic trends. The results provide details into the relations between obesity, insulin resistance, and demographic parameters in NAFLD patients, with implications for clinical screening and preventive strategies.

Although the mean age was slightly higher in NAFLD patients compared to controls, age-related trends indicated that the prevalence of NAFLD increased in participants over 40 years. This finding supports previous epidemiological data suggesting that advancing age is associated with increased metabolic dysfunction and higher NAFLD risk (9).

5.1. Comparison Between NAFLD and Controls

NAFLD patients demonstrated significantly higher HOMA-IR, HbA1c compared to controls, FBG expressed non-significant differences between both groups. These results corroborate the established links between NAFLD and glycemic parameters (9).

The markedly elevated BMI observed among NAFLD patients highlights the central role of obesity in disease pathogenesis. The strong correlation between BMI and HOMA-IR suggests that excess adiposity contributes to insulin resistance, which in turn promotes hepatic lipid accumulation. These findings are consistent with previous studies demonstrating that obesity, particularly visceral adiposity, is a major driver of NAFLD development and progression (3).

5.2. Insulin Resistance as a Central Marker

ROC analysis demonstrated excellent diagnostic performance for HOMA-IR and fasting insulin in distinguishing NAFLD patients from controls, with high sensitivity and specificity. These findings align with prior studies highlighting insulin resistance as a pivotal pathogenic factor in NAFLD. These differences likely reflect population-specific metabolic profiles and the interplay with insulin resistance (9).

5.3. Glycemic Predictors

HbA1c outperformed fasting glucose in predicting NAFLD (AUC = 0.82 vs. 0.55), reflecting its utility as a marker of long-term glycemic control and insulin resistance (10).

5.4. Regression Analysis and Predictive Model

HbA1c was significantly associated with HOMA-IR ($R^2 = 0.078$, $P = 0.039$), reinforcing the importance of glycemic dysregulation in NAFLD pathogenesis. Logistic regression including insulin, BMI, cholesterol, HbA1c, and HOMA-IR achieved 97.6% classification accuracy and an AUC of 0.998, outperforming previously reported predictive models (11).

Study Limitations

Waist circumference was not assessed, limiting evaluation of central obesity. In addition, cross-sectional design prevents causal inference. Moreover, single time-point measurement of insulin and lipids limits assessment of dynamic changes and treatment response; sensitivity may vary by disease severity.

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6.Conclusion

The study underscores the central role of insulin resistance and obesity in NAFLD risk and provides evidence for their use in early screening. HbA1c, is particularly useful as non-invasive indicators. These results targeted metabolic and lifestyle interventions for NAFLD prevention and management

This study demonstrated a strong association between (NAFLD and insulin resistance. Overall, these findings support the concept that NAFLD is not solely a liver disorder but a systemic metabolic disease in which insulin resistance plays a central role.

Recommendations

Routine insulin measurement could be benefit in early detection. Standardized imaging methods are recommended for consistent staging and follow-up. Optimal control of obesity and diabetes must be done. A multidisciplinary cooperation (dietitians, endocrinologists, radiologists) is recommended to improve patient outcome.

Future Directions

Future research should involve larger multicenter and longitudinal studies to clarify disease progression. Advanced statistical analyses are needed to explore the mediating role of insulin resistance and the modifying effects of comorbidities such as diabetes and Polycystic Ovary Syndrome (PCOS). Incorporating biomarkers of De novo Lipogenesis (DNL), adipokines, and genetic variants (e.g., Patatin-Like Phospholipase Domain-Containing Protein 3(PNPLA3), Transmembrane 6 Superfamily Member 2 (TM6SF2) may improve mechanistic understanding. Interventional trials evaluating pharmacologic and lifestyle therapies are warranted.

ETHICAL STATEMENT:

The study was conducted in accordance with guidelines established by the World Health Organization (WHO) and the Libyan Ministry of Health. Approval was granted by the Misurata Libyan Academy, the Zliten Medical Center (ZMC), and a selected private laboratory (AlQalb Laboratory). All cases participated in the research received a comprehensive detail about the study objectives, procedures, and benefits. Verbal consent was collected from each participant before starting the data collection. All information about the cases was kept confidential and used solely for research purposes.

CONFLICT OF INTEREST

There is no conflict of interest to be declared

AUTHORS' CONTRIBUTIONS

SA developed the concept and structure of the review. EA led the literature search and drafted the initial manuscript, provided critical revisions.

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