ORIGINAL ARTICLE

Association of Nutritional Status and Serum Leptin in Offsprings of Diabetic Parents of Karachi, Pakistan

Meraj Rahim[1], Mariam Rahim[2], Munim Abdul Rahim[3], Mozaffer Rahim Hingorjo[4], Shaheen Sharafat[5], Zaman Shaikh[6] and Masood Anwar Qureshi[1]

ABSTRACT

Objective: Prevalence of diabetes in Pakistan in the year 2014 was 6.9 million and is expected to rise to approximately 13 million in 2035, ranking Pakistan at 8th position among world's top 10 countries having diabetes.

Materials and Methods: The study design is young subjects were taken aged 18 to 24 and were classified according to their family history of type 2 diabetes mellitus (T2DM) into those with single diabetic parent (SDP), both diabetic parents (BDP) and subjects having no family history of diabetes (NDP). Body composition was assessed by measuring body mass index (BMI), waist circumference (WC) and waist-hip ratio (WHR). Fasting venous blood was analyzed for glucose and leptin levels (measured by immunoenzymetric assay).

Results: The offspring of BDP had significantly higher body weight as compared to those of SDP and NDP ($p<0.05$). The mean fasting serum leptin levels among NDP, SDP and BDP were significantly different ($p<0.05$), and were respectively, 4.91±6.78, 15.55±13.49 and19.04 ±14.57 ng/mL.

Conclusion: Hyperleptinemia and anthropometric indices are the most prominent indicators of T2DM in individuals with a history of diabetes in the family.

Key words: Serum leptin, BMI, type 2 diabetes mellitus.

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INTRODUCTION

The prevalence of diabetes is rising throughout the world. In Pakistan, its prevalence was reported as 6.9 million cases in 2014; this is expected to rise to a approximately 13 million in the year 2035, which would rank Pakistan at 8th position among the top 10 countries with increased prevalence of diabetes[1]. In Pakistani urban population the prevalence of diabetes and its associated impaired fasting glucose is reported to be 6.0% in males and 3.5% in females[2]. Diabetes Mellitus is a syndrome due to deficiency of insulin secretion by the beta cell or resistance to the peripheral actions of insulin leading to raised plasma glucose levels. Although this disease has been studied at larger scales, due to the multifactorial nature its exact pathogenesis remains unclear. In this regard, obesity and the rise in adipocytes result in increased secretion of Leptin[3]. This hormone works with insulin and helps in the homeostasis of normal blood glucose[4]. Leptin binds to soluble leptin receptor in blood and produce its effect at the satiety center in the brain[5]. The level of soluble leptin receptors are key indicators of presence of leptin[6]. Just like insulin resistance, genetic factors are involved in the production of leptin resistance. Leptin receptor shows an ob gene mutation resulting in decreased action of leptin. This leads to hyperleptinemia which does not act on target tissues leading to leptin resistance. The receptors of leptin are regulated by the levels of circulating leptin in blood. Due to hyperleptinemia down regulation of its receptors occur resulting in leptin resistance[7]. This disorder results in those whose genes are affected due to mutation of leptin receptors[8]. Concurrently, higher centers are unresponsive to the circulating leptin thus resulting in disordered signaling to the satiety center[9].

Department of Physiology/[1] Graduate, Dow Medical College/[2] Dr. Ishrat-ul-Ebad Khan Institute of Oral Health Sciences/[3] Dow International Medical College/[5] Dow University of Health Sciences, Karachi, Pakistan.

4 Jinnah Medical & Dental College, Karachi, Pakistan.

6 South City Hospital, Karachi, Pakistan.

Correspondence: Dr. Meraj Rahim, Department of Physiology, Dow International Medical College, Dow University of Health Sciences, Karachi, Pakistan.

Email: meraj.rahim@duhs.edu.pk

The objective of this research was to compare the levels of serum leptin and body composition among healthy young adults with a history of diabetes in the family.

MATERIALS & METHODS

Study design: This was a cross-sectional study performed during 2010 to 2011. The participants were young adults aged 18 to 24 years with no known underlying medical problem. The sampling technique was non probability convenient .

Data collection was done at the campus of Dow University of Health Sciences. Permission for research was approved by the university to visit different campuses which included College of Pharmacy, Diabetes and Endocrinology (NIDE), and Institute of Nursing. First the different parts of campuses were visited and an account of the present research was given. The volunteered participants were given a consent form and questionnaire and were invited to come after 12 hours fast for their blood parameters and anthropometric measures. Apart from subjects having diabetes mellitus, those with a history of or having currently any other endocrine disorder were also excluded. The sample size was 180 subjects estimated by taking into consideration prevalence of diabetes as 13.5%[10]. This research was approved by ethical board Reference No:[IRB-164/DUHS-10] of Dow University of Health Sciences, Pakistan.

The participants were organized in accordance to history of diabetes in their family into those having

i. No diabetic parent (NDP)
ii. A single diabetic parent (SBP)
iii. Both diabetic parents (BDP)

Measurement of Anthropometric Indices: The body weight was measured in kilogram (kg) while asking them to remove shoes and heavy garments and then advising them to stand in the center of balance. Height was measured in meters using a stadiometer. The subjects were advised to remove their shoes and stand upright and straight during the measurement. Body mass index (BMI) was then calculated by dividing the weight with the square of height. The Asian Pacific criteria were used to categorize BMI into underweight, normal weight, overweight and obese[11]. For waist circumference (WC) a non-elastic tape was used and measurement done in cm. The tape was placed between lower margin of rib and upper margin of iliac crest. Hip circumference (HC) was taken at the broadest part of hip. Waist circumference was then divided by HC to get the waist to hip ratio (WHR).

Biochemical Analysis: Fasting venous sample was taken (12 mL) and serum separated at a centrifugation speed of 3000 G for 10 minutes. The serum was stored in aliquots at -20^{O}C. Quantitative assay of serum leptin was performed via immunoenzymetric assay using commercially available kit, DIA Source Leptin-EASIA (KAP2281) Kit, Belgium. The detection limit was 0.04 ng/ml.

Statistical Analysis: Means and standard deviation of descriptive data were presented. One way analysis of variance (ANOVA) was used for comparing means between the three groups. Scheffe's method was applied for multiple comparisons between pairs. Data was analyzed using SPSS version 16. A p-value < 0.05 was considered significant.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from all patients for being included in the study.

RESULTS

Table 1 shows the mean BMI as well as the frequency of distribution of underweight, normal weight and overweight/obese among the study population. After categorizing BMI, it was observed that most of the subjects having BDP belonged to overweight/obese category. In contrast, the majority of subjects in underweight category were those with NDP. Furthermore, the body weight of offspring of BDP was significantly greater than the other two categories ($p < 0.05$)[12-15]. Waist-Hip ratio was normal in NDP group while it was raised in the other two groups with a higher percentage of females than males. This was seen especially in the BDP group; 37.5% females and 14.4% males having more than normal WHR[12-15].

Serum leptin in offspring of BDP was 19.04 ± 14.57 as compared to 15.55±13.49 and 4.91±6.78 in SDP and NDP offspring, respectively (Table 2). The levels of leptin were statistically significant between the groups (Table 3). In Figure 1 and Figure 2 increasing levels of BMI showed increased levels of leptin in

Table 1: Body Mass Index of study participants

Parameters	Mean BMI (kg/m^2)	Under-weight* (%)	Normal* (%)	Overweight* (%)
NDP	21.02±6.19	31.4	50.0	18.6
SDP	22.26±6.80	19.7	50.7	29.6
BDP	25.58±5.15	2.6	20.0	76.9

*Note: BMI (kg/m^2) was categorized as follows: < 18.5 = underweight; 18.5 to 22.9 = Normal; Overweight/Obese = 23
Abbreviations: BMI, body mass index; NDP, no diabetic parent; SDP, single diabetic parent; BDP, both diabetic parent

Table 2: Biochemical parameters of offspring of BDP, SDP & NDP

Parameters	BDP	SDP	NDP
Serum Leptin (ng/dL)	19.04 ± 14.57	15.55 ± 13.49	4.91 ± 6.78

Abbreviations: BMI, body mass index; NDP, no diabetic parent; SDP, single diabetic parent; BDP, both diabetic parent

Table 3: Scheffe' multiple pair wise comparison of biochemical parameter

Parameters	BDP		SDP		NDP	
	r	p value	R	p value	r	p value
Serum Leptin-BMI	0.663	<0.005	0.719	<0.005*	0.891	<0.005*

Abbreviations: BMI, body mass index; NDP, no diabetic parent; SDP, single diabetic parent; BDP, both diabetic parent

Table 4: Intragroup correlation (r and p value) of physical and biochemical parameters

Parameters	NDP vs SDP p-value	NDP vs SDP p-value	NDP vs SDP p-value
Serum Leptin	0.00<0.05	0.00<0.05	0.326

Abbreviations: BMI, body mass index; NDP, no diabetic parent; SDP, single diabetic parent; BDP, both diabetic parent

blood. In both genders the BDP offspring had greater serum leptin at a BMI (14-18) compared to especially NDP. Intragroup correlation was calculated and the p-value in all 3 groups was found to be statistical significant i.e < 0.005 (Table 3). In figure 3 the scatter plot showed a positive correlation between BMI and Leptin.

DISCUSSION

The present study was conducted to predict the development of diabetes in individuals having high levels of serum leptin. Once established, measures including dietary alteration and regular exercise, may decrease serum leptin levels thereby preventing T2DM and its complications.

Leptin and BMI have been documented to show positive correlation in offspring having positive history of diabetes. High levels of circulating leptin are associated with raised BMI and leptin resistance. This is especially seen in children of diabetic parents who show increased levels of both leptin and insulin. The higher leptin concentration found in children of diabetic parents may be partly to the dysregulation of adipo-insular axis as suggested previously[16].

Presence of T2DM in one or more parents increases the chance of developing diabetes in the offspring. Studies have observed presence of risk factors in offspring that if measured may be able to predict future diabetes[16].

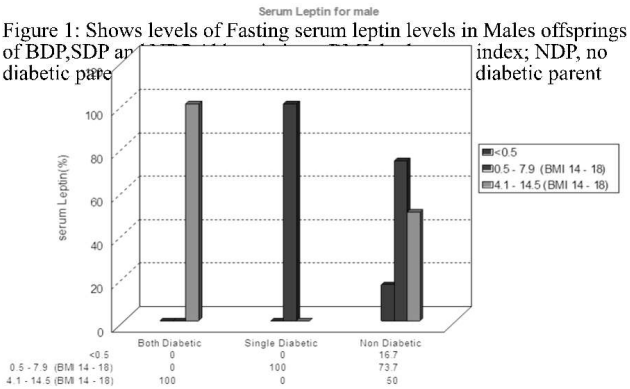

Figure 1: Shows levels of Fasting serum leptin levels in Males offsprings of BDP,SDP and NDP. Abbreviations: BMI, body mass index; NDP, no diabetic parent; SDP, single diabetic parent; BDP, both diabetic parent

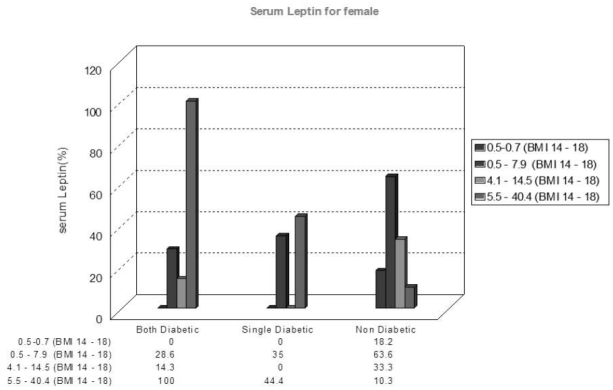

Figure 2: Shows levels of Fasting serum leptin levels in Females offsprings of BDP,SDP and NDP.

Abbreviations: BMI, body mass index; NDP, no diabetic parent; SDP, single diabetic parent; BDP, both diabetic parent

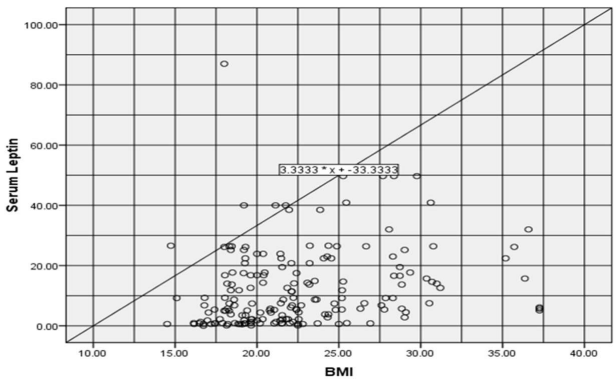

Figure 3:Shows scatter plot between Serum Leptin and BMI

Mannucci et al (2008) pointed out that obesity is linked to hypertension and abnormal lipids. National Education Cholesterol Programme has laid down the criteria to diagnose metabolic syndrome and prediction of diabetes[17]. It is consistent with many research studies that hypertension, stroke and cardiovascular risks are increased when there are raised abdominal circumferences and established diabetes mellitus[18-20]. Accumulation of central or visceral fat leads to infiltration by macrophages resulting in a state of chronic systemic inflammation which is the predisposing factor to the development of insulin resistance, T2DM, metabolic syndrome, hypertension and atherosclerosis[21,22]. It has been suggested that there is involvement of leptin in lipid metabolism through lipolysis stimulation[23].

The present study highlights the role played by a history of diabetes in parents that may later lead to development of diabetes in children. This study shows the potential value of estimating body composition by measuring the body weight, WHR and BMI in young adults. If increased, it influences the metabolism of carbohydrate and lipid and becomes a risk factor for the onset of diabetes in future. A family history of diabetes leads to increase in central obesity that sets the stage for chronic inflammation and is suggested to be a cause of hyperinsulinism in offspring in contrast to offspring having NDP.

Our study also highlights the fact that women are more predisposed to later onset of diabetes if they have a family history of such disease. This part played by genetic factors is not well understood. The FTO (fat mass obesity associated) gene may predispose the individual to become obese with greater BMI and later develop into diabetese[24].

The raised BMI and WHR in offspring of diabetic parents in our study may be due to mutation of receptors and improper signaling of the target tissues resulting in metabolic derangement. In another study it was stated that raised BMI consequently lead to cardiovascular risks[25]. It has been documented that family history of diabetes also showed raised BMI[26]. Cassano et al found abdominal circumference to be predictors of onset of diabetes[27].

Globally, impaired blood glucose levels, dyslipidemias, insulin resistance, raised blood pressure and metabolic syndrome is increasing at a rapid pace and consequently leading to diabetes mellitus. Central obesity is a precursor of insulin resistance due to its association with infiltration by macrophages and its effects on generating both insulin as well as leptin resistance thereby affecting glucose homeostasis adversely[28]. Therefore there is dire need of lifestyle modifications to prevent onset of diabetes[29-31].

This study also supports the previous suggestion that leptin increase has a positive contribution to increase insulin levels as well as decreasing insulin sensitivity in later years and predates the development of diabetes. Leptin has an active role in the pathogenesis of insulin resistance[32]. Serum leptin level is independently correlated with beta cell mass and insulin sensitivity[33-35]. Findings on relationship of leptin with insulin resistance may suggest leptin as a biomarker for identification of risk of T2DM in children having diabetic parents[33]. The dysregulation of adipo insular axis leads to higher leptin levels in individuals who have diabetic parents. Obesity favors a state of chronic hyperinsulinism that predisposes to hyperleptinemia. This rise in leptin increases resistance to the peripheral actions of insulin, further increasing the already high insulin levels[36]. In the present study it is documented that raised BMI offspring having diabetic parents showed raised leptin. Positive correlation in positive history of diabetes in offspring
showed its association between BMI and leptin.

The present study supports the part played by genes in T2DM and has found some diabetes identifying risk factors in children of diabetic individuals, which if not controlled in the young age may affect the metabolic profile of the person and later play a part in development of diabetes. This calls for lifestyle modification to prevent the risk factors causing further harm.

CONCLUSION

It is concluded that increase leptin levels as well as raised anthropometric indices of obesity such as BMI and WHR, may predict the development of T2DM in future in subjects with a history of diabetes in the family.

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