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STUDY ON INSULIN RESISTANCE IN NORMAL WEIGHT INDIVIDUALS – HOSPITAL BASED CROSS SECTIONAL DESCRIPTIVE STUDY

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ABSTRACT :

Background: The increasing prevalence of obesity becomes main factor for epidemic of various metabolic diseases, causing massive health and socioeconomic burden worldwide. Accurate assessment of insulin resistance helps in identifying individuals at increased risk of these diseases and may help target preventive and therapeutic efforts more effectively. Hence we aimed to evaluate the prevalence of insulin resistance (IR) in normal weight individuals in Indian population and also whether triglyceride index and various other factors including waist hip ratio, fasting insulin can be used as surrogate markers for identifying insulin resistanc
Methods: Data was collected from patients attending the Department of General Medicine of Sree Mookambika Institute of Medical sciences, kanyakumari, tamil nadu, from march 2023 to september 2024. inclusion criteria is normal weight individuals aged 21 to 50 years attending medicine opd.
Results: The prevalence of Metabolic syndrome according to JIS definition was 25% in males (95% CI 16.8% - 35.5%) and 47% in females (95% CI 39.06% -55.3%). The prevalence of Insulin resistance (HOMA-IR) was 7.5% in males (95%). There was no significant difference in fasting blood sugar, triglycerides, HDL, LDL, total cholesterol, HOMA index and triglyceride index by gender.
Conclusion: In conclusion, our study provides evidence for prevalence of Insulin resistance and Metabolic syndrome in normal weight individuals. There was no evidence for using triglyceride index to identify metabolically risky group among normal weight population.
Keywords: normal weight obesity,body mass index.

INTRODUCTION:

The increasing prevalence of obesity becomes main factor for epidemic of various metabolic diseases, causing massive health and socioeconomic burden worldwide.
Insulin resistance is the key pathophysiologic defect in metabolic syndrome and type 2 diabetes mellitus which

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is currently measured by HOMA-IR. [1-4]

Accurate assessment of insulin resistance helps in identifying individuals at increased risk of these diseases and may help target preventive and therapeutic efforts more effectively.
Obesity, defined as excess body fat has been evaluated in various studies using mainly of body mass index(BMI) which doesn't differentiate lean body mass from fat mass.[5,6] In general, this indicator has limited ability for diagnosing individuals with excess BF presenting BMI within the normal range.

Ruderman et al, in early eighties described a type of obesity defined as metabolically obese normal weight subjects (MONW). These individuals were characterized by normal BMI , but presented with insulin resistance, hyperinsulinemia ,type 2 diabetes, hypertriglyceridemia and cardiovascular diseases predisposition.[7,8]
De Lorenzo et al, described the term normal weight obesity (NWO) to identify individuals who have normal BMI but high % BF, accompanied by total lean mass deficit.[9]

In a study conducted in Switzerland, which included only females aged 35– 75 years, women with NWO had a high waist circumference (WC), hyperglycemia, high triglycerides and low high-density lipoprotein (HDL) cholesterol, and higher cardiometabolic risk but a similar prevalence of hypertension compared to lean women.[10]Currently various investigations reveal that metabolically obese but normal weight (MONW) individuals also called metabolically abnormal normal weight or normal weight obesity are common and they are characterized by insulin resistance,increased levels of adiposity and a higher susceptibility to type 2 diabetes and cardiovascular diseases (CVD).

Hence early identification of MONW individuals would have important benefits by implementing preventive and early intervention in individuals even with normal weight.
In a Singapore based study, Kavitha Venkatraman et al concludes triglycerides and WHR combined with fasting insulin levels provide a better estimate of insulin resistance and identification of individuals with future risk of CVD, compared to HOMA-IR. [11]

S-H Lee et al described that TyG index is a simple marker that correlates well with the degree of insulin resistance measured by hyperinsulinemic euglycemic clamp studies which is the gold standard for Insulin resistance measurement.[12]
However, to our knowledge, there are few studies reporting an association between NWO and metabolic disorders in Indian population.

Hence we aimed to evaluate the prevalence of insulin resistance (IR) in normal weight individuals in Indian population and also whether triglyceride index and various other factors including waist hip ratio, fasting insulin can be used as surrogate markers for identifying insulin resistance.

AIM AND OBJECTIVES OF THE STUDY:

- To study the prevalence of Insulin resistance using HOMA Index and Metabolic Syndrome in Normal Weight Individuals.
- To study the usefulness of Triglyceride Glucose Index in identifying Insulin resistance among Normal

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Weight Individuals.

MATERIALS AND METHODS:

Data was collected from patients attending the Department of General Medicine of Sree Mookambika Institute of Medical sciences, kanyakumari, tamil nadu, from march 2023 to september 2024. inclusion criteria is normal weight individuals aged 21 to 50 years attending medicine opd.exclusion criteria are patients with: known h/o diabetes mellitus or fbs≥126 during study,known h/o hypertension, dyslipidemia,known h/o chronic renal, liver, cardiac disease, malignancy, thyroid disease or tuberculosis,patients on steroids, diuretics, statins and anti- psychotic drugs.

Screening for insulin resistance and metabolic syndrome even in normal weight individuals will prevent diabetes mellitus and cardiovascular disease risk by risk factors modification and early intervention.

Statistical analysis was done using the statistical package for social sciences (SPSS).Different statistical methods were used as appropriate. Mean ± SD was determined for quantitative data and frequency for categorical variables. The independent t- test was performed on all continuous variables. The normal distribution data was checked before any t-test. The Chi-Square test was used to analyze group difference for categorical variables. In logistic regression models, age was adjusted for estimation of each or all the independent effects of hypertension, ischemic heart disease and diabetes mellitus . A p- value < 0.05 was considered significant.

RESULTS:

COMPARISON OF BASELINE CHARACTERISTICS OF THE STUDY

POPULATION BASED ON GENDER

S. No	Parameter	Male (n=80)		Female (n=140		P value	Statistical test
		Mean	SD	Mean	SD		
1	Age (years)	38.71	7.8	37.5	7.5	0.26 (NS)	Unpaired ‘t’ test

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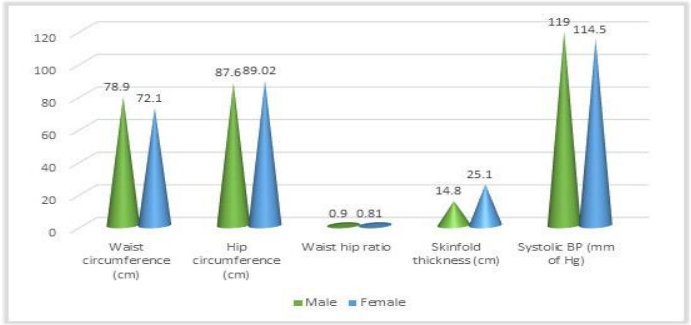
2	Weight (Kg)	56.77	5.27	51.2	6.04	<0.0001**	Unpaired 't' test
3	Height (cm)	161.2	6.1	152.4	5.7	<0.0001**	Unpaired 't' test
4	BMI (Kg/m^2)	21.9	1.6	22.01	1.68	0.646 (NS)	Unpaired 't' test
5	Waist circumference (cm)	78.9	5.8	72.1	5.81	<0.0001**	Unpaired 't' test
6	Hip circumference (cm)	87.6	4.01	89.02	5.61	0.04*	Unpaired 't' test
7	Waist hip ratio	0.9	0.05	0.81	0.05	<0.0001**	Unpaired 't' test
8	Skinfold thickness (cm)	14.8	4.64	25.1	7.5	<0.0001**	Unpaired 't' test
9	Systolic BP (mm of Hg)	119	9.08	114.5	11.08	0.002*	Unpaired 't' test
10	Diastolic BP (mm of Hg)	73.1	7.56	71.3	8.06	0.112 (NS)	Unpaired 't' test

Data are expressed as mean with standard deviation. * indicates $p<0.05$ and considered statistically significant and ** indicates $p<0.0001$ which is considered extremely significant.

COMPARISON OF CLINICAL PARAMETERS BASED ON GENDER



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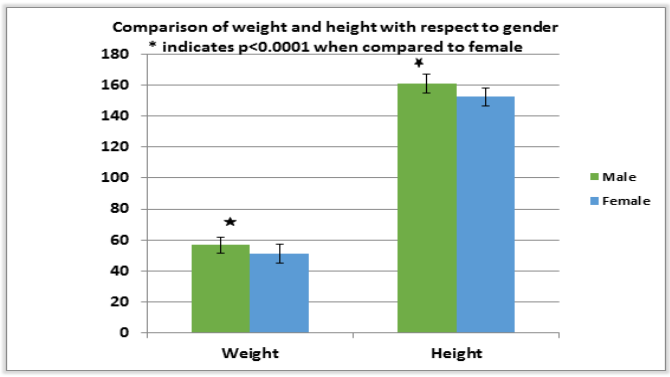

COMPARISON OF LABORATORY PARAMETERS OF THE STUDY POPULATION BASED ON GENDER

S. No	Parameter	Male (n=80)		Female (n=140		P value	Statistical test
		Mean	SD	Mean	SD		
1	Fasting blood sugar (mg/dl)	99.8	12.86	99.1	15.4	0.758 (NS)	Unpaired 't' test
2	Total Cholesterol (mg/dl)	192.3	31.54	193.3	36.8	0.83 (NS)	Unpaired 't' test
3	Fasting triglycerides	185.4	42.6	186.7	54.07	0.854 (NS)	Mann Whitney U test
4	HDL CHolesterol (mg/dl)	44.3	8.38	45.5	7.39	0.29 (NS)	Unpaired 't' test
5	LDL cholesterol (mg/dl)	108.4	28.5	165.1	31.3	0.32 (NS)	Mann Whitney U test

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6	Fasting insulin (IU/ml)	7.17	2.59	7.93	2.86	0.053 (NS)	Unpaired 't' test

CORRELATION OF HOMA INDEX WITH THE CLINICAL PARAMETERS OF THE PATIENTS IN THE STUDY

S. No	Parameter	Overall (n=220)			Male (n=80)			Female (n=140)		
		R value	95% CI	P Value	r value	95% CI	P Value	r value	95% CI	P value
1	Age	0.14	0.009 to 0.26	0.03*	0.17	-0.04 to 0.38	0.11 (NS)	0.13	-0.03 to 0.29	0.11 (NS)
2	BMI	0.16	0.03 to 0.29	0.01*	0.08	-0.13 to 0.29	0.44 (NS)	0.21	0.05 to 0.36	0.01*
3	Waist Hip ratio	0.02	-0.1 to 0.16	0.67 (NS)	0.001	-0.2 to 0.22	0.99 (NS)	0.2	0.04 to 0.36	0.01*
4	Skin fold thickness	0.29	0.17 to 0.41	<0.0001*	0.54	0.36 to 0.68	<0.0001*	0.2	0.04 to 0.36	0.01*
5	Systolic Blood Pressure	0.02	-0.1 to 0.15	0.766 (NS)	0.04	-0.17 to 0.26	0.67 (NS)	0.04	-0.125 to 0.2	0.62 (NS)
6	Diastolic Blood Pressure	0.02	-0.1 to 0.16	0.66 (NS)	0.17	-0.05 to 0.37	0.12 (NS)	-0.03	-0.19 to 0.13	0.69 (NS)

Pearson correlation was used to test the correlation between the variables. * indicates $p<0.05$ and considered statistically significant for the reliability of r value.

CORRELATION OF TyG WITH CLINICAL PARAMETERS OF THE PATIENTS IN THE STUDY

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S. No	Parameter	Overall (n=220)			Male (n=80)			Female (n=140)		
		r value	95% CI	P value	r value	95% CI	P Value	r value	95% CI	P value
1	Age	0.13	0.001 to 0.26	0.04*	0.09	-0.12 to 0.31	0.39 (NS)	0.16	-0.002 to 0.32	0.053 (NS)
2	BMI	0.06	-0.06 to 0.19	0.329 (NS)	-0.06	-0.22 to 0.21	0.95 (NS)	0.1	-0.06 to 0.26	0.22 (NS)
3	Waist Hip ratio	0.1	-0.03 to 0.23	0.132 (NS)	0.02	-0.2 to 0.23	0.85 (ns)	0.26	0.1 to 0.41	0.0013*
4	Skin fold thickness	-0.06	-0.19 to 0.07	0.35 (NS)	0.1	-0.12 to 3.14	0.37 (NS)	-0.1	-0.3 to -0.03	0.01*
5	Systolic Blood Pressure	0.14	0.003 to 0.26	0.03*	0.01	-0.2 to 0.23	0.88 (NS)	0.22	0.05 to 0.37	0.008*
6	Diastolic Blood Pressure	0.13	0.003 to 0.26	0.04*	0.12	-0.09 to 0.33	0.27 (NS)	0.15	-0.014 to 0.31	0.07 (NS)

Pearson correlation was used to test the correlation between the variables. * indicates $p<0.05$ and considered statistically significant for the reliability of r value.

CORRELATION OF TyG INDEX WITH BIOCHEMICAL PARAMETERS OF THE PATIENTS IN THE STUDY POPULATION

S. No	Parameter	Overall (n=220)			Male (n=80)			Female (n=140)		
		r value	95% CI	P value	r value	95% CI	P Value	r value	95% CI	P Value

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1	Fasting blood sugar (mg/dl)	0.33	0.2 to 0.44	<0.0001*	0.21	-0.002 to 0.41	0.052 (NS)	0.38	0.23 to 0.52	<0.0001*
2	Total Cholesterol (mg/dl)	0.2	0.07 to 0.33	0.0019*	0.17	-0.04 to 0.38	0.11 (NS)	0.22	0.06 to 0.37	0.007*
3	Fasting triglycerides	0.67	0.59 to 0.74	<0.0001*	0.54	0.36 to 0.68	<0.0001*	0.74	0.65 to 0.81	<0.0001*
4	HDL CHolesterol (mg/dl)	-0.05	-0.18 to 0.007	0.39 (NS)	-0.1	-0.31 to 0.11	0.36 (NS)	-0.03	-0.19 to 0.13	0.683 (NS)
5	LDL cholesterol (mg/dl)	0.03	-0.1 to 0.16	0.63 (NS)	0.18	-0.03 to 0.38	0.1 (NS)	-0.04	-0.2 to 0.12	0.62 (NS)
6	Fasting insulin (uIU/ml)	0.01	-0.11 to 0.14	0.82 (NS)	0.04	-0.17 to 0.26	0.69 (NS)	-0.01	-0.17 to 0.15	0.9 (NS)

Pearson correlation was used to test the correlation between the variables. * indicates $p<0.05$ and considered statistically significant for the reliability of r value.

CORRELATION BETWEEN HOMA INDEX & TyG INDEX IN THE STUDY POPULATION

		Correlation between HOMA index and TyG index

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S. No	Condition	r value	95% CI	P Value
1	Overall	0..14	0.01 to 0.27	0.03*
2	Male gender	0.11	-0.1 to 0.32	0.29 (NS)
3	Female gender	0.06	-0.01 to 0.31	0.06 (NS)

Pearson correlation was used to test the correlation between the variables. * indicates $p<0.05$ and considered statistically significant for the reliability of r value.

CORRELATION OF HOMA INDEX & TyG INDEX – R VALUE

The prevalence of Metabolic syndrome according to JIS definition was 25% in males (95% CI 16.8% - 35.5%) and 47% in females (95% CI 39.06% -55.3%). The prevalence of Insulin resistance (HOMA-IR) was 7.5% in males (95%CI 3.5% - 15.4%) and 8.6% in females (95% CI 5.0% - 14.3%) .

The baseline characteristics of the study subjects are described in.The Mean Weight, Height, Waist circumference, Waist-Hip ratio, Skinfold thickness were significantly higher among men when compared with women whereas the skinfold thickness was significantly higher among women than men.
There was no significant difference in fasting blood sugar, triglycerides, HDL, LDL, total cholesterol, HOMA index and triglyceride index by gender.
There was no significant correlation between HOMA index and any of the clinical parameters studied.

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HDL cholesterol was negatively correlated with HOMA index in both gender and was statistically significant.

DISCUSSION:

In this study, we tested the prevalence of Insulin resistance and Metabolic syndrome in Normal Weight Individuals according to BMI.he prevalence of Insulin Resistance according to HOMA-IR was 8.18% (overall) in which 7.5% in male and 8.57% in female in comparison with previous prospective study resulted with 2.0% in male and 2.6% in female.[17]
The prevalence of Metabolic syndrome according to JIS Definition was 39.1% (overall) in which 25% in male and 47.1% in female in comparison with previous prospective study resulted with 3.1% in male and 0.9% in female.[17]

Our data suggest that accounting only BMI to identify subjects who are at risk of metabolic syndrome in their later life may fail to identify important fraction of population who despite having normal BMI.
It seems that together with epidemic of high BMI obesity, there is normal BMI obesity epidemic is also evident in developing countries like India.
Our study showed that metabolic syndrome and insulin resistance were found to be higher in women than men with normal weight by BMI.
A recent study carried out in U.S. showed fourfold increase in prevalence of metabolic syndrome among NWO subjects. Our study has some different characteristics compared to that U.S. study.[13] We used the JIS definition[14] because it reflects the new emergent consensus to define, instead of NCEP-ATPIII.

In 2006, De Lorenzo et al[9] described the association between normal weight and high fat content with metabolic abnormalities. Our study also found similar results in normal weight individuals.
Marques Vidal et al in 2008[15] found association between NWO and CV risk factors. They demonstrated women with NWO had high blood pressure, lipids and blood sugar levels.A cohort study conducted in Brazil proved that NWO was associated with metabolic syndrome and insulin resistance.[16] This study also showed significant association between NWO and high WC, low HDL and high triglyceride level. Our study showed similar association between HOMA index and HDL cholesterol in normal weight individuals.

Our study didn't show any significant association between HOMA index and any of the clinical and biochemical parameters except HDL cholesterol.
In our study, Insulin resistance was found to be more around the age group of 43years in men whereas 38years in women.There is a statistical significance (P0.0004) of skinfold thickness which is found to be higher in women (29.3mm) compared with men (21.7).
Also Fasting blood sugar value is found to be statistically significant (P0.008) higher in men (121 mg/dl) compared with women (109 mg/dl).

A Singapore based study conducted by Kavita Venkatraman et al[11] proved fasting triglycerides and waist-hip ratio combined with fasting insulin level can be used to predict insulin resistance and CVD risk more than HOMA-IR .But our study didn't show any association between triglyceride index and HOMA index.

CONCLUSION:

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In conclusion, our study provides evidence for prevalence of Insulin resistance and Metabolic syndrome in normal weight individuals. There was no evidence for using triglyceride index to identify metabolically risky group among normal weight population.

Considering these observation, it has been proved that having a normal BMI doesn't mean no risk for metabolic disorders and consequently for CVD. This situation reveals the need for change in routine screening of obese individuals defined by BMI alone and requires the incorporation of other clinical and biochemical parameters. There is a need for comprehensive studies addressing the complex interaction between fat content/distribution/activity, muscle mass and their effect on metabolism, CVD risk and survival.

LIMITATIONS OF THE STUDY

As this is a cross-sectional study the future outcome of the study population could not be explained. In future this can be done as a prospective study for identification of development of metabolic disorders and CVD risk.

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