TYPE 2 DIABETICS: RELATIONSHIP OF GLUCOSE AND INSULIN LEVELS IN THE ASYMPTOMATIC OFFSPRINGS OF PATIENTS WITH TYPE 2 DIABETES.

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ABSTRACT

OBJECTIVE: To measure and compare the glucose and Insulin levels of asymptomatic offspring of type 2 diabetic patients with asymptomatic offspring of non diabetics.

STUDY DESIGN: Case control study.

PLACE AND DURATION: Department of Pathology PGMI, Lahore and Diagnostic Laboratory of UVAS, Lahore, from 1st October 2009 to 30th June 2010.

METHODOLOGY: Non diabetic healthy offspring of diagnosed patients with type 2 diabetes mellitus attending the medical departments of LGH Lahore, both male and female below 30 years of age, documented by normal fasting blood glucose level and not having any symptom of diabetes were included.

RESULTS: In this study glucose and insulin were measured in 100 subjects. Glucose was measured by GOD PAP method and Insulin by ELISA technique. Mean ± SD of glucose in control group was 80.75±14.21and in study group was 80.92±13.38having non significant difference having P value 0.081. Mean±SD of insulin in control group was 16.80± 4.09 and in study group was 18.40±13.32 having non significant difference having P value 0.098.

CONCLUSION: Insulin and glucose concentrations were within normal limits, and were not having any significant direct or inverse relationship (p=0.076).

KEY WORDS: Glucose oxidase paraaminophenazone (GOD PAP), Enzyme linked immunosorbent assay (ELISA), Type 2 diabetes mellitus (T2DM), Insulin, Glucose.

INTRODUNTION

Type 2 diabetes mellitus (T2DM) is the most common form of hyperglycemia (High blood sugar level), comprising approximately 90% of all cases of diabetes[4,5]. Disease exists in all populations and recently the prevalence has risen. In the pre-diabetic state, Type 2 diabetes mellitus involves two defects: increased peripheral insulin resistance and hyper-insulinemia which is followed by the failure of insulin secretion[4]. T2DM is an extremely polygenic disease and no single cause is adequate to explain the progression from normal to impaired glucose tolerance to diabetes. The fundamental molecular defect in insulin resistance and insulin secretion result from combination of environmental and genetic factors[5].

Insulin is the major regulator of glucose metabolism, directly by suppressing endogenous glucose production (glycogenolysis; gluconeogenesis) and indirectly by suppressing glucagonsecretion and lipolysis. Insulin's role is to facilitate the movement of glucose from the bloodstream into the body's cells, where it is used for energy. In T2DM the body still produces insulin, but the body's cells become resistant to its effects[6]. Insulin acts on target tissue by binding to specific "insulin receptors" which are 'glycoproteins'. The human insulin receptor gene is found in chromosome 19[7]. Most patients acquire disease after the age of 40, but it may occur in younger people. T2DM in children and in adolescents is an emerging, significant problem. Among children in Japan, type 2 diabetes is now more common than type 1[8].Identical twin of a patient with T2DM have a greater than 90% chance of developing diabetes and about 25% of other patients have a first-degree relative at risk for T2DM. These observations suggest a strong genetic component which predisposes to T2DM[9].

The most recent published information in the United States is from the Centers for Disease Control and Prevention (CDC), which estimated prevalence in 2011, to be 26 million people. From 1980 through 2011, the number of Americans with diabetes has increased more than four times (from 5.6 million to 26 million) [10]. Note that in 1987, the prevalence of diagnosed diabetes was 6.8 million.This large increase in diabetes has been observed globally. The prevalence of diabetes worldwide was estimated to be 4.0% in 1995 and is anticipated to rise to 5.4% by the year 2025. The prediction is that in 2025 there will be 300 million people with diabetes, greater than 75% of them live in developing countries. These statistics have led to diabetes being described as one of the main threats to human health in the twenty-first century. The prevalence of diabetes mellitus increases with age. An estimated 186,000 deaths annually are attributable to diabetes[8].

The diagnosis of diabetes mellitus depends, solely on demonstration of hyperglycemia. Recognition of T2DM may be difficult because the hyperglycemia is often not severe enough for the patient to notice symptoms of diabetes. Initially, the risk

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of complications makes it important to identify people with the disease[8].

The criteria for diagnosis of DM have been adjusted recently by the expert committee. An individual who has symptoms of diabetes (polyuria, polydipsia, unexplained weight loss) and casual plasma glucose levels equal to or greater than 200 mg/dl is diagnosed to be suffering from diabetes. Casual is defined as occurring any time of day independent of time since the last meal. If this individual's symptoms are confirmed on a subsequent day, the individual would be diagnosed as having diabetes, if repeated fasting plasma glucose level is greater than 126 mg/dl are strongly suggestive of diabetes[11]. Individuals with serum fasting glucose greater than 110 but less than 126 mg/dl, or OGTT values of greater than 126 but less than 200 mg/dl, are considered to have impaired glucose tolerance. Individuals with impaired glucose tolerance have a significant risk of progressing to overt diabetes over time, with as many as 5% to 10% advancing to full-fledged diabetes mellitus per year[8]. Upper limit of 110 mg/dl on the fasting glucose is designated as the upper limit of normal blood glucose[12].

By dietary and lifestyle modification weightreduction can be achieved which leads to increased insulin sensitivity and improvement of glucose uptake and utilization. By these measures we can delay the start of type 2 diabetes mellitus in the offsprings of patients with T2DM.This study was planned to measure and compare the glucose and Insulin levels of asymptomatic offspring of type 2 diabetic patients with asymptomatic offspring of non diabetics in our population. In this setting no such data is recorded in past.

METHODOLOGY

It was a case control study conducted in Department of Pathology PGMI, Lahore and Diagnostic Laboratory of University of Veterinary and Animal Sciences, Lahore.The sampling technique was a purposive non-probability sampling. Non diabetic healthy offspring of diagnosed patients with type 2 diabetes mellitus attending the medical departments of Lahore General Hospital Lahore, both male and female below 30 years of age, documented by normal fasting blood glucose level and not having any symptom of diabetes were included. Patients with systemic and endocrine ailments and offspring in which one of the parents were not alive were excluded. The study was completed in nine months, from October 2009 to June 2010. The study was performed on 100 subjects, including 64 males and 36 females, divided into groups A & B. A group included age and sex matched 50 non-diabetic healthy subjects as controls documented by normal fasting blood glucose level and not having any symptom of diabetes, being offspring of parents with normal fasting blood glucose level and no history of T2DM. In this group 19 were females and 31 were males. Group B included 50 non-diabetic healthy subjects, documented by normal fasting blood glucose level and clinical history, consisting of 33 males and 17 females below 30 years of age, being offspring of patients having T2DM.

Cases were selected using the inclusion and exclusion criteria. From anticubital veins of all the subjects, 5.0 ml blood was taken aseptically without prolonged venous stasis in disposable syringes. The samples were allowed to clot and the serum obtained was transferred into properly labeled sterile vials and stored at -20°C until analysis of glucose and insulin levels[13].The personal information of the subjects was recorded on the prescribed Proforma and registered cases were asked to sign an informed consent on the consent Proforma for allocating them into the groups and using their data in the research.

STATISTICAL ANALYSIS

The collected data was entered into SPSS version 15 and analyzed through it.Mean ± SD were given for normally distributed quantitative variables(glucose and insulin). Independent samples "t" test was applied to observe differences. The Pearson test was used to calculate correlation between variables. A "p" value of 0.05 or less was considered statistically significant.

RESULTS

SEX DISTRIBUTION IN GROUP A AND B

In total of 50 controls (group A), 19(38%) were females and 31(62%) were males. In group B 33(66%) were males and 17(34%) were females as shown in figure 1.

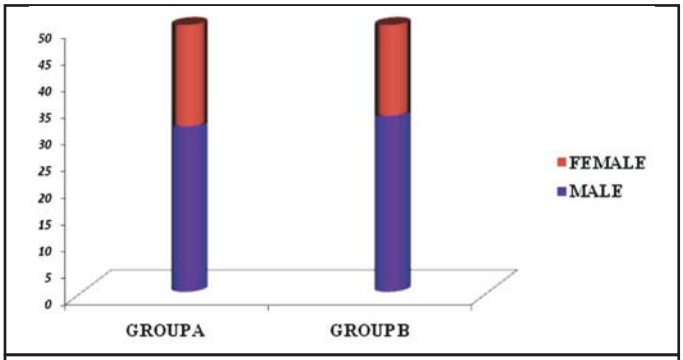

FIGURE-1: SEX DISTRIBUTION IN GROUP A AND B

AGE DISTRIBUTION IN GROUP A AND B

Mean SD values of age in groups A & B are 22.2±3.4 years and 23.1±3.5 years with ranges from 18-29 years in each group. Age distribution in group A shows that 12 (24%) were between 18-23 years and 38 (76%) were between 23-29 years. Age distribution in group B shows that 30 (60%) were between 18-23 years of age and 20 (40%) were between age of 24-29 years (Table-I).

TABLE-I: COMPARISON OF AGE IN GROUP A AND B (IN YEARS)

AGE (years)	GROUP A	GROUP B
Mean±1SD	22.16±3.42	23.14±3.50
Range	18-29	18-30

A Vs B P=0.0878(Non-significant)

WEIGHT DISTRIBUTION IN GROUP A AND B

Mean SD values of weight in groups A&B were 58.32±9.16 kg and 63.36±14.54 kg with ranges of 47-85 kg and 42-90 kg,

respectively. Weight distribution in group A shows that 43 (86%) are between Weight 47-65 kg and 7 (14%) were between weight 66-84 kg. Weight distribution in group B shows that 33 (66%) were between 47-66 kg of weight and 17 (34%) were between 67-85 kg respectively (Table-II)

TABLE-II: COMPARISON OF WEIGHT IN GROUP A AND B

Weight (kg)	Group A	Group B
Mean±SD	58.32±9.16	63.36±14.54
Range	47-85	42-90

A Vs B P= 0.25(Non-significant)
Group A= Offspring of non diabetics.
Group B= Offspring of patients with T2DM

INSULIN LEVELS IN GROUP A AND B

Fasting serum insulin in female study subjects was found to be 20.1±9.3 µIU/ml and in female controls was 26.3±6.36 µIU/ml. Similarly fasting plasma insulin in male study subjects was 18.1±4.11 µIU/ml and in the male controls was 17.6±3.34 µIU/ml (Table-III). The fasting insulin level of male and female subjects in group B was 18.4±13.32 (95%CI=17.24- 19.55) µIU/mland in the control group A was 16.8± 4.09 (95% CI = 15.64 -17.96) µIU/ml (Table-III) with ranges of 10.57-30 µIU/ml and 4.99-28.91 µIU/ml respectively.

TABLE-III: COMPARISON OF INSULIN LEVELS IN GROUP A AND B

INSULIN µIU/ml)	GROUP A	GROUP B
Mean±SD	16.80± 4.09	18.40±13.32
95%CI	15.64-17.96	17.24-19.55
Ranges	10.57-30.00	4.99-28.91
Males	17.61±3.34	18.12±4.11
Females	26.30±6.36	20.10±9.30

Avs B P= 0.081(non-significant)
Group A= Offspring of non diabetics. Group B= Offspring of patients with T2DM

GLUCOSE LEVELS IN GROUP A AND B

The fasting glucose level of male and female subjects in group B was 80.92±13.38 (77.19 - 85.20) mg/dl and in control group A was 80.75±14.21 (77.79 - 85.38) mg/dl (Table-IV) with range of 65-112 mg/dl and 60-110 mg/dl, respectively. The comparison between two groups A&B showed non-significant difference having p value=0.098 (Table-IV).

TABLE-IV: COMPARISON OF GLUCOSE LEVELS IN GROUP A AND B

Glucose (mg/dl)	GROUP A	GROUP B
Mean±SD	80.75±14.21	80.92±13.38
95% CI	77.19-85.20	77.79-85.38
Ranges	60-110	65-112
Males	80.95±14.34	79.77±22.39
Females	78.98±14.41	85.11±15.03

A VsBP=0.098 (non-significant)
Group A= Offspring of non diabetics.
Group B= Offspring of patients with T2DM

Fasting glucose level in female controls was found to be 78.98±14.41 mg/dl with range from (66-92 mg/dl) which was not significant (p >0.05) as compared to the fasting glucose level of female study subjects which was 85.11±15.03 mg/dl with range from 69-100 mg/dl, respectively. Similarly fasting glucose level in male study subjects was 79.77±22.39 mg/dl with range from 66-94 mg/dl and was not significant (p>0.05) than the male controls who had mean fasting glucose level of 80.95±14.34 mg/dl with range from 65 to 94 mg/dl. For glucose 95 % confidence interval for lower bound was 78.6791 and for upper bound were 84.0989.

DISCUSSION

Age distribution in groups A & B showed mean SD values 22.16±3.42 years and 23.14±3.50 years with ranges of 18-29 years of each group (Table-I). Comparison of two groups showed non-significant difference (p=0.0878). Age distribution in group A showed that 12 (24%) were between 18-23 years and 38 (76%) were between 24-29 years. Age distribution in group B showed that 30(60%) were between 18-23 years of age and 20 (40%) were between age of 24-29 years (Table-I) and the difference was non-significant (p>0.05). Our study was in accordance with the study of Petersen et al (2004)14. As regards age distribution their study was in younger aged and insulin resistant offspring of parents having type 2 diabetes mellitus, while Yamamoto et al studied in subjects having age between 30-65 years[15]. Our study was not in agreement with the study of Tsou et al, their study was in boys having age between 15 to 18 years of age and girls having age between 11 to 14 years[16].

Regarding sex distribution out of 50 subjects, 19(38%) were females and 31(62%) were males in group A. In Group B 33(66%) were males and 17(34%) were females (Figure 1). Comparison of two groups showed non-significant difference (p>0.05). Our study was not in accordance with the study of Nishizawa et al (2002)[17]possibly due to ethnic differences. Our study was not in accordance with the study of Tsou et al[16]. Anthony et al have their study in persons having age between 28 to 52 years Hispanic and 28 to 52 years African-American, they saw in their study that males have higher glucose levels[18]. Our study was in accordance with the study of Yokoyama et al who showed that there were no differences in distribution of gender in their study[19].

Mean SD values of weight in groups A&B were 58.32±9.16 kg and 63.36±14.54 kg with ranges of 47-85 kg and 42-90 kg respectively (Table-II). Weight distribution in group A showed 43 (86%) were between weight 47-65 kg and 7 (14%) were between weight 66-84 kg. While weight distribution in group B showed 33(66%) were between weight 47-66 kg and 17 (34%) were between 67-85 kg respectively. Comparison of two groups showed non-significant difference. Our observation was consistent with the study of Zou et al (2005)[20]. Our study was in accordance with the study of Yokoyama et al who showed that there were no differences in distribution of weight in their study[19]. Our study was in accordance with the study of Ura et al

who showed similar results in their study[21].

Fasting serum insulin in male study subjects was found to be 18.12±4.11 µIU/ml which was not significant (p>0.05) as compared to the fasting serum insulin of male controls which was 16.8±4.09 µIU/ml. Similarly fasting serum insulin level in female study subjects was 20.1±9.3 µIU/ml and in the female control group was 18.06±4.54 µIU/ml (Table-III) which was not significant (p>0.05). The comparison between groups A&B showed that in group A mean±SD was 16.8±4.09 µIU/ml and in group B mean±SD was 18.4±13.3 µIU/ml with ranges of 10.57-30 µIU/ml and 4.99-28.91 µIU/ml respectively, which had non - significant difference (p>0.05). Tsou et al have shown similar results in their study[16] that was in non diabetic children, boys aged 15-18 years and girls aged 11-14 years. Our study was in accordance with the study of Anthony et al but their study was in subjects having ages between 26 to 56 years[18]. Our study was against the study of Yokoyama et al; their study was in children having group ages between 6-10 years in first, 11-14 years in second and 15-18 years in third group[19]. Our study was against the study of Ura et al who showed significant difference in insulin levels in two groups[21].

Fasting glucose level in female controls was found to be 78.98 ± 14.41 mg/dl with range from 66 to 92 mg/dl, which was not significant (p >0.05) as compared to the fasting glucose level of female study subjects which was 85.11 ± 15.03 mg/dl with range from 69 to 100 mg/dl. Similarly fasting serum glucose level in male study subjects was 79.77 ± 22.39 mg/dl with range from 66 to 100 mg/dl and in the male controls was 80.95 ± 14.34 mg/dl with range from 65 to 94 mg/dl (Table-IV) which was not significant (p>0.05). The fasting serum glucose level of subjects in group B was 80.92 ± 13.38 mg/dl and in control group A was 80.75±14.21 mg/dl with ranges of 65-112 mg/dl and 60-110 mg/dl respectively. The comparison between two groups A&B showed non-significant difference. Our study was in accordance with the study of Yamamoto et al (2002)[15], their study was in the subjects having age between 30-65 years. Anthony et al have shown in their study that males have higher glucose levels than females, their study was in persons having age between 26 to 54 years of Hispanics and 28 to 56 years African-American18. Our study was in accordance with the study of Ura et al[21]. Our study was not in accordance with the study of Tschritter et al, they studied in subjects with impaired glucose tolerance which were more obese than subjects with normal glucose tolerance[22]. The authors could not find national data on the relationship of glucose and insulin levels in asymptomatic offsprings of patients with type 2 diabetes.

CONCLUSIONS

Both glucose and insulin levels were within normal limits and were not having any significant direct or inverse relationship.

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