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PREVALENCE OF METABOLIC SYNDROME AND INSULIN RESISTANCE IN NORMAL AND ABNORMAL GLUCOSE TOLERANT SUBJECTS IN SOUTH INDIA.

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Background: Type 2 diabetes prevalence is increasing world wide, due to underline insulin resistance leading to metabolic syndrome. Subjects with abnormal glucose metabolism are at increased risk for Coronary artery disease. Thus the diagnosis of insulin resistance is useful to prevent the increasing complication of diabetes.

Aims & Objectives: The present study was done in subjects with normal and abnormal glucose metabolism to find out the prevalence of metabolic syndrome and insulin resistance.

Methodology: By oral glucose tolerance test (OGTT), 136 subjects were divided into normal glucose tolerance (NGT) , Impaired glucose tolerant (IGT) and diabetes mellitus (DM). Fasting glucose, total cholesterol, triglycerides, HDL – c, insulin, hsCRP were measured in all the groups. HOMA IR was calculated and based on IDF(International Diabetic Federation) Criteria each group is divided into with MS and with out MS.

Results: All the parameters were compared between the groups. p value <0.05 considered as significant. Prevalence of metabolic syndrome in NGT was 26%, in IGT 43% and 86% among those with DM. The prevalence of insulin resistance was more in MS group compared to subjects without MS (NGT: 40% Vs 13.15%, DM 52% Vs50%).

Conclusion: Metabolic Syndrome is one of the earliest detectable risk factors with increased insulin resistance.Thus diagnosing the subjects with metabolic syndrome can reduce the increasing prevalence of diabetes & helps in preventing the complication of type 2 diabetes.

Keywords: Glucose tolerance, insulin resistance, Metabolic syndrome, Oral glucose tolerance test

INTRODUCTION

Prevalence of type 2 diabetes is rapidly increasing world wide, primarily due to global increase in obesity & sedentary life style. Subjects with abnormal glucose metabolism are at increased risk for coronary artery disease(CAD) and they often exhibit various cardiovascular disease risk factors, like hyper triglyceredemia, dyslipidimia, hypertension, obesity etc. The clustering of these risk factors has been called as metabolic syndrome(MS) and this MS is closely associated with type 2 diabetes mellitus (DM) & impaired glucose tolerance (Pirjo Ilanne et al).Many newly diagnosed subjects already suffer from so called late complications. Thus type 2 diabetes is 'a tip of ice berg' of long existing metabolic abnormalities (Ele Ferranini et al, GT Ko et al). Insulin resistance is the disturbance underlying a cluster of abnormalities designated as MS and there is abundant evidence that insulin resistance (IR) is a precursor of type 2 diabetes (DM) and cardiovascular disease(CVD)as well. IR can be measured based on fasting insulin & fasting glucose by HOMAIR (Lyn Steffen et al, Steven E .Stern et al , H Yeni- Komshian et al). The main idea of the study is to assess the prevalence of MS in normal and abnormal glucose tolerant subjects and to know the association of Insulin resistance with metabolic syndrome. The diagnosis of IR and MS which are pre diabetic conditions, will be useful to prevent the further increase in prevalence of diabetes

MATERIALS & METHODS

The study included the subjects referred to central research laboratory for the Oral Glucose Tolerance Test(OGTT). 137 subjects of age group 25-60 yrs were included in the study. Among 137 subjects , 73 were normal glucose tolerant (NGT), 35 were impaired glucose tolerant (IGT) and 29 were type diabetes (DM). Both males & females were included in the study. Each group was classified as with metabolic syndrome ,without metabolic syndrome based on International Diabetes Federation criteria (IDF).

The data on family history, personal history of diabetes, smoking habits, alcohol consumption , hypertension and treatment history for any other disease were collected by a questionnaire. Anthropometric measures like waist circumference, height &weight were measured.

Blood samples were collected after 12 hrs of fasting for estimation of glucose lipid profile, Apo A_1, hsCRP and insulin .Blood glucose & lipid profile(Total cholesterol (TC), triglycerides (TGL) , HDL) were measured in kone-lab 60 automated systems using commercial kits. Apo A_1 & hs CRP were measured by immuno nephelometric method.Serum insulin was estimated by automated chemiluminescence method.

RESULTS

Data evaluation was done using SPSS programme. The results were expressed as mean (Standard Deviation (SD)). The p value was used to compare the different groups. p value <0.05 was considered significant.

The mean and standard deviation of both biological & biochemical parameters of the 3 groups were calculated. There is age difference between the groups. The mean age of DM is 50.9 (8,18) yrs. & NGT 44.9(10.9). DM group had higher waist circumference, BMI, systolic & diastolic blood pressure compared with IGT and NGT.Figure 1 and 2 representing the mean and standard deviation of the biological and biochemical parameters of the all 3 groups.

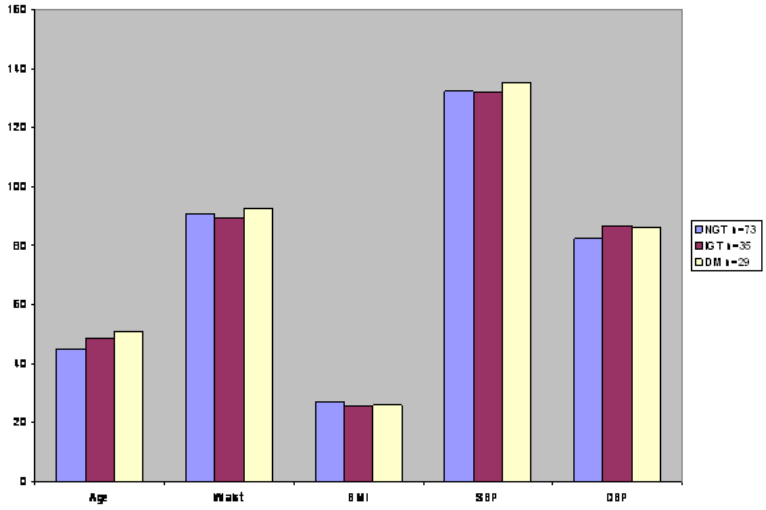

Figure 1: Biological parameters in NGT, IGT &DM

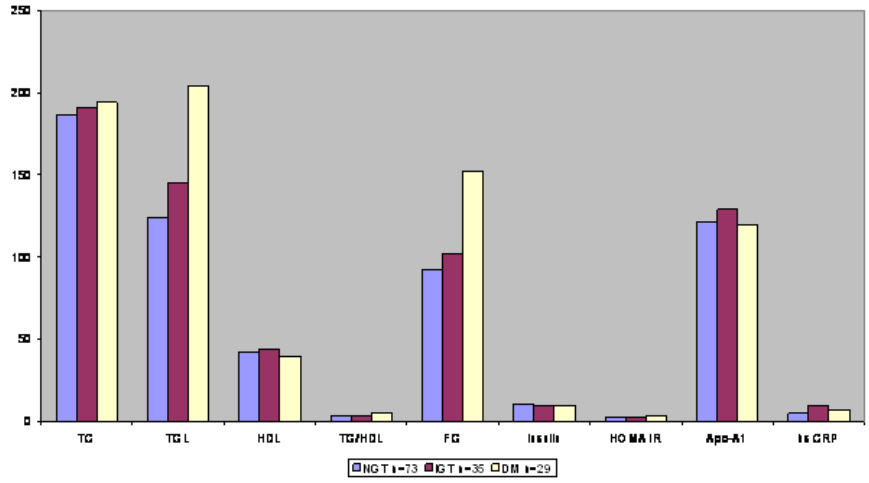

Figure 2: Biochemical parameters in NGT, IGT & DM

Table 1: Showing the mean (SD) of parameters in NGT subjects with MS had higher BMI, WC & SB than in non MS group P value is significant for WC(P.0.000), BMI(0.020) & systolic BP(0.002).Among biochemical parameters in NGT with MS & with out MS, The p value is significant for TGL, (0.001). TG/HDL (0.000), Insulin (0.022), HOMAIR(0.017), and APOA_1 (0.033).

Table 1: Biological and biochemical parameters in NGT

Sub group	MS n=35	Non MS n=38	p value
Age (yrs)	45(9.7)	44.7(12.4)	0.197
Waist (cm)	95.4(8.2)	86.15(12)	0.000***
BMI kg/ m^2	28.2(4.5)	25.8(3.6)	0.020*
SBP mm Hg	136.2(8.07)	128.6(11.6)	0.002*
DBP mm Hg	83.797.30	81.05(5.5)	0.87
TC mg/dl	189(50)	183.5(44.4)	0.587
TGL mg/dl	144.5(51)	104.6(40)	0.001**
HDL mg/dl	39.3(9.3)	45.15(13.1)	0.031*
TG/HDL	3.72(1.2)	2.4(1.0)	0.000***
FG mg/dl	93.17(12.5)	91.7(9.1)	0.574
Insulin mu/ L	12.6(7.3)	8.7(6.9)	0.022*
HOMA	2.93(1.7)	1.97(1.5)	0.017*
Apo A1	113.5(27.6)	128.3(30.3)	0.033*
hs CRP mg/l	6.1(12.7)	4.14(7.4)	0.431

p value < 0.05 significant , n= number of subjects

Table 2 : Showing the biological & biochemical parameters in IGT with MS & with out MS. Table 3: Showing the parameters in MS and without MS in DM. Figure 3 represents the HOMAIR in NGT ,IGT and DM.

Table 2: Biological and biochemical parameters in IGT

Sub group	MS n=19	Non MS n=16	p value
Age (yrs)	48.15(7.5)	49.3(9.8)	0.690
Waist cm	94.05(7.9)	83.62(26)	0.141
BMI kg/m^2	26.9(3.7)	23.6(3.05)	0.007*
SBP mm Hg	135.2(8.4)	128.7(12.5)	0.090
DBP mm Hg	89.4(7.05)	83.75(7.1)	0.024*
TC mg/dl	192.2(44.2)	188.9(36)	0.812
TGL mg/dl	169.3(111)	116.4(45.8)	0.071
HDL mg/dl	40.42(10.6)	48.8(9.5)	0.018*
TG/HDL	3.86(2.1)	2.88((1.3)	0.006*
FG mg/dl	103.8(12.5)	100.12(11.4)	0.371
Insulin mu/l	9.4(5.8)	9.5(6.3)	0.967
HOMA IR	2.38(1.4)	2.37(1.6)	0.990
Apo A1 mg/dl	123.16(25.6)	135.7(27.8)	0.178
hs CRP mg/l	7.07(11.4)	13.4(23.8)	0.340

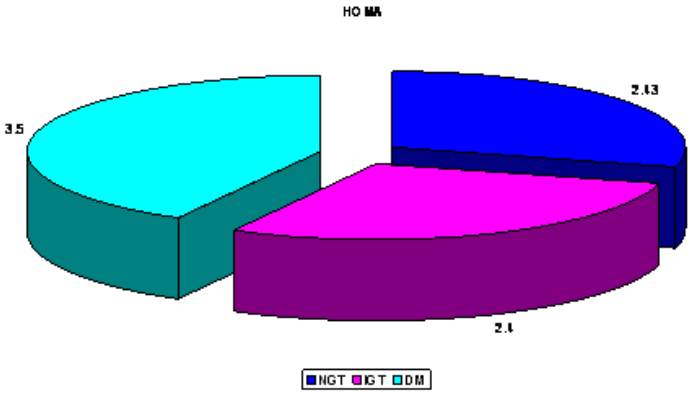

Figure 3 : HOMAIR in NGT ,IGT and DM

Table 3: Biological and biochemical parameters in DM

Sub group	MS n=25	Non Ms n=4	p value
Age (yrs)	52.4(6.1)	41.5(13.6)	0.205
Waist cm	93.6(11.1)	85.7(3.09)	0.009*
BMI mm Hg	26.3(4.5)	23.9(1.5)	0.072
SBP mm Hg	137.2(11.7)	123.7(11)	0.087
DBP mm Hg	86.8(5.5)	81.25(2.5)	0.009*
TC mg/dl	195.2(51)	187.2(47.8)	0.775
TGL mg/dl	159(64.8)	486(76.02)	0.453
HDL mg/dl	39.8(8.5)	38.7(6.8)	0.779
TG/HDL	4.56(3.2)	3.96(2.5)	0.073
FG mg/dl	146.8(38.7)	187.7(168)	0.662
Insulin mu/l	9.9(5.2)	9.4(6.6)	0.898
HOMA IR	3.6(2.0)	3.2(1.5)	0.636
Apo A1mg/dl	121.4(25.5)	109.5(19.2)	0.326
Hs CRP mg/l	6.2(6.8)	14.4(15)	0.350

DISCUSSION

Metabolic syndrome is common phenotype increasing the risk for type 2 diabetes and cardiovascular disease (DeFronzo et al , Richard Kahn et al). Among Framingham off spring white subjects the age and sex adjusted prevalence of MS was 24%. Subjects with MS had higher level of predicted CVD risk after adjusting for age, sex & ethnicity. In our study also we observed higher levels of insulin, HOMAIR, lipid profile, blood pressure & anthropometric measurements in MS than in those with out MS (Anthoni J.G et al , James B. Meigs et al).

Subjects with MS are more insulin resistant and are at increased risk for CVD than those without MS. NHANES III(national health and nutrition examination survey III) showed the prevalence of MS as 26% among persons with NGT, 33% among IGT & 86% among those with DM (Charles M. Alexander et al , Francisco J. Novoa et al). The prevalence rates in our study for NGT 47% & for IGT 45.7% and for DM it is 86.2% which is clearly explaining the increase prevalence of MS in diabetes subjects. And it also clear that the prevalence is little high in NGT group compared to NHANES III. It is mainly due to ethnicity.

The typical phenotype observed in Asian Indians consists of higher percentage of body fat at a lower value of BMI, high waist hip ratio at a relatively low waist circumference . This is due to less lean body mass as compared to Caucasians, & other Asian ethnic groups (Scott M. Grundy , Steven Haffner et al , GA Bay).

Pouliot et al emphasized the importance of visceral obesity as a possible cause of MS. The prevalence of MS increases as the degree of obesity increases. The best way to measure obesity is to measure waist circumference. The advantage of measuring WC is that an excess abdominal fat is correlated more closely with the presence of metabolic risk factors that the total body fat (14,15).

In this study which is done on Asian Indians, there is a good positive correlation between WC and MS in NGT, IGT and DM. There is a significant difference in waist circumference between subjects with MS & with out MS.

According to Copenhagen study, Telde study , MS group has higher systolic & diastolic blood pressure values than non MS group.Consistent with their findings in NGT, MS subgroup has higher mean systolic blood pressure of 136.2(8.07) than in non MS sub group with p value of 0.002. Similarly in IGT & DM mean systolic & diastolic blood pressure were high in MS than Non MS sub group (Robert J. Huggett et al ,) . Metabolic Syndrome is a state of sympathetic nerve hyperactivity and the additional presence of hyper tension further intensifies this hyperactivity contributing to high CVD risk & metabolic abnormalities.

Recently IRAS showed a link between a direct measure of IR itself and atherosclerosis. Insulin resistance at the level of adipose tissue is the initiating event for dyslipidemia in MS. Due to IR, Free fatty acids(FFA) are released from adipose tissue . Thus there will be increased availability of FFA to liver ,this leads to increased triglyceride (TGL) synthesis & overproduction of VLDL. CETP mediates the exchange of TG-CE between LDL, VLDL and HDL forming TG rich HDL. These TG rich HDL are prone to be catabolised leading to low HDL levels in MS(Scott .M Grundy , Cecil M. Burchfiel et al)

IR may cause destabilization of ABCA1. Hence in the absence of sufficient cholesterol efflux apo A1 is rapidly cleared from the circulation by the kidneys. HONOLOLU heart programme found that the risk of CAD was increased in subjects with low HDL-C, high TGL, high TG/HDL ratio. TG/HDL ratio positively correlates with IR. In this study an increase in the mean of lipid parameters & decrease in ApoA1 values were observed in DM & IGT compared to NGT . MS sub group which is considered to be high risk of development of CAD had higher lipid profile (TG, TG/HDL, HDL-c) values & decreased apo A1 values than in subjects with out MS sub group in all the NGT, IGT & DM groups(Attila Brehm et al , Karen L. Cheal et al).

IR is presumed to be the baseline defect leading to MS. In RIAD(Rsk factor in Impaired Glucose Tolerance for Atherosclerosis study), IR calculated by HOMA was significantly increased in IGT & DM compared to NGT.According to

SHS (Strong Heart Study) as tertiles of HOMA IR increase ,the percentage of MS prevalence was also increased (Helaine E.Resnick et al) . A population based study by Ramachandra et al showed that IR as assessed by HOMAIR was higher in MS than in subjects without MS. In our study, we observed the same.We also found that prevalence of IR, taking 75th percentile of HOMA as cut off (>3) was more in MS than in non MS group of NGT ,IGT & DM groups. NGT (40%, Vs 13.15%), in DM (52% Vs 50%) IGT (16%Vs 31.25%).

Elevated levels of hsCRP an inflammatory marker is founding type 2 diabetes patients and in IRS. NHANES III showed that subjects with MS were more likely to have elevated levels of hs CRP than individuals without syndrome. . In our study IGT, & DM had higher mean levels of hs CRP than NGT. In MS sub group the mean hs CRP levels were elevated in NGT. But in the sub group of IGT & DM the relation is not observed due to less sample size. Thus in type 2 DM & MS the inflammatory markers will be elevated due to release of cytokines IL-6 & TNF α .(Andreas Festa et al, Andreas Festa $_a$)

Thus from our study we conclude that abnormal glucose metabolism is associated with altered lipid profile & insulin resistance. In this study we found that the prevalence of MS & IR is high DM than in NGT. MS is one of the earliest detectable risk factor with increased Insulin resistance. Thus diagnosing the subjects with metabolic syndrome can reduce the increasing prevalence of diabetes & helps in preventing the complications of type 2 diabetes.

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