Original Article

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Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) as Predictor of Pre-diabetes in Non-Alcoholic Fatty Liver Disease (NAFLD)

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Abstract

Background: India is the diabetes capital of the world with every fifth diabetic in the world is an Indian. **Subjects and Methods:** We studied Sixty non-alcoholic, non-diabetic, normotensive obese NAFLD subjects with WHR:>0.9 in males and >0.85 for females according to inclusion and exclusion criteria. **Results:** NAFLD, a chronic condition ranging from benign steatosis, (i.e., hepatic triglyceride accumulation >5.5% using magnetic resonance imaging or >5% corresponding to 50 mg/g by wet weight), to more significant liver injury, i.e.,non-alcoholic steato-hepatitis(NASH).**Conclusion:** Association of NAFLD with features of insulin resistance and was more prevalent among subjects with IGT. The increased risk for cardio-metabolic diseases in NAFLD might be due to hepatic overproduction of glucose, VLDL, inflammatory factors as a result of insulin resistance.

Keywords: HOMA-IR, NAFLD and USG.

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Introduction

India is the diabetes capital of the world with every fifth diabetic in the world is an Indian.[1] In India, the diabetic population is estimated to rise from its current level of 30 million to 57 million by 2025. The country is also facing an obesity crisis in the middle class especially in urban population where obesity prevalence is as high as 30%.[2] NAFLD is a chronic condition, ranging from benign steatosis to non-alcoholic steato- hepatitis(NASH).[3] Indian study reported NAFLD prevalence rate of 24.6% with a preponderance of males.[4]

Rationale

The complications of DM affect many organ systems and are responsible for the majority of morbidity and mortality associated with the disease.Excess liver fat is extremely common and prevalence of NAFLD has been increasing mainly because of the increased prevalence of obesity.Patients with NAFLD are at increased risk for cardio-metabolic complications such as type 2 diabetes (T2DM) and cardiovascular disease (CVD)[5,6]The real prevalence is unknown since NAFLD is often undiagnosed.USG abdomen a very common noninvasive routine investigation at present which can trace NAFLD cases to predict prediabetes, thus preventing T2DM.

Justification

India is facing a double threat due to obesity and diabetes epidemics. It is important that diabetes mellitus should be recognised early in order to identify a particularly high-risk population, often underestimated and undertreated.

Aims and Objectives

- To identify the HOMA-IR cut off values that best differentiates prediabetic NAFLD cases from age, sex, adiposity matched control group.
- To find the association between NAFLD and prediabetes.

Research Design and Methodology

Place of study: Department of Biochemistry in collaboration with department of General Medicine VIMSAR, Burla.
Period of study: May 2017 to may2018.
The study was approved by the institutional ethics committee, and informed written consent was obtained from each patient before participation.
Study design: Case Control study.

Inclusion Criteria

Study Population:
Selection of Cases:

- Sixty non-alcoholic, non-diabetic, normotensive obese NAFLD subjects with WHR:>0.9 in males and >0.85 for females.
- AGE: 20- 50 years.

NAFLD diagnosis: There are four sonographic findings of diffuse fatty change in the liver:

a) Diffuse hyperechoic echo texture (bright liver),
b) An increased liver echo texture compared with the kidney,
c) Vascular blurring, and
d) Deep attenuation.[7]

A combination of these parameters allowed the diagnosis of fatty liver with a sensitivity of 83% and a specificity of 100%.[8]

Selection of controls:

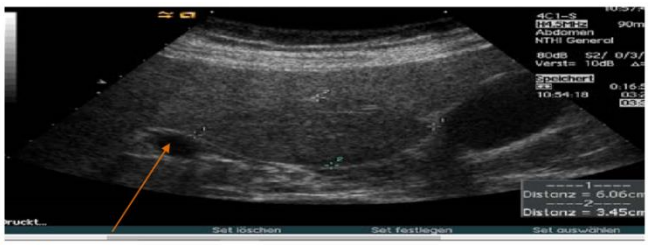
- Sixty age, sex, ethnicity and adiposity matched non diabetic, non alcoholic, normotensive without NAFLD.

Exclusion Criteria

- H/O heavy alcohol use (>12 to 15 g of alcohol per day, or >12 oz of beer, 5 oz of wine, or 1.5 oz of distilled spirits);
- Fasting glucose level of ≥126mg/dL (13.3 mmol/L);
- H/O diabetes mellitus
- H/O Heart disease (congestive heart failure, New York Heart Association functional class ≥II),
- H/O Hepatic disease other than non-alcoholic steatohepatitis
  - ❖ Hepatitis B or C
  - ❖ Autoimmune hepatitis
  - ❖ Hemochromatosis
  - ❖ Wilson disease
  - ❖ Drug-induced disease, other)
- H/O renal disease
- Receiving metformin, thiazolidinedione's

Subjects and Methods

- WHR (waist hip ratio): waist circumference ÷ hip circumference
- USG: (Xario 100, Toshiba Japan.)
- Blood Glucose: glucose oxidase method
- OGTT: glucose oxidase method
- INSULIN: IFA (AIA -360 Tosoh Japan)
- HOMA-IR: fasting insulin (micro U/L) × fasting glucose (nmol / L) / 22.5).
- Lipid profile: (cobasintegra 411) TC, HDL, LDL, TG
- LIVER FUNCTION TEST:(cobasintegra 411) Bilirubin, AST, ALT,GGT.



Focal hypoechoic area

Most important sign of hepatic steatosis

- Presence of focal hypoechoic areas (FHA) corresponds to parenchymal islands with (close to) normal fat content
- Surrounded and contrasted by bright echogenic parenchyma with fatty infiltration.

Statistical analysis

All values were reported as the mean ± SD of the mean for continuous variables and the number (percent) for categoric variables. Comparison of groups (i.e., with versus without NAFLD or by glucose tolerance status) was performed using ANOVA. Statistical significance was set at $P < 0.05$.

Result & Discussion

NAFLD, a chronic condition ranging from benign steatosis, (i.e., hepatic triglyceride accumulation >5.5% using magnetic resonance imaging or >5% corresponding to 50 mg/g by wet weight),[10,11] to more significant liver injury, i.e.,non-alcoholic steato-hepatitis(NASH).[3] Prevalence of NAFLD has been increasing mainly because of the increased prevalence of obesity. Most subjects with NAFLD, even those with diabetes, have normal liver aminotransferases and clinicians do not suspect the potential presence of NAFLD.[9–11] Cross-sectional studies have associated T2DM with worse histology in NAFLD.[12] Compared with NGT subjects, subjects with IGT are believed to have an increased risk of developing NAFLD,[13,14] but the true prevalence of prediabetes and T2DM has never been systematically assessed by means of an oral glucose tolerance test (OGTT) among patients with NAFLD. This study aims to find whether NAFLD is associated with insulin resistance (IR) and increases the risk of developing T2DM.

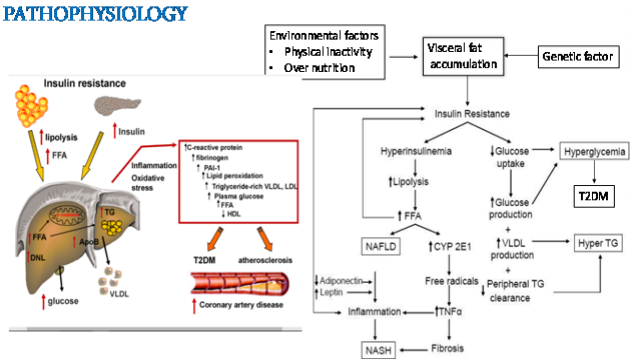


Figure 1:

Table 1: Patient characteristics

Variables	No NFALD	Nfald	P value
AGE	34.98± 6.85	34.98± 6.85	1
SEX(M:F)	42:18	42:18	
WHR	0.93 ± O.05	0.93 ± 0.05	1
FBS	86.85 ±13.15	100.98 ±12.99	<0.0001
INSULIN	7.525 ± 1.87	9.358 ± 2.658	0.0001
TC	180 ± 8	190 ± 7	<0.0001
HDL	50 ± 4	35 ± 2	<0.0001
LDL	103 ± 7	120 ± 5	<0.0001
TG	92 ± 15	159 ± 9	<0.0001
AST	25 ± 4	49 ± 3	<0.0001
ALT	29 ± 3	57 ± 5	<0.0001
HOMA-IR	1.665 ±0.636	2.393 ± 0.905	<0.0001

- Fasting plasma insulin, HOMA-IR, FBS, plasma TG, AST,ALT, LDL and HDL values of cases were significantly differ from controls because of insulin resistance in cases.
- Our observations were similar to observations of Ortiz-Lopez C et al, 2012.[15]

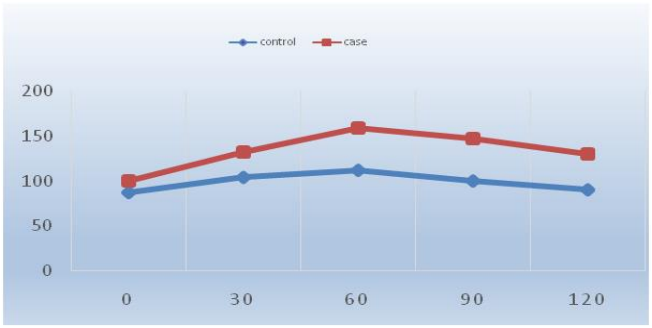


Figure 2: Comparative values for blood glucose levels during oral tolerance test in controls and NAFLD groups

- Higher values in cases than the controls were observed in all studied points.
- Our observations were similar to observations of Salgado et al, 2010.[16]

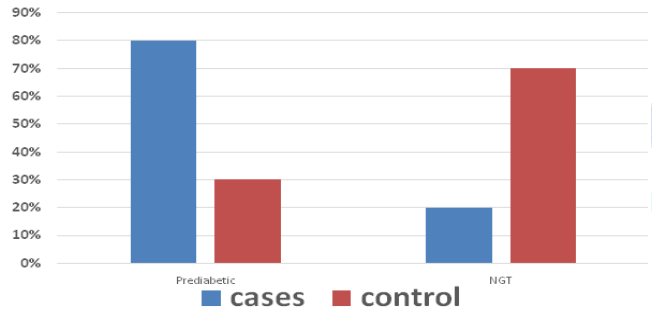


Figure 3: Prevalence of NGT (Normal Glucose Tolerance) and IGT (Impaired Glucose Tolerance) in patients with and without NAFLD

- NGT – 70% in controls and in 20% of cases.
- IGT – 30% in controls and in 80% of cases.

Our observations were similar to observations of Ortiz-Lopez C et al,2012.[15]

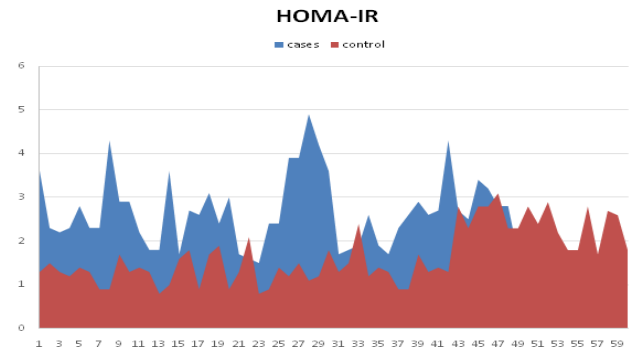


Figure 4: comparative value of HOMA-IR in cases and controls

- Mean value of HOMA-IR (2.393±0.905) in cases was significantly higher than the control group (1.665±0.636).
- This shows the presence of insulin resistance in the cases.
- 30% of the controls also showed higher values indicating evidence of insulin resistance.
- As observed by Salgado et al, 2010, their Control group presented HOMA-IR mean value of 1.27 ± 0.63 which is different from the mean value of 1.665±0.636 in our population.

Conclusion

- Association of NAFLD with features of insulin resistance and was more prevalent among subjects with IGT.
- The increased risk for cardio-metabolic diseases in NAFLD might be due to hepatic overproduction of glucose, VLDL, inflammatory factors as a result of insulin resistance.
- Larger trials that investigate the incidence of T2DM, CVD and related mortality in subjects with NAFLD are needed to confirm these observations.

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