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Original Research Paper

Does The Parental History of Type 2 Diabetes Mellitus Affect The Prevalence of Insulin Resistance Syndrome in Adolescents?

Biochemistry

KEYWORDS : Insulin Resistance Syndrome, Type II Diabetes Mellitus, Adolescents.

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ABSTRACT

Objectives: *The objectives of our study were to compare biochemical and anthropometric parameters and prevalence of IRS in adolescents of diabetic and non-diabetic parents.*

Material and methods: *It is an observational analytical case-control study. In this study 100 adolescents of non diabetic parents (control group) and 50 age and sex matched adolescents of diabetic parents (study group) participated. All subjects were evaluated for WC, BMI, BP, FBS, fasting Lipid profile, insulin levels, IR and β-cell function by standard methods.*

Results: *Mean WC in study and control group were 83.49 ± 11.35 cm and 78.31 ± 11.38 cm respectively. It was significantly high in study group as compared to control group (p= 0.01). Other parameters were also high in study group. According to Adult Treatment Panel III criteria the prevalence of IRS was 6% and 12% in control and study group respectively.*

Conclusion: *On the basis of our study we can conclude that adolescents of diabetic parents are on the edge of IRS and later the DM, as IRS is a constant precursor for type-2 DM, which starts 10-20 years before development of type-2 DM.*

Introduction:

Type-2 DM is reaching epidemic proportions in children and adolescents, along with obesity. One out of three newly diagnosed Type-2 diabetics is adolescent. It is not completely clear what relationship exists between the components of insulin resistance (IR) and Type-2 DM. Studies demonstrate that IR is a precursor to Type-2 DM [1].

The concurrence of disturbed glucose and insulin metabolism, overweight and abdominal fat distribution, mild dyslipidemia, and hypertension and its association with subsequent development of type-2 DM and cardiovascular disease has given rise to the concept of insulin resistance syndrome (IRS). IR is considered as the underlying abnormality in this syndrome [2]. The precise way in which IR develops is unclear, although genetics, diet and level of physical activity are believed to play a role. Identifying patients with IR and those who are likely to develop IR offers the hope that some or all of the components of the syndrome can be prevented [3].

Studies in populations at risk of developing Type-2 DM reported that IR is an early and primary abnormality detectable in the normoglycemic, pre-diabetic state and the worsening of IR leads to fasting hyperglycemia, impaired glucose tolerance and clinical DM [4]. IR has been suggested to constitute one of the primary and key pathogenic factors for the development of glucose intolerance and type-2 DM [5].

IR occurs 10–20 years before the onset of the disease and that it is the best predictor of whether or not an individual will later become diabetic [6].

Insulin Resistance Syndrome:

Reaven GM in 1988 first described IRS to comprise central obesity, hyperinsulinemia, hyperuricemia, hypertriglyceridemia, and a propensity to coronary heart disease (CHD) and stroke. Insulin resistant syndrome is the constant precursor of Type-2 DM, and it begins in childhood. Earlier an intervention in the natural history of the disease, more effective it will be [7].

Despite abundant epidemiologic and experimental research that has been published on the metabolic syndrome, definitions of this syndrome and the various cutoffs for its components have varied widely [2, 8].

The third National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) criteria modified for age (for children and adolescents) defines the insulin resistance syndrome as the presence in an adolescents of at least three of the following five risk factors (Table 1) [9, 10]:

Table 1: ATP III criteria for IRS [9, 10]:

Component	Risk Category Definition
Triglycerides	≥ 110 mg/dl
High density lipoprotein cholesterol (HDL-C)	≤ 40 mg/dl
Systolic blood pressure or diastolic blood pressure	≥ 90th percentile for age and gender [11]
WC	≥ 90th percentile for age and gender[12]
Fasting blood glucose	≥ 110 mg/dl

In present study this criterion was used for calculating prevalence of IRS.

Need of study:

Prevalence of IR is more in adolescents. Since IRS begins in childhood we can add the preventive measures in early years of life, like- life style modification, healthy eating habits, exercise etc. so that the onset of disease process can be prevented or delayed in the children having IRS.

Aim of our study was to measure the burden of IRS in adolescents of diabetic parents, using various anthropometric and biochemical parameters and also to compare the β-cell function in both the groups.

Material and Methods:

It was an observational analytical case-control study which was carried out after Institutional ethical committee permission. Written consent was also obtained from all the participants.

Study included total150 subjects which were divided into two groups:

Control Group: 100 adolescents (age: 17± 2 years) having non diabetic parents.

Study Group: 50 age and sex matched adolescents having type II diabetic parents.

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Inclusion criteria:
Adolescents within the age group of 15-19 years.

Exclusion criteria:
Adolescents having DM or any other major illness which can directly or indirectly affect the result.

Anthropometric and Biochemical parameters:
Body mass index (BMI) and waist circumference (WC) were recorded for all subjects.

BMI was calculated using the measured height and weight [Weight (Kg)/height^2 (metres^2)].

WC was measured midway between the rib cage and the superior border of the iliac crest in mid respiration.

WC >90th percentile was considered as risk factor for IRS [10].

BP (mmHg) was recorded in either of the arm in the condition of complete physical and mental rest, in sitting position using sphygmomanometer.

SBP and DBP >90th percentile were considered as risk factor for IRS [10].

Sample Collection:
After overnight fasting samples were collected. Fasting plasma glucose levels, lipid profile and glycosylated Hb were measured on the same day. The remaining serum sample was aliquot and stored at -20^o C for insulin level detection.

Fasting plasma glucose (glucose oxidase and peroxidase method[13]), HbA1c (Latex agglutination inhibition assay [14]), serum fasting insulin (Sandwich ELISA [15] DRG International, USA), serum total Cholesterol (Enzymatic CHOD- POD method [16]), high density lipoprotein (Enzymatic end point method [16]), serum triacylglycerols (GPO-POD Enzymatic method [16]) low density lipoprotein and very low density lipoprotein (Indirect method- Friedewald Equation [17]). All the above mentioned biochemical parameters were estimated by using IFCC approved procedures.

Insulin estimation was done on B4B ELISA reader, rest all the parameters were analyzed by using a commercially available reagent kit (RANDOX Laboratories, Crumlin,UK) with the help of Randox Daytona auto analyzer serial number 5826-0965.

Homeostatic Model Assessment (HOMA) was used to estimate insulin resistance (HOMA IR) and % beta cell functioning (HOMA β)[18].

Following formulae were used.

$$\text{HOMA-IR} = \frac{\text{Fasting Plasma Glucose X Fasting Insulin}}{405}$$

$$\text{HOMA-}\beta = \frac{360 \text{ X Fasting Insulin}}{\text{Fasting Plasma Glucose} - 63}$$

(When glucose in mg/dl and insulin in μIU/ml).

Data Analysis:
Statistical analysis was done by using descriptive statistics, proportion and Student t statistic at 5% level of significance.

Observation and Results:

Table 2: Anthropometric parameters in control and study groups.

S.N.	Parameters	Control group (Mean ± SD)	Study group (Mean ± SD)	t Statistic	P-value
1.	WC (cm)	78.31 ± 11.38	83.49 ± 11.35	-2.628	*0.01
2.	BMI (kg/m^2)	21.61 ± 3.88	22.94 ± 4.76	-1.822	0.071

***p≤0.05 was considered significant.**

Table 3: Blood pressure in control and study groups.

S.N.	Parameters	Control group (Mean ± SD)	Study group (Mean ± SD)	t Statistic	P-value
1.	SBP (mmHg)	111.90 ± 8.86	114.64 ± 9.41	-1.748	0.082
2.	DBP (mmHg)	73.49 ± 6.97	74.48 ± 8.04	-0.778	0.438

***p≤0.05 was considered significant.**

Table 4: Biochemical parameters in control and study groups.

S.N.	Parameters	Control group (Mean ± SD)	Study group (Mean ± SD)	t Statistic	P-value
1.	FPG (mg/dl)	89.05 ± 10.26	90.67 ± 7.76	-0.988	0.325
2.	HbA1c (%)	5.57 ± 0.66	5.72 ± 0.66	-1.341	0.182
3.	TG (mg/dl)	84.66 ± 40.50	85.16 ± 34.84	-0.075	0.941
4.	T. Cholesterol (mg/dl)	166.24 ± 34.82	171.60 ± 29.43	-0.934	0.352
5.	HDL (mg/dl)	48.85 ± 12.54	48.39 ± 10.89	0.218	0.827
6.	LDL (mg/dl)	100.38 ± 30.31	103.88 ± 30.38	-0.665	0.507
7.	VLDL (mg/dl)	16.93 ± 8.10	17.11 ± 7.24	-0.132	0.895
8.	Insulin (μIU/l)	14.53 ± 5.64	15.58 ± 7.03	-0.993	0.322
9.	IR	3.24 ± 1.50	3.53 ± 1.72	-1.07	0.287
10.	β- Cell function (%)	222.61 ± 110.72	215.05 ± 107.69	0.398	0.691

***p≤0.05 was considered significant.**

Fig 1: Comparison of anthropometric parameters and blood pressure between control and study groups.

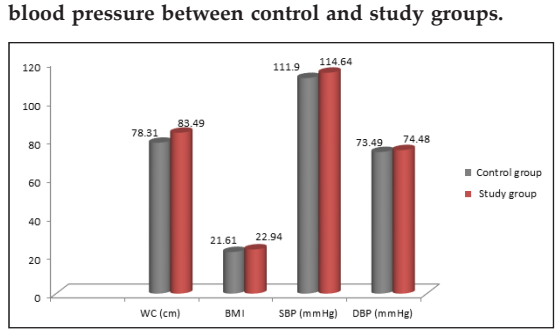
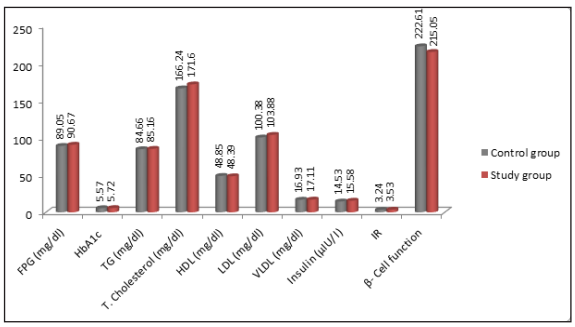


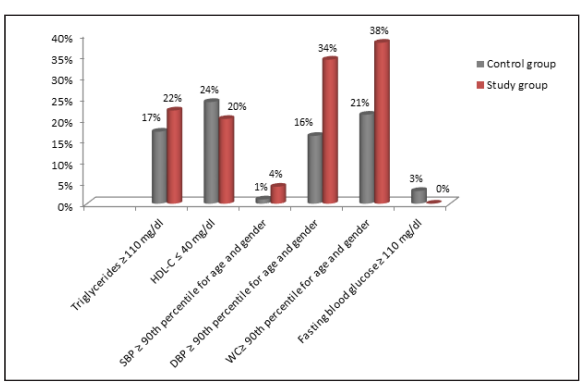
Fig 2: Comparison of biochemical parameters between control and study groups.



The mean WC was 83.49 (± 11.35) in study group which was significantly higher (p=0.01) as compared to control group (78.31 ± 11.38). Rest other parameters like- BMI, SBP, DBP, HbA1c, lipid profile (total cholesterol, TG, LDL, VLDL), insulin level and insulin resistance (IR) were high in study group as compared to control group, but the rise was not statistically significant (p=> 0.05), as shown in table 2-4 and fig 1-2. Likewise no significant difference was found in the level of serum HDL and β- cell function (HOMA-β) between study and control group (p>0.05), although both were low in study group as compared to control group.

According to ATP III criteria, as shown in fig 3, 17% adolescents of control group were having high TG levels as compared to 22% in study group, 24% were having low HDL-C in control group as compared to 20% in study group. Similarly 1%, 16% and 21% adolescents of control group were having high (≥ 90th percentile for age and gender) SBP, DBP and WC respectively as compared to 4%, 34% and 38% in study group respectively.

Fig 3: Percent distribution of Insulin Resistance Syndrome components according to ATP III criteria



When we compared the prevalence of IRS in both the groups by considering any three components (given in table 1), it was 6% in control as compared to 12% in study group.

Discussion:

The incidence of the Insulin Resistant Syndrome (IRS) is rising worldwide. This is partly due to a significant increase in the prevalence of obesity. The early diagnosis of IRS in population might hold promise for enhanced prevention of type-2 DM. The etiology of the IRS is multi-factorial. The family history of type-2 DM contributes greatly for the onset of IRS [19].

The mean WC was significantly high in study group than control, which is one of the components of IRS and represents the central obesity in adolescents of diabetic parents. 17% more adolescents were obese in study group compared to control group, according to ATP III criteria. Srinivasan et al. reported that the offspring with parental diabetes versus those without such history had significantly excess generalized and truncal adiposity beginning in childhood [20].

BMI was more in study group than in control group. The difference was not statistically significant. Supporting our results, *Benigno* et al reported highest proportion of BMI > 95 of the entire group of offspring with both diabetic parents [21]. Recently, a common variant in the FTO (fat, mass, and obesity) gene has been identified that predisposes to diabetes through an effect on the BMI.

It was shown that individuals homozygous for this particular SNP (allele A) had a higher BMI as compared to heterozygote individuals. Evidence also supports the association of FTO gene with high WC in genetically susceptible individuals [22].

In our study 22% adolescents were having high TG levels and 20% were having low HDL levels in study group, according to ATP III criteria. Insulin resistance and type-2 DM are generally accompanied by high plasma TG levels and low levels of HDL. Similar findings have also been found in the offspring of individuals with type-2 DM, this mainly attributed to the increased risk of obesity, hyperinsulinemia and glucose intolerance. However, it is not yet clear whether a family history of DM per se is associated with dyslipidemia or

dyslipidemia is related to the obesity, hyperinsulinemia or glucose intolerance, usually present in subjects with family history of type 2 DM [23].

In accordance with our results, A. Shahid et al [22] reported that the offspring with diabetic parents shows significantly high serum triglyceride levels versus those without diabetic parent.

4% and 34% adolescents of study group were having high (≥90th percentile) SBP and DBP respectively as compared to 1% and 16% in control group. A.Shahid et al [19] and Anjana RM et al [24] in their study found no significant difference in SBP when they compare control and children of one diabetic parent, but significant difference were found when both parents were diabetic. The findings of DBP by A.Shahid et al [19] were similar to our findings. While Altinli S et al [25] showed significant difference in SBP and statistically non-significant difference in DBP between children of diabetic and non-diabetic parents. The cause of hypertension in IRS is exactly not known, but some correlate it with hyperinsulinemia. According to them; hyperinsulinemia can increase blood pressure by increased renal sodium absorption or by increased activity of the sympathetic nervous system or via Free Fatty Acid-induced sensitivity to adrenergic stimuli and antagonized nitric oxide vasorelaxation [15].

We found no significant difference in FPG level in study and control groups. In favor of our findings Michael I. Goran et al [26] also found same result.

β- cell function was higher in control group than in study group, which was supported by various other studies. The mechanisms underlying the progressive decline in β-cell function are not fully understood. Miriam Cnop et al [27] found that the development of central adiposity was asso-

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ciated with loss of β-cell function, suggesting that changes in central or visceral fat– derived factors may predispose β-cell dysfunction in high-risk individuals.

According to ATP III criteria modified for age, our study estimated a significantly high prevalence of IRS in adolescents with diabetic parents as compared to those with non-diabetic parents. This was comparable to other studies too. A study carried out by Anjana RM et al [24] found higher prevalence of IRS in adolescents of diabetic parents as compared to adolescents of non-diabetic parents, which support our finding. Mithun Das et al [28] also found significant difference in prevalence of IRS in adults of diabetic and non-diabetic parents.

Conclusion:

It has been proved by various studies that the offspring's of diabetic parents are genetically more prone to develop type-2 DM in future, which is proved by our study too. IRS is a constant precursor for type-2 DM, which starts 10-20 years before development of type-2 DM. We can say that adolescents of diabetic parents are on the edge of development of insulin resistant syndrome and later the Diabetes mellitus.

By identifying these offspring at early adolescent age, we can recommend them to adopt healthy life style changes- the fundamental approach is weight reduction, increased physical activity, decrease junk food consumption and by developing healthy food habits, we can save the high risk from many deadly complications like type-2 DM, and many cardiovascular morbidities for which IRS is responsible.

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