

Correlation Among BMI, Fasting Plasma Glucose and HbA1c Levels in Subjects with Glycemic Anomalies Visiting Diabetic Clinics of Lahore

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Abstract.- This study was aimed at determining correlations among body mass index (BMI), fasting plasma glucose (FPG) and HbA1c levels in glycemic anomalies in local population. A total number of 508 subjects (males 228, females 280) of age between 27–87 years with glycemic anomalies visiting Amin Memorial Trust Hospital (diabetic clinic) of Lahore were included in the study. Of the people identified with diabetes type 2 and impaired glucose tolerance (IGT) 58% were not previously diagnosed. The subjects were divided into two different categories on the basis of fasting plasma glucose level and oral glucose tolerance test (OGTT), viz., 130 IGT subjects and 378 Diabetes mellitus type 2 subjects using Diabetes Expert Committee criteria of 2003. The OGTT diagnosed IGT subjects constituted were 65% and OGTT diagnosed diabetic subjects were 30%. In IGT subjects 22.3% subjects had normal HbA1c (5-6%), while 55% subjects had elevated HbA1c (6-8%) and 22.6% subjects had poor glycemic control with HbA1c > 8%. In diabetic subjects 29.1% subjects had HbA1c 6-8%, 63.3% diabetic subjects had 8-10% hemoglobin, while 7.6% diabetic subjects had HbA1c 10-18%. In IGT subjects 10% had normal BMI, 30% were overweight and 60% were obese. Among diabetic subjects 14% had normal weight, while 16% were overweight and 70% subjects were obese. A positive and highly significant correlation was observed with HbA1c in IGT and diabetics ($r = 0.298$, $r = 0.460$). In multiple regression analysis HbA1c was important predictor of FPG both in IGT and diabetic.

Key words: Fasting plasma glucose, IGT, BMI, HbA1c, diabetics, OGTT.

INTRODUCTION

Type 2 diabetes is the predominant form of diabetes worldwide accounting for 90% of cases. An epidemic of type 2 diabetes is underway in both developed and developing countries. Life style modification as a result of urbanization leading to sedentary habits and nutritional changes has an important contribution. Demographic projections by WHO with reference to the prevalence data of Pakistan 1995, National Diabetes Survey estimate an increase in Type 2 diabetes in Pakistan from 4.3 million in 1995 to 14.5 million in 2025 making Pakistan the fourth country among the top 10 countries of the World (King *et al.*, 1998). In under-developed countries especially low income groups a large number of cases remain undetected. The overall prevalence of abnormal glucose tolerance in Pakistan was 20.5% in women and 15.9% in men.

A larger percentage of subjects both women and men belonged to age group 45-54 years (27%), while glucose intolerance was reported to be 22.04% in urban areas and 17.15% in rural area (Shera *et al.*, 2007).

Normal glucose homeostasis relies on a balance between insulin secretions and tissue sensitivity to insulin (Masharani, 2006). Tissue insensitivity to insulin has been noticed in most type 2 patients irrespective of the weight. Approximately 20-40 % of diabetic patients are non obese. Though these percentages vary according to the population studied *e.g.*, higher in Asian populations and lower in pacific islanders and Pima Indians of the American southwest and Mexico (Greenspan and Gardner, 2004).

Type-2 diabetes represents a heterogeneous group comprising milder form of diabetes that occurs predominantly in adults. Impaired glucose tolerance (IGT) is an intermediate category between normal glucose tolerance and diabetes. It is common with an incidence varying widely among population. IGT goes undiagnosed for many years since the

hyperglycemia develops gradually and is generally asymptomatic initially (Holt and Hanley, 2006; Zimmet *et al.*, 2001). Despite the mild glucose homeostasis it is well documented that these subjects are at increased risk of developing macrovascular and microvascular complications as compared to diabetics (Weigand *et al.*, 2005). IGT subjects have a greater risk of developing diabetes. Several recent studies have reported that early detection of hyperglycemia and intervention with life style changes can delay or even revert the onset of diabetes among the high-risk adults (Nathan *et al.*, 2007). Diabetic patients with IGT have been the subject of studies reporting the effectiveness of early intervention (Shimazaki *et al.*, 2007).

Glycosylated haemoglobin (HbA1c) is an indicator of sustained hyperglycemia for monitoring glycemic level. Glycated hemoglobin is abnormally high in diabetics with chronic hyperglycemia and reflects their metabolic control. It is produced by non-enzymatic condensation of glucose molecule with free amino groups on the globin component of hemoglobin. Higher the prevalent ambient levels of blood glucose, higher will be the levels of glycated hemoglobin (Masharani, 2006).

The aim of present study was to determine the correlation of fasting plasma glucose (FPG) with BMI and HbA1c in prediabetics and newly diagnosed type 2 subjects in population visiting a diabetic clinic in Lahore.

MATERIALS AND METHODS

A total of 508 subjects of either sex (male 228, female 280) visiting Amin Memorial Trust Hospital (diabetic clinic) of Lahore during the year 2006 were included in this study. On the study day, the subjects were in a fasting state without taking any medication. Their demographic data, medical history, family history of diabetes, and duration of the disease were recorded. Height and weight (measured to the nearest 0.1 kg) were measured with the subject wearing light clothing and without shoes. All subjects underwent 75g oral glucose tolerance test (OGTT) for diagnosis of diabetes and IGT under the expert supervision of hospital management. The subjects were categorized using

Diabetes Expert Committee criteria 2003. According to it, the FPG of 100–125 mg/dl was diagnostic of IGT and ≥ 126 mg/dl is diagnostic of diabetes if confirmed on a subsequent day and two hours after glucose load ≥ 200 mg/dl was diagnostic of diabetes and ≥ 140 –199 was diagnostic of IGT. OGTT diagnosed IGT subjects were 65% with FPG ranging 74–100 mg/dl.

The out come based on this criterion was that IGT subjects were 130 and diabetic were 378.

BMI was calculated according to Asian standards (Dhiman *et al.*, 2005) as the weight (Kg) divided by the square of the height (m^2). Plasma glucose was measured by a glucose oxidase method (Diagnostic Chemicals reagent kit, Hitachi, 902). HbA1c was measured by using Glycosal (HbA1c) kit. HbA1c was assessed on whole blood (Diasat Analyzer, Bio Rad, USA). It was based on low pressure cation exchange chromatography in conjunction with gradient elution to separate human hemoglobin subtype and variants from hemolyzed whole blood. The DiaSTAT software program was used for analysis of the chromatogram.

The study was approved by the ethical committee of hospital. A written consent was taken from hospital management. They provided all the facilities to carry on the study and cooperated throughout the period of study.

Statistical analysis

Statistical analysis was performed using the SPSS (version 13.0) software. All Results are expressed as Mean \pm SEM. FPG and HbA1c were cross-tabulated. Pearson correlation was used to find correlation and t-test was applied to find significance between the two groups. Stepwise multiple regression analysis was employed to study the joint effect of variables on the fasting plasma glucose levels.

RESULTS AND DISCUSSION

In this study a total number of 508 subjects (male 228, female 280) of age between 27–87 years with glycemic anomalies were included in the study. Two categories of subjects were targeted. The subjects were divided into IGT (n=130 and Diabetes

mellitus type 2 subjects (n=378). On the basis of fasting plasma glucose level and OGTT. OGTT diagnosed diabetics were 25% with FPG range of 100 mg/dl to 125 mg/dl and IGTs were 65% with FPG range of 74-100.

Demographic data

Demographic data of the study group is presented in Table I. Females were comparatively younger than males in diabetic group.

BMI of IGTs and diabetics was observed and both the groups fell in the category of over weight and obese. Their BMI showed non-significant difference ($P>0.05$) in IGT and diabetic group (Table I).

Biochemical analysis

The FPG in IGT group was 104.00 ± 1.96 mg/dl and in diabetic group was 184.14 ± 3.26 mg/dl showing a significant difference ($p<0.005$) between the groups. No significant gender difference was observed in IGT subjects, while a significant difference was observed in diabetics males and female ($P<0.05$) (Table I).

HbA1c is related to metabolic control of glucose in blood and it increases with increase in FPG and its value reflects the long-term glycemic control in the blood. The HbA1c of IGT group and the diabetic group showed the highly significant difference ($P<0.005$) (Table I).

In IGT group the fasting plasma glucose was inversely correlated with age and it was significant ($r = -0.310$, $p<0.05$) while negative and non-significant correlation was observed with BMI ($r = -0.091$, $p>0.05$). A positive and highly significant correlation was observed with HbA1c ($r = 0.298$, $p<0.005$).

In diabetic group the FPG was inversely correlated with age and it was highly significant ($r = -0.166$, $p<0.005$), while negative and non-significant correlation was observed with BMI ($r = -0.093$, $p>0.05$). A positive and highly significant correlation was observed with HbA1c ($r = 0.460$, $p<0.005$).

The data was further analyzed on the basis of age to find out the frequency of hyperglycemia in different age groups. The data revealed that the highest frequency of abnormal glycemia (both in

IGT and DM) was observed between age groups (41-60) years, while it was lowest between 27-40 years in the study population.

When FPG was cross-tabulated with HbA1c in IGT subjects, HbA1c percentage was normal (5.1-6.0%), with FPG in range of 110-120 mg/dl. When FPG was cross-tabulated with HbA1c in diabetic subjects poor glycemic control ($>6.5\%$) was observed among them. When stepwise multiple regression analysis was employed considering FPG as a dependent variable and age, BMI and HbA1c as independent variable HbA1c was important determinant in the model (adjusted $R^2 = 0.675$) both in IGT and diabetic (Table II).

Demographic data of the study population revealed that in diabetic and IGT groups, females were younger as compared to males. This finding is in line with other studies (Ahmadani *et al.*, 2008). Moreover, females had higher BMI as compared to the males. Habib and Aslam (2003) reported a higher prevalence of obesity among diabetic females as compared to males. When the data was analyzed on the basis of age, it revealed that highest frequency of abnormal glycemic control, both in IGT and DM was present in age group ranging 41-60 years and it was lowest in group ranging 27-40 years. Shera *et al.* (1999) reported that advanced age and obesity were associated with higher rates of diabetes. In our study, FPG was inversely related to the age in IGT and diabetic subjects. Obviously type-2 diabetes incidence increase with age but whether the aging process *per se* is contributory remains unclear (Degroot and Jameson, 2006). Contradictory reports from the previous studies have been observed, aging is associated with decrease in glucose tolerance, which appears to be due to a decline in both insulin sensitivity and insulin secretion (Chen *et al.*, 1985), however, age related factors such as reduced physical activity and increased fat accumulation are at least partly responsible for this phenomenon.

In our study we failed to find significant correlation of FPG with BMI. This is in discordance with findings of Fawwad *et al.* (2006) who observed strong association of obesity with insulin insensitivity in type 2 diabetic subjects. In other study, Bakari *et al.* (2007) reported a non-significant correlation between causal blood sugar and BMI

Table I.- General characteristics of studied population.

Variables	All (n = 508)	Female (n = 280)	Male (n = 228)	Female vs. Male (p value in t test)	Diabetic Subjects (n = 378)	IGT subjects (n = 130)	Diabetic vs. IGT (p value in t-test)
Age (years)	51.35±0.51	49.10±0.81	54.10±0.79	0.000**	51.15±0.57	51.93±1.02	0.505
BMI (Kg/M ²)	27.97±0.24	29.26±0.34	26.41±0.34	0.000**	27.91±0.27	28.20±0.53	0.621
FPG (mg/dl)	164.00±2.92	173.40±4.10	153.57±4.00	0.000**	184.14±3.26	104.38±1.96	0.000**
HbA1c (%)	8.90±0.09	8.92±0.13	8.89±0.15	0.824	9.50±0.10	7.12±0.17	0.000**
Smokers	90	5	85	0.00**	70	15	0.00**
Non-smokers	418	275	143	0.00**	308	115	0.00**
Physical activity							
Sedentary (n)	235	160	190	0.00**	180	55	0.00**
Moderate (n)	273	120	38	0.00**	198	75	0.00**
Disease status							
Newly diagnosed	330	185	175	-	245	83	0.00**
Previously diagnosed	178	95	120	-	133	47	0.00**
Family history of diabetes	390	217	199	-	300	75	0.00**
Family history of thyroid	20	-	3	-	12	NA	-
Socioeconomic Status							
Low	400	197	203	-	360	115	-
Mediocre	108	83	25	-	18	15	-

* = P<0.05; ** = P<0.01

Data expressed: Mean ± SEM

Table II.- Multiple regression analysis with fasting plasma glucose as dependent variable in IGT and diabetic subjects.

Model	Unstandardized coefficients		Standardized coefficients	t	P-value
	B	Std. Error	Beta		
IGT group (n=130)					
1 (Constant)	96.730	3.620		26.720	0.000
HbA1C	2.415	0.490	0.399	4.930	0.000
Diabetic group (n=378)					
1 (Constant)	58.732	12.694		4.627	0.000
HbA1C	12.348	1.322	0.434	9.338	0.000

among female subjects, while in the males the correlation between these variables was significant.

BMI alone has been shown to be prospective marker for development of type-2 diabetes (Rolandson *et al.*, 2001) but other studies show that obesity/hereditary background of diabetes will fail to detect majority of subjects with IGT (Colditz *et al.*, 1995; Lindahl *et al.*, 1999). This may be due to genetically predisposed diabetic subjects screened for study. Keeping in view ethnic background,

variations in environment and life style features may account for this disparity.

Glycemic control indicated by HbA1c was poor in both the genders of diabetic groups although no statistically significant difference was observed but HbA1c was higher in males as compared to females. There was a significant positive association between fasting plasma glucose and HbA1c in diabetic group, while the relationship was weak in IGT group. This finding is in line with Habib and

Aslam (2003). They reported poor glycemic control (HbA1c >7.5%) among diabetic subjects (46.7%).

Nakagami *et al.* (2007) reported that glycated hemoglobin is significantly correlated with 2 hours plasma glucose at OGTT but not with fasting plasma glucose in subjects without diabetes.

In our study OGTT diagnosed IGT were 65% with FPG (74-100), while OGTT diagnosed diabetic subjects were 30% (FPG, 100-140) indicating that FPG alone is not sufficiently sensitive for high-risk groups of previously undiagnosed subjects. In stepwise multiple regression analysis HbA1c maintained independent association with fasting plasma concentration both in IGT and diabetics. For early diagnosis of IGT subjects OGTT seems to be a better option.

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