Prevalence Of Insulin Resistance and Its Correlation with Fatty Liver Index In Overweight Non-Diabetic Patients

Suhail Aamir. A[1], Vimalkumar Anandan Govindaraj[2]* [3]Vikrannth Vasanthakumar, Gowtham Ganapathy P[4], Gada Kanaka Durga Chandu[5] & Mahendra Kumar Kalappan[6]

Department Of General Medicine, Saveetha Medical College and Saveetha Institute of Medical And Technical Sciences, Saveetha University, Saveetha Nagar, Thandalam, Chennai Bengaluru, Nh 48, Chennai, Tamilnadu 602105, India
Corresponding Author: Name: Suhail Aamir.A Email: Drsuhail25@Gmail.Com

KEYWORDS

Predictive Accuracy, Ultrasonography Among, Non-Diabetic Patients

ABSTRACT

Introduction: The increasing prevalence of both obesity and type 2 diabetes due to easy access to high calorie foods and sedentary lifestyles resulted in NAFLD to be one of the ,major public health concern in India. Due to the asymptomatic nature of NAFLD, imaging techniques like ultrasonography and CT scan have been used as diagnostic tool though liver biopsy is gold standard test. Inspire of this, non-invasive algorithms like fatty liver index have been used nowadays in clinical as well as community to detect fatty liver. The current study aimed to determine the diagnostic accuracy among overweight non-diabetic patients.

Methods: An observational cross sectional study was conducted in a internal medicine department of tertiary care center situated in South India between 2022 to 2023 .Convenient sampling technique was followed. A structured questionnaire was used to collect data on socio-demographic and relevant clinical details. Fatty liver index was enumerated with waist circumference, Body Mass Index, serum triglycerides and gamma glutaryl transferase. Ultrasonography was performed as diagnostic test.

Results: A total of 107 study subjects were included. Majority of the study subjects were in age category of 40-60 years (66%). Both male and female genders were equal in number. The prevalence of non alcoholic fatty liver disease identified by fatty liver index was 57 % whereas by ultrasonography it was 54.2%. The sensitivity and specificity of fatty liver index validated against ultrasonography were 77.1% and 76.1% respectively. Conclusion: Fatty liver index has been found to be acceptable diagnostic tool which could be used especially when imaging techniques are not available.

INTRODUCTION:

Diabetes mellitus is a systemic condition characterized by hyperglycemia. This results from a defect in insulin secretion by the pancreatic β cells or a decrease in insulin sensitivity.. [1] The Pathogenesis behind Type II Diabetes is Resistance to insulin, the development of tolerance to insulin and its action, making the hormone less effective. The main causes of rising burden of diabetes globally are due to high prevalence of overweight and obesity along with unhealthy lifestyles especially in developing countries like India. 2 As per WHO reports, about 77 million people are affected by diabetes in India and it was estimated that by 2045 it would reach over 134 million. Only 43% of these people are in adequate treatment.3 Sedentary lifestyles, combined with expanding urbanization and the consumption of processed foods, indicate that the incidence of diabetes mellitus will triple over the next 25 years, affecting younger demographics as well. 4 The multi-organ complications caused by type 2 diabetes can be broadly divided into micro and macro-vascular complications. Early morbidity and mortality among diabetes patients have been

attributed to these complications, resulting in economic burden to both the patients as well as the health care system of the country.[3]

Non-alcoholic fatty liver disease (NAFLD) is one of the prevalent hepatic disorder which is characterized by the excessive fat accumulation in the liver, among the patients who do not consume excess amount of alcohol, identical to that is present in alcoholic fatty liver disease. NAFLD involves a group of pathological conditions, covering a range from simple steatosis (NAFL), non-alcoholic steatohepatitis (NASH), cirrhosis and carcinoma of liver .[5] Type 2 diabetes and Non-alcoholic fatty liver disease (NAFLD) always coexist.[6] Release of pro-arthrogenic and nephrotoxic factors due to systemic inflammation cuased by inulsin reistance in the liver and extra hepatic tissues is the main pathogenic mechanism behind NAFLD[7] In India, the combined pooled prevalence of NAFLD is 35.4% in children and 38.6% in adults. The frequency is comparable in both genders.[8]

. Fatty liver index (FLI) which is estimated from waist circumference, serum triglyceride levels , body mass index, and gamma-glutamyl transferase can be used as a non-invasive method to predict Non-alcoholic fatty liver disease.[9]Various studies have shown associations between the NAFLD and obesity (BMI), abdominal obesity (Waist Circumference), Resistance to Insulin, hyperglycaemia, and other individual elements of the metabolic syndrome.[10-13] Due to the simplicity of its measurement and calculation, identification of insulin resistance by Homeostasis Model Assessment of Insulin Resistance test (HOMA-IR), has been the most commonly utilized method both in clinical settings and in commnity.[11] The current study was conducted to identify the prevalence of insulin resistance using HOMA-R and to evaluate its relationship with fatty liver index among the overweight non-diabetic patients.

METHODOLOGY:

It was descriptive cross sectional study conducted in General medicine department belonging to a tertiary care medical college and hospital located in Chennai, Tamil Nadu of South India. the study period was between 2022 and 2023 .All patients who were attending the OPD of General Medicine department of the study setting with no history of diabetes were selected as the study subjects. The study period was between 2022 and 2023 According to Mohamed RZ et al[12], considering the sensitivity of fatty liver index as 82.8%, the estimated sample size was 107 with 80% power, 95% confidence interval of 95% and precision taken as 5%.Convenient sampling method was employed to recruit the study participants into the study. Only those study subjects who were in the age of 20-70 years and with the BMI of 25-30 kg/m2 were included in the study. Standardized techniques were used by trained personnel to measure weight and height across studies. Those patients with known status of type 2 Diabetes or any types of diabetes, alcoholic fatty liver disease, an Severe infections, any other Chronic illness e.g., severely damaged liver functions (AST levels or ALT levels more than 2 upper limit of normal) and known alcoholic with intake more than two occasions a week were excluded from the study.

Patients coming to general medicine OPD and IPD of study setting were selected according to inclusion and exclusion criteria. An informed Consent was taken from each candidate. History taking after providing a informed written consent were done. Full clinical examination which includes Fatty Liver Index, Anthropometric parameters such as height, weight, waist circumference and body Mass Index (BMI)were done as per proposed in research protocol. The subject was dressed modestly and wore no shoes when their weight was recorded on a digital scale. The participant stood without shoes, and the height of participant was measured with a tape

measure to the nearest millimeter. Unclothed, the subjects' waist and hip circumferences were measured with a tape measure. Between the iliac crest and the costal margin, the WC was thought to have the smallest circumference. Body mass index (BMI) was computed by dividing weight (in kilograms) by height (in meters) squared. AS per WHO BMI classification, only those study subject were overweight i.e BMI of 25-30 kg/m2 were taken into the study.

The formula for HOMA-IR, which predicts insulin resistance by simulating the dynamics of glucose and insulin under fasting conditions, is as follows: fasting insulin (mU/dL) x fasting blood glucose (mmol/L)/22.5. [13] this HOMA-IR was used to categorise the presence of insulin resistance in the current study if the values are greater than 2. All the patients have undergone comprehensive assessment of diabetes and microvascular complications related to it such as Fasting and 2 hours of post prandial blood glucose levels, HbA1C%, HOMA-IR, Fasting insulin and Lipid profile were also done. The FLI's formula is as follows, as proposed in previous research[14,15] : FLI is equal to [e0.953 = H loge (serum triglycerides) + 0.139 = × loge (BMI) + 0.718 = × loge (gamma-glutamyltransferase) + 0.053 = × loge (waist circumference–15.745)]/[1 + e0.953 + H + loge (triglycerides) + 0.139 + × + BMI + 0.718 + × + loge (γ-glutamyltransferase) + 0.053 + × + waist circumference – 15.745] / 100; Waist circumference measurements are given in centimeters, triglyceride levels are expressed as milliliters per liter, and γ-glutamyltransferase levels are expressed as units of unit (U/L). The score is between 0 and 100. A score of above 100 was considered as positive for fatty liver disease. Institutional Ethical Committee approval from the institution was obtained before the start of the study. All the details were entered in a semi-structured questionnaire.

MS-Excel was used to data entering and analysis was done using the SPSS software version 24. On applying KOLMOGOROV-SMIRNOV test, all numerical data was found to be normally distributed. Descriptive statistics such as percentages, frequencies, mean and standard deviation were used to present all the quantitative data. For categorical variables, chi square test was done. Pearson correlation test was applied to identify the corelationship between the continuous variables.

RESULTS:

A total of 100 study subjects were recruited in the study.The mean age of the study participants was 48.43+8.71 years. Maority of the study subjects belonged to the age category of 40-49 years(35.5%) followed by 50-59 years(33.6%). Very less proportion of subjects were in the age category of more than and equal to 60 years as shown in table 1. There was almost equal proportion of male(49.5%) and females (50.5%). Table 2 shows the average of all the anthropometric measurements such as height (in cm), weight in (kg), waist circumference (in cm) and Body mass index (in kg/m2) done among the recruited participants. In table 3, the mean values of parameters related to diabetic control such as fasting blood gluocose, 2 hour post-prandial glucose and glycosylated hemoglobin were illustrated.

Table 4 shows that the prevalence of insulin resistance identified using HOMA-IR with the cut off of greater than or equal to 2 was 76.6% among the non-diabetic overweight patients, whereas the proportion of fatty liver index among these study subjects as per fatty liver index (with cut-off of above 100) was 54.2% as shown in table 5. In table 6, it was shown that there was a significant positive correlation between insulin resistance and fatty liver index. This means that with every unit increase of HOMA-IR , there will be an increase in fatty liver index unit which signifies the relationship of insulin resistnace and fatty liver disease (Fig 1)

Table 1-Age distribution of the study subjects (N-107):

Age Categories	Frequencies	Percent(%)
<40	20	18.7
40-49	36	33.6
50-59	38	35.5
≥60	13	12.1
Total	107	100.0

Table 2- Mean values of Heightt,weightt,bmi and wasist circumferences of the study subjets (N-107)

S.No	Parameters	Mean	Std. Dev.
1	Height (cm)	164.019	13.7422
2	Weight (kg)	74.2467	13.4657
3	WAISTCIRCUMFERENCE(cm)	40.4019	1.40659
4	BMI(kg/$m^{2)}$	27.243	1.67017

Table 3- Mean values of blood glucose parameters of the study subjects (N-107)

S.No	Parameters	Mean	Std. Dev.
1	HBA1c (%)	5.1318	0.38987
2	FBS(mg/dl)	89.5794	11.2309
3	PPBS(mg/dl)	104.682	14.7089

Table 4- Prevalence of Insulin resistance as per HOMA-IR among study subjects (N-107)

HOMAR-IR	Frequency	Percent
Insulin Resistance	82	76.6
No Insulin Resistance	25	23.4
Total	107	100.0

Table 6- Proportion of fatty liver identified through fatty liver index among the study subjects (N-107)

FATTY LIVER INDEX	Frequency	Percent
Fatty Liver	58	54.2
No Fatty Liver	49	45.8
Total	107	100.0

Table7- correlation between Insulin resistance (by HOMA-IR) and fatty liver index:

		FATTYLIVERINDEX
HOMA-IR	Pearson Correlation	0.283
	p-value	.003

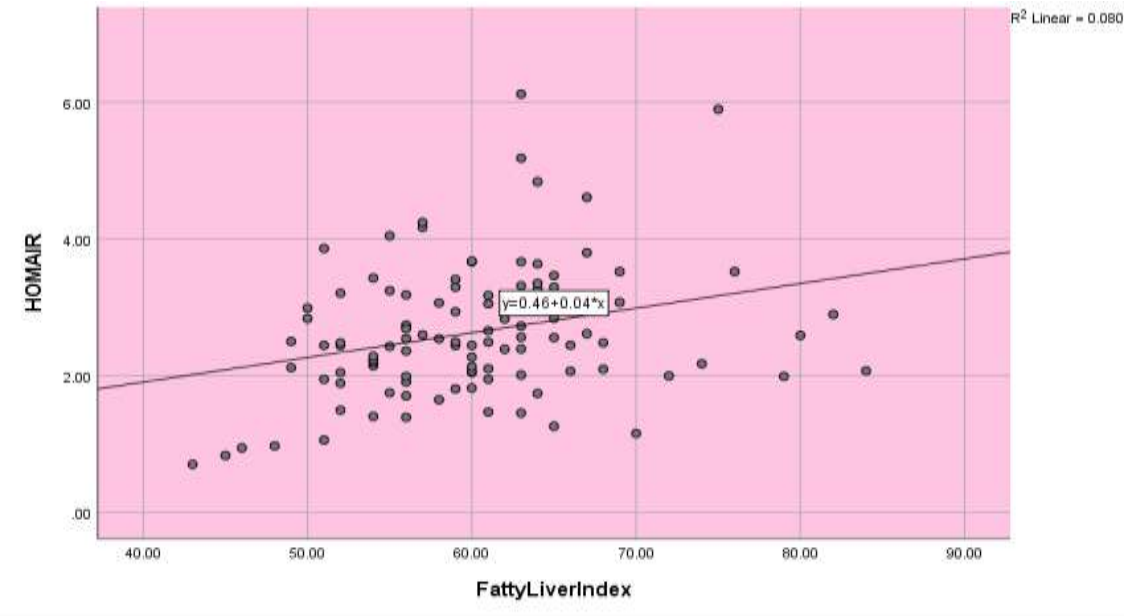

Fig -1- Scatter plot depicting correlation between HOMA-IR and Fatty liver index

DISCUSSION:

In this study, the mean age among the study population is 48.42 with a Standard Deviation of 8.7. Majority of the study population belong to age group of 50-59 (38, 35.5%), followed by age group of 40-49(36, 33.6%). This finding of mean age and majority of subjects being between 40-60 years was also observed in a similar studies conducted by Khang ARet al, Kim JH et al and Scapaticci S et al.[14-16] In the present study, there was no gender preponderance among the study subjects. But the role of gender in the determination of progression of insulin resistance and fatty liver have been studied especially when obesity and polycystic ovarian disease is common among the female population.[17] This difference in finding could be due to different study area and being a hospital based study setting.

HbA1c reflects the recent three-months control of diabetes and type 2 diabetes pathophysiology is linked to insulin resistance. HbA1c was studied to rule out diabetes in the study population. In this study, The HbA1c was ranging from 4.5 to 5.9. The mean HbA1c was 5.1 with SD of 0.39. The eligibility criteria of the study population was nondiabetic population, and the Minimum and Maximum values of the Fasting blood sugar were 71 and 108, respectively. The Minimum value and Maximum value of the Postprandial blood sugar were 81 and 135, respectively. The Mean of FBS and PPBS were 89.5794 and 104.68, respectively. The above findings are comparable to the similar studies conducted by Naguib H et al and Zupa R et al.[18,19]

In this current study, BMI, Fasting Insulin and Triglycerides were significantly correlated with the Insulin Resistance (by HOMA-IR) with p-value less than 0.05. Similarly Jorge Parcha V et al, which studied the relationship of Insulin resistance with triglyceride levels, waist circumference and BMI values among lean and overweight non-diabetic adults, observed that Insulin resistance was found to be significantly associated with the presence of NAFLD but not associated with waist circumference value or BMI.[20] HOMA-IR is a tool to measure insulin resistance and an independent predictor of severe liver fibrosis among non-diabetic overweight NAFLD cases..[21,22] Although liver biopsy is the gold standard technique to correctly diagnose the presence of NAFLD, the usage of this non-invasive marker in prediction of the Fatty liver could be efficient for clinicians. In addition, it is a useful and simple clinical biomarker to detect at risk diabetes patients.In our study population of overweight non-diabetic population, Fatty Liver was present in 58 (54.2%) using Fatty liver index >60.The baseline prevalence of the hepatic steatosis among the prediabetic population was found to be (i.e., FLI ≥60) 56%.[23] But in a Japanese study prevalence of hepatic steatosis among the prediabetic population was found to be (i.e., FLI ≥60) 19%.[24]

Diabetes mellitus is an independent risk factor of commencement and progression of NAFLD and the progress of cirrhosis. [9]In this study, When HOMA-IR is correlated with the Fatty Liver Index; the correlation coefficient was 0.283 with a p-value of 0.003, which is significant. In the scatter plot there was a positive correlation (increase in HOMA-IR with Increase in Fatty Liver Index) between HOMA-IR and Fatty liver index. Our findings indicate that once the presence of insulin resistance identified among the high risk patients using HOMA-IR, these patients could be screened with fatty liver index when ultra-sonography is not available or in community settings.

CONCLUSION:

Insulin resistance (HOMA-IR >2) was present in three fourth of the study population. Half of the study subjects have Fatty Liver using Fatty liver index. There was significant positive correlation identified between HOMA-IR . This proves the importance of insulin resistance on deciding the occurrence of NAFLD since we studied especially amongst the non-diabetic overweight patients who are at risk.

REFERENCES:

1. Ramamurthy J. CORRELATION BETWEEN DIABETES AND HYPERTENSION IN PATIENTS WITH PERIODONTITIS-A RETROSPECTIVE STUDY. Ann Trop Med & Public Health; 23(S22): SP232319. Nov 2020 Vol. 23 Issue 22. DOI: http://doi.org/10.36295/ASRO.2020.2323**19**

2. Banday MZ, Sameer AS, Nissar S. Pathophysiology of diabetes: An overview. Avicenna journal of medicine. 2020 Oct;10(04):174-88.

3. Tinajero MG, Malik VS. An update on the epidemiology of type 2 diabetes: a global perspective. Endocrinology and Metabolism Clinics. 2021 Sep 1;50(3):337-55.

4. Roy JR, Janaki CS, Jayaraman S, Periyasamy V, Balaji T, Vijayamalathi M, Veeraraghavan VP. Carica papaya reduces muscle insulin resistance via IR/GLUT4 mediated signaling mechanisms in high fat diet and streptozotocin-induced type-2 diabetic rats. Antioxidants. 2022 Oct 21;11(10):**2081**.

5. Targher G, Corey KE, Byrne CD, Roden M. The complex link between NAFLD and type

2 diabetes mellitus—mechanisms and treatments. Nature reviews Gastroenterology & hepatology. 2021 Sep;18(9):599-612.
6. Petroni ML, Brodosi L, Bugianesi E, Marchesini G. Management of non-alcoholic fatty liver disease. Bmj. 2021 Jan 18;372.
7. Yu W, Xie D, Yamamoto T, Koyama H, Cheng J. Mechanistic insights of soluble uric acid-induced insulin resistance: Insulin signaling and beyond. Reviews in Endocrine and Metabolic Disorders. 2023 Apr;24(2):327-43.
8. Pradeepa R, Mohan V. Epidemiology of type 2 diabetes in India. Indian journal of ophthalmology. 2021 Nov 1;69(11):2932-8.
9. .Kim J-Y, Lee G-N, Song HC, Park Y-M, Ahn Y-B, Han K, et al. Association between Fatty Liver Index and Periodontitis: the Korea National Health and Nutrition Examination Survey. Sci Rep. 2020;10(1):3805.
10. Peng L, Wu S, Zhou N, Zhu S, Liu Q, Li X. Clinical characteristics and risk factors of nonalcoholic fatty liver disease in children with obesity. BMC pediatrics. 2021 Dec;21:1-8..
11. Zeng P, Cai X, Yu X, Gong L. Markers of insulin resistance associated with non-alcoholic fatty liver disease in non-diabetic population. Scientific reports. 2023 Nov 22;13(1):20470
12. Mohamed RZ, Jalaludin MY, Zaini AA. Predictors of non-alcoholic fatty liver disease (NAFLD) among children with obesity. Journal of Pediatric Endocrinology and Metabolism. 2020 Feb 1;33(2):247-53.
13. Ganta GK, GSR K. Anthropometric Measurements as Predictors of Metabolic Health in Young Adults (19–24 Years): Investigating the Correlation of Anthropometrics with Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) and Quantitative Insulin Sensitivity Check Index **(QUICKI)**.
14. Sheba W, Morsy E, Altahan S, Ayaad M, Lashen SA. Nonalcoholic fatty liver disease is associated with early left ventricular diastolic dysfunction in patients with type 2 diabeteS. Alexandria Journal of Medicine. 2022;58(1):117-24.
15. Lee MJ, Bae JH, Khang AR, Yi D, Yun MS, Kang YH. Triglyceride-glucose index predicts type 2 diabetes mellitus more effectively than oral glucose tolerance test-derived insulin sensitivity and secretion markers. Diabetes Research and Clinical Practice. 2024 Apr 1;210:111640.
16. Kim JH, Moon JS, Byun SJ, Lee JH, Kang DR, Sung KC, et al. Fatty liver index and development of cardiovascular disease in Koreans without pre-existing myocardial infarction and ischemic stroke: a large population-based study. Cardiovasc Diabetol. 2020;19(1):51.
17. Scapaticci S, D'Adamo E, Mohn A, Chiarelli F, Giannini C. Non-Alcoholic Fatty Liver Disease in Obese Youth With Insulin Resistance and Type 2 Diabetes. Front Endocrinol (Lausanne). 2021;12:127.
18. Won YB, Seo SK, Yun BH, Cho S, Choi YS, Lee BS. Non-alcoholic fatty liver disease in polycystic ovary syndrome women. Scientific reports. 2021 Mar 29;11(1):7085
19. Naguib H, Kassab H. Potential relation between non-alcoholic fatty liver disease and glycemic and metabolic parameters in subjects without diabetes. Egyptian Liver Journal. 2021 Dec;11:1-7.

20. Zupo R, Castellana F, Panza F, Castellana M, Lampignano L, Cincione RI, Triggiani V, Giannelli G, Dibello V, Sardone R, De Pergola G. Non alcoholic fatty liver disease is positively associated with increased glycated haemoglobin levels in subjects without diabetes. Journal of Clinical Medicine. 2021 Apr 15;10(8):1695.

21. Parcha V, Heindl B, Kalra R, Li P, Gower B, Arora G, Arora P. Insulin resistance and cardiometabolic risk profile among nondiabetic American young adults: insights from NHANES. The Journal of Clinical Endocrinology & Metabolism. 2022 Jan 1;107(1):e25-37..

22. Motamed B, Vajargah MK, Kalantari S, Shafaghi A. HOMA-IR index in non-diabetic patient, a reliable method for early diagnosis of liver steatosis. Caspian journal of internal medicine. 2022;13(3):519..
23. Lee JH, Park K, Lee HS, Park HK, Han JH, Ahn SB. The usefulness of metabolic score for insulin resistance for the prediction of incident non-alcoholic fatty liver disease in Korean adults. Clinical and molecular hepatology. 2022 Oct;28(4):814.
24. Li N, Tan H, Xie A, Li C, Fu X, Xang W, Kirim A, Huang X. Value of the triglyceride glucose index combined with body mass index in identifying non-alcoholic fatty liver disease in patients with type 2 diabetes. BMC Endocrine Disorders. 2022 Apr 15;22(1):101.
25. Shida, T., Oshida, N., Suzuki, H., Okada, K., Watahiki, T., Oh, S., Kim, T., Isobe, T., Okamoto, Y., Ariizumi, S.I. and Yamamoto, M., 2020. Clinical and anthropometric characteristics of non-obese non-alcoholic fatty liver disease subjects in Japan. *Hepatology Research*, *50*(9), pp.1032-1046