CIUSTERING OF CARDIOVASCULAR RISK FACTORS IN IMPAIRED FASTING GLUCOSE AND IMPAIRED GLUCOSE TOLERANCE

C. Snehalatha, A. Ramachandran, K. Satyavani, S. Sivasankari, V. Vijay.

ABSTRACT

The study was done to look for clustering of cardiovascular risk factors in impaired fasting glucose (IFG) and impaired glucose tolerance (IGT). Cardiovascular risk factors such as insulin resistance (HOMA-IR), obesity (BMI $\geq$ 23 kg/m^2), upper body adiposity ($\uparrow$ WHR), dyslipidemia ($\uparrow$chol, $\uparrow$ TG and / or $\downarrow$ HDL chol) and hypertension were determined using standard procedures in normal glucose tolerance (NGT) (n = 129). IFG (n = 65), and IGT (n = 68). Clustering was considered as the presence of $\geq$ 2 abnormalities. Statistical analyses were done using chi-square test and multiple logistic regression analysis.

Increased prevalence of the clusters was observed in IFG (76.9%), IGT (80.9%) than in NGT (58.1%). In the multiple logistic regression analysis the clustering of the cardiovascular risk factors was found to be associated with IFG and IGT, independent of the presence of family history of diabetes. In conclusion both the dysglycemic conditions, IFG and IGT were associated with cardiovascular risk factors and seem to carry high risk for future diabetes and CVD.

KEY WORDS: Impaired fasting glucose; Impaired glucose tolerance; Clustering of cardiovascular risk factors; Asian Indians.

INTRODUCTION

The American Diabetes Association (ADA) [1] and the World Health Organization (WHO) [2] have clearly defined two separate categories of glucose intolerance namely impaired fasting glucose (IFG) and impaired glucose tolerance (IGT). As IFG is related to impaired fasting and IGT is related to post-load glucose responses, these categories may be distinct in their pathophysiological features. These subclinical stages have been shown to be predictive of future diabetes and clustering of cardiovascular risk factors could also occur in these categories. This analysis was done to see the clustering of cardiovascular risk factors in IFG and IGT subjects. Subjects with normal glucose tolerance (NGT) were used as controls.

MATERIAL AND METHODS

Three hundred and twenty six asymptomatic subjects without known history of diabetes who underwent an oral glucose tolerance test with 75 gm glucose load, at Diabetes Research Centre, Chennai were selected for the study. Glucose tolerance status was classified based on the WHO criteria [2].

Subjects with NGT (Fasting Plasma Glucose (FPG) < 110 mg/dl and 2h < 140 mg/dl) were used as the control group. A total of 262 subjects (M:F; 141:121) who were classified as having NGT, IFG (FPG $\geq$ 110 - < 126mg/dl and 2h <140 mg/dl) and IGT (FPG < 126mg/dl and 2h $\geq$ 140 - < 200 mg/dl) were selected for this study. Newly diagnosed diabetic subjects (n=37) (FPG $\geq$ 126 mg/dl and / or 2h $\geq$ 200 mg/dl) and those subjects having a combination of IFG + IGT (n=27) (FPG $\geq$ 110 - < 126 mg/dl and 2h $\geq$ 140 - < 200 mg/dl) were excluded from the study.

Age, height, weight, waist, hip and family history of diabetes were recorded. Body mass index (BMI) (kg/m^2) and waist to hip ratio (WHR) were calculated. Informed consent was obtained from all the study subjects. Fasting and 2h plasma samples were collected for estimation of plasma glucose. The fasting serum sample was used for estimation of lipids. Plasma glucose was estimated by glucose oxidase-peroxidase method (Boehringer – Mannheim, Germany) and total cholesterol (T-chol), high-density lipoprotein cholesterol (HDL-chol) (direct assay). Triglycerides (TG) were estimated by enzymatic procedures. Clinical, anthropometric and biochemical evaluations were done by standard procedures [3].

Diabetes Research Centre & M. V. Hospital for Diabetes, 4 Main Road, Royapuram, Chennai, India.

The normal cut off values for BMI and WHR were derived from a population based study by computing their risk associations with diabetes. The cut off value for normal BMI for men and women was 23kg/m^2. The cut off values for normal WHR were 0.88 for men and 0.80 for women. The normal cut off values for (T-chol 209 mg/dl, TG 165 mg/dl and HDL- chol men 35 mg/dl, women 40 mg/dl) were obtained from 700 normoglycemic, non-hypertensive subjects using mean ± one SD. The presence of one or more abnormal lipid parameters was termed as dyslipidemia.

Hypertension was defined as the presence of systolic blood pressure (SBP) of 140 mmHg or more and / or diastolic blood pressure (DBP) of 90 mmHg or more or if any person was being treated with anti-hypertensive drugs.

Insulin resistance (HOMA-IR) in the fourth quartile was considered abnormal. The cut off value for IR was ≥ 5.2.

Statistical Analysis: Mean ± SD are reported. Group means were compared by analysis of variance or't' test. The difference in proportions was compared by Chi-square test. Multiple logistic regression analysis was done using clustering of abnormalities as the dependent variable with family history of diabetes and IFG, IGT vs. NGT as independent variables. Presence of ≥ 2 abnormalities indicated clustering of the risk factors. Statistical analysis was done using SPSS PC package version 4.0.1.

RESULTS

NGT was present in 129, IFG in 65 and IGT in 68 study subjects. Table 1 shows the anthropometric and biochemical characteristics of the study groups. Subjects with IFG and IGT were older than NGT subjects ($p < 0.05$). BMI of men with IFG was significantly higher than NGT ($p < 0.05$). Serum cholesterol and triglycerides levels were significantly higher in IGT than in NGT.

Table 1: Anthropometrical and Biochemical Characteristics of the Study Groups[#]

Variables	NGT n=129	IFG n=65	IGT n=68
Age (yrs)	39.1±11.1	44.6±10.9*	45.9±10.6*
BMI (kg/m^2)			
Men	23.7±4.0	25.9±4.3*	24.1±3.2
Women	25.2±3.6	27.0±5.8	25.4±4.5
WHR			
Men	0.89±0.07	0.92±0.06	0.92±0.06
Women	0.86±0.07	0.88±0.06	0.85±0.06
Plasma glucose (mg/dl)			
Fasting	98.0±7.6	116.3±4.4*	95.0±10.8*, **
2h	106± 17.3	112.0±18.1*	158.0±12.9*, **
Lipid profile (mg/dl)			
T-chol	184 ±33.5	196±34.6	212±30.2*, **
TG	135±78.2	141 ± 66.3	171±112*
HDL-chol			
Men	41.0±8.8	40.5±7.7	41.7±10.0
Women	46.6±9.4	46.8± 9.6	47.0±11.1

*$p < 0.05$; * vs NGT, ** vs IFG; NGT – Normal glucose tolerance; IFG – Impaired fasting glucose; IGT – Impaired glucose tolerance;[#]Values are mean ± SD*

Table 2 shows the prevalence of risk variables in categories of glucose tolerance. Prevalence of insulin resistance was significantly higher in IFG and in IGT than NGT. Subjects with IGT had significantly higher prevalence of dyslipidemia than NGT and IFG. Prevalence of hypertension was significantly higher in IGT subjects.

Table 2: Prevalence of Risk Variables in Categories of Glucose Tolerance

Variables	NGT n=129	IFG n=65	IGT n=68
↑BMI	81 (63.3)	47 (72.3)	42 (61.8)
↑WHR	77 (63.6)	48 (82.8)	48 (71.6)
↑HOMA-IR	34 (26.6)	32 (49.2)*	29 (42.6) **
Dyslipidemia	70 (54.3)	37 (56.9)	55 (80.9)*, #
Hypertension	18 (13.9)	14 (21.5)	21(30.9)*

**p < 0.008 vs. NGT, ** p < 0.03 vs. NGT; # p = 0.005 vs. IFG by chi-square test; Values are n (%).*

Subjects with IFG (76.9% vs. 58.1%, p = 0.02) and IGT (80.9% vs. 58.1%, p = 0.002) had a significantly higher prevalence of clustering of risk variables than the NGT subjects (58.1%). Prevalence of clustering of risk variables between IFG and IGT were similar.

Results of multiple logistic regression analysis showed that IFG and IGT were significantly associated with risk of having a combination of two or more abnormalities, independent of the effect of the family history (Table 3).

Table 3: Results of Multiple Logistic Regression Analysis

Dependent variable – clustering of risk factors.
Independent variables – IFG, IGT

Variables	β	SE	OR	p value
FH-DM	0.606	0.29	1.83	0.03
IFG	0.74	0.35	2.1	0.03
IGT	1.11	0.36	3.03	0.002

FH-DM- Family history of diabetes.

DISCUSSION

In Asian Indian population, prevalence of IFG was similar to that of IGT (4). The results of this study showed that IFG and IGT were equally associated with several cardiovascular risk factors. Clustering of the risk factors occurred more frequently in IFG and IGT than in NGT. The association of cardiovascular events with either fasting or post load hyperglycemia had been demonstrated in a number of studies (5-9). The Hoorn study had shown that the cumulative incidence of diabetes was strongly related to IFG and IGT at baseline and to the combined presence of IFG and IGT (10). The Funagata Diabetes Study from Japan had shown that while IGT had two risks i.e. development of diabetes and CVD, IFG category posed only a risk of developing diabetes (11). The sensitivity of IFG as predictor of subsequent development of diabetes was shown to be less than that of IGT (12). Long-term prospective studies are required to determine its predictive nature, both for diabetes and its complications (10).

The study results imply that the cardiovascular risk factors being equally high in IGT and IFG, the risk of future CVD could be high and similar in both the categories. Both categories of glucose intolerance seem to carry risks for future diabetes and CVD.

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