Original Article

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Prevalence of Obesity, Non-Alcoholic Fatty Liver and Insulin Resistance and their inter relationship among type II diabetic patients attending Diabetic Centre, Teaching Hospital, Jaffna.

Rajendra.S[1], Nalini.R[2], Aravinthan M[2]

[1]Department of surgery, Faculty of Medicine, Jaffna,
[2]Teaching Hospital, Jaffna,

Introduction

Obesity plays an important role in the pathogenesis of type II diabetes (1). The percentage of patients with type II diabetes and obesity has shown a rising trend in Asia (2). Sri Lankan guideline committee has given BMI cut off values to define overweight and obesity. BMI of 23-24.9 kg/m^2 will be overweight , and 25- 30 , 30-35 and >35will be class 1, class 2 and class 3 obesity respectively (3). Prevalence of overweight and obesity among adults in Sri Lanka was 25.2% and 9.2% respectively (4). Obesity can lead to type II diabetes,hypertension, heart diseases, chronic kidney diseases, obstructive sleep apnoea and osteoarthritis (5).

NAFL is detected frequently by Ultrasonographic(USS) examination of abdomen. The sensitivity and specificity of abdominal USS in detecting NAFL is 89% and 93% respectively (6).Liver biopsy is the gold standard for diagnosing NAFL but it is invasive and has associated morbidity (7).The prevalence of NAFL in urban adult Sri Lankan population was 61.5% and annual incidence of NAFL was6.2% and the incident NAFL was associated with diabetes and obesity (8). Type II DM patients are likely to have increased prevalence of NAFL because of obesity and insulin resistance (9).

Subnormal biologic response to givenconcentration of insulin is known as insulin resistance(IR). IR plays an important role in diabetes, hypertension, dyslipidaemia, obesity and cardiovascular diseases (10). IR can be assessed based on the score on the homeostasis model assessment of insulin resistance (HOMA-IR) (11). A study carried among type II DM patients in Galle Sri Lanka, revealed that 93% of DM patients had IR when assessed by HOMA method (12). There are established molecular mechanisms describing the role of IR in the pathogenesis of DM, NAFL and obesity (1). No studies have been carried out in Sri Lanka to assess the interrelationship between these factors in diabetic patients.

Method

This institutional based prospective analytical cross sectional study was carried out at the Diabetic Centre, Teaching Hospital, Jaffna, from April to September 2017. Type II DM patients attending the diabetic centre, TH Jaffna for follow-up care were selected. These patients, who consented to take part in the study, were consecutively included in the study. Those patients with significant renal, cardiac and respiratory diseases and also with malignancies as well as those who have the habit of alcohol consumption were excluded from the study. The study was carried out from the 1st of April 2017 to the 30th of September 2017. Sample size was calculated using the equation, $n=z^2 p (100-p) / d^2$ the calculated sample size was 250.

Information was gathered from the patient using an interviewer administered questionnaire. Demographic data such as the age& sex of patients

Corresponding author: Dr.S. Rajendra, email- dr.s.rajendra@gmail.com, https://orcid.org/0000-0002-3303-603X, Submitted 14th October 2019, Accepted 25th November 2019

were recorded. Anthropometric measurements (height and weight)were measured utilizing the standard methods with calibrated equipment. All these measurements were done by two specially trained pre intern doctors. Body mass index was calculated by using the standard formula (BMI = weight in kg /height in meters^2). Asian criteria values for BMI cut off was utilized as advised by Sri Lankan guideline committee

Fasting blood sample was obtained from each patient to measure the fasting sugar and insulin levels and subsequent estimation of IR by HOMA-IR method. Fasting blood sugar was measured by Glucose oxidase using DDS T240 Auto Chemistry Analyzer machine. HOMO-IR was assessed by Electro ChemiLuminescence Immune Assay(ECLIA) method in ROCHE Hitachi Cobas E 411 Fully automated hormone analyzer machine. HOMO –IR index > 2 infers insulin resistance.

Each patient underwent an USS assessment of liver by consultant radiologist to detect and grade the NAFL. Liver echogenicity equal to the echogenicity of kidney would be considered a normal liver. Increased hepatic echogenicity with visible periportal and diaphragmatic echogenicity will be grade I NAFL. Increased echogenicity of liver with imperceptible periportal echogenicity would be grade II NAFL. Increased liver echogenicity with imperceptiblediaphragmatic margin would be grade III NAFL.

Data were analyzed by Statistical Package for Social Sciences (SPSS) version 21. P value of 0.05 was deemed statistically significant.

Ethical approval was obtained fromthe Ethical Review Committee of the Faculty of Medicine, the University of Jaffna and all the patients were recruited after obtaining informed consent from the patient.

Results

There were 240 type II DM patients (n=240) recruited for this study. Mean age of the study population was 58.38 years (SD 10.15). There were 150 female patients (62.5%) and 90 male patients (37.5%).

Prevalence of Obesity in Type II DM

The mean BMI of this study population was 25.85 Kg/m^2 (SD 3.91). Among this study population of type II DM patients, 138 patients (57.5%) were obese, having a BMI of >25 Kg/m^2 (Table1).

Table 1: The distribution of BMI

BMI	Frequency (n)	Percentage (%)
Underweight	5	2.1
Normal	55	22.9
Over weight	42	17.5
Obese – Type I	106	44.2
Obese – Type II	28	11.7
Obese – Type III	4	1.7
Total	240	100

The association between age of type II DM patients and obesity was statistically significant ($p<0.05$). The prevalence of obesity in type II DM patients was high in the 60-70 years age group. (Table2)

Table 2: The association between age and obesity

Age	Obese patients	Non obese patients	Total
20-39	8	4	12
40-59	72	34	106
60-79	58	64	122
Total	138	102	240

The association between sex of type II DM patients and obesity was statistically significant ($p<0.05$). The prevalence of obesity was high among females (37.9%).

Prevalence of NAFL in Type II DM

In this cohort of 240 type II DM patients, 178 of them (70%) had NAFL. There was no statistically

significant association of NAFL with age or sex of type II DM patients. (Table3)

Table 3: Prevalence of NAFL

Liver Echog -enecity	Grades of Liver Echog -enecity	Freq -uency (n)	Perce -ntage
Normal liver	Grade 0	72	30.0
Fatty liver	Grade 1	146	60.8
	Grade 2	22	9.2
	Grade 3	-	-

Prevalence of IR in Type II DM

Among this cohort of 240 type II DM patients, 178 (74.2%) had IR (HOMO-IR index >2).There was no statistically significant association between IR and age of type II DM patients.(Table 4)

Table 4: The association of IR with age

Age	IR +	No IR	Total
20-39	10	2	12
40-59	80	26	106
60-79	88	34	122
Total	178	62	240

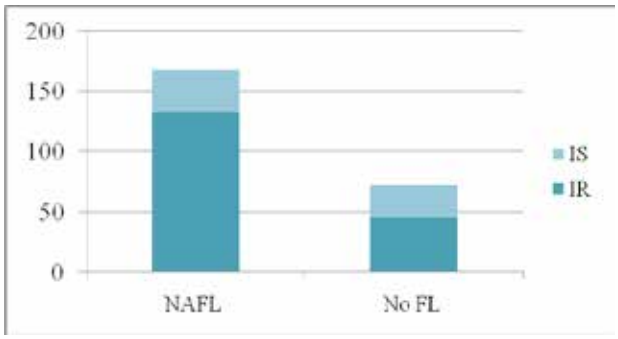
There was no statistically significant association between IR and sex of type II DM patients. Majority were females (48.33%).

Interrelationship between IR and NAFL in Type II DM

In the type II DM patients with IR (n=178), 74.7% had NAFL(n=133).

The association between IR and NAFL in this cohort of type II DM patients was statistically significant (p<0.05)(Chart1)

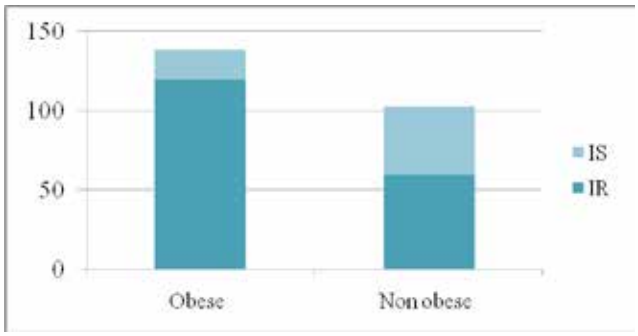
Chart 1: The association between IR and NAFL



Interrelationship between IR and Obesity in Type II DM

Out of 178 type II DM patients with IR, 119(86.23%) were obese. The association between IR and obesity in this cohort of type II DM patients was statistically significant (p<0.05)(Chart 2)

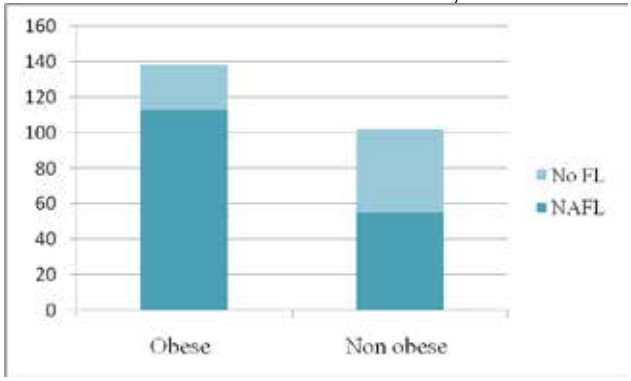
Chart 2: Relationship between IR and obesity



Interrelationship between obesity and NAFL in Type II DM

Out of the 138type II DM patients who had obesity, 113 (81.88%) were NAFL. The association between obesity and NAFLin this cohort of type II DM patients was statistically significant (p<0.05). (Chart3)

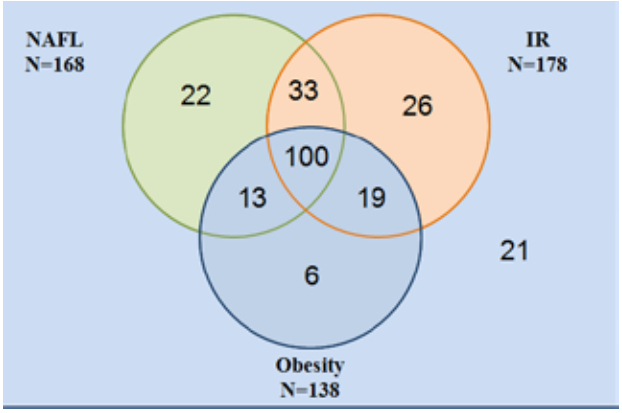
Chart 3 Association between obesity and NAFL



Interrelationship between obesity, NAFL and IR among type II DM patients

Out of 240 type II diabetic patients, 100 (41.6%), had obesity, NAFL and IR. 21 (8.75%) out of 240 diabetic patients, did not have either obesity, NAFL or IR.

Picture 1:'Ominous triad' of NAFL, IR and Obesity



Discussion.

Impaired function of insulin (IR) occurs early in type II DM whereas impaired insulin secretion occurs in later stages (13). The onset of type II DM is heralded by the ability of IR to bring about a failure of beta cell compensation in susceptible individuals (10). Prevalence of IR among type II DM patients in our study group in Jaffna was 74.2%.The prevalence of IR in diabetic patients in Galle was 93% (12). The difference in prevalence in these two regions may be due to the difference in the total number of type II DM patients recruited for the study (240 Vs 42) and also because of the difference in ethnicity and socio cultural and diet patterns (14).Among the 240 type II DM patients 25.8% (n=62) did not have IR. This could be explained by the long term use of medications (eg. Metformin) that reduce IR, and also could be due to good dietary and life style modification practiced by patients (13) . A patient who has other type of DM (eg. Maturity Onset Diabetes of Young-MODY) could have been categorized as type II DM and this may be another reason for not having IR despite having DM.

Development of type II DM was accompanied by progressive weight gain and obesity (14). Obesity is commonly associated with subclinical inflammation in white adipose tissue, enhancing the production of pro inflammatory mediators to cause IR and type II DM (15). Prevalence of obesity (57.5%) in type II DM patients in our study group was comparable with that in SouthEast Asian countries and in USA.

Lack of suppression of lipolysis in adipose tissue causes increased delivery of fatty acid to liver. Triglyceride synthesis and accumulation of excess liver fat (NAFLD) occurs. Impaired fatty acid oxidation due to IR further aggravates the condition in type II DM (9). The prevalence of NAFL (70%) in type II DM patients in our study group was comparable with its prevalence in other parts of Sri Lanka (eg.Ragama), India and the USA (8,15,16,18). Effective treatment of type II DM and NAFLD can prevent the progression to inflammation and fibrosis (NASH) (19).

Fatty liver had positive association with IR and body weight in nonobese, non diabetic patients (20). Treatment with insulin sensitizing agents (eg. metformin) has shown improvement in NAFL and even in hepatic histology (21).The positive association between NAFL and IR in DM patients in our study was statistically significant($p<0.05$).Similar correlation has been observed in India(19). Insulin resistance state and subsequent hyperinsulinaemia induces lipogenesis and hepatic fat deposition.

Obesity and type II DM are closely related to the degree of insulin resistance and hyperinsulinaemia (13). The association between IR and obesity in type II DM patients in our study was statistically significant. Adipocytokines , including adiponectin, have been attributed have effect on IR and thereby causing obesity in type II DM patients (22).

The prevalence of NAFL among diabetic patients and among obese patients in Asia Pacific Region ranges from 30% to 90% and 15% to 80% respectively (23). The prevalence of NAFL in obese diabetic patients was 100% in USA (18). In our study the prevalence of NAFLin obese type II diabetic patients in our group was 81.88%. Obesity, type II DM and metabolic syndrome have been considered major risk factors for NAFL (23). These patients have higher risk of development and progression of cardiovascular disease (24).

Interestingly 41 % (100 out of 240) patients with type II DM in our study had obesity,IR and NAFL all together. This is a new finding and no such comparable studies were found nationally or internationally.These patients are at risk of developing cardio vascular and cerebro vascular events apart from complications of DM (11, 25). This alarmed finding in our study highlights the importance ofthe primary and the secondary health care based interventions (lifestyle modifications and pharmacological interventions), improving public awareness and promoting health education to prevent such overwhelming catastrophes.

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Conflicts of interest

Non declared by principal investigator and co- investigators. Expenses for biochemical investigations were self funded by principal author

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