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Research Article

COMPARATIVE STUDY OF INSULIN RESISTANCE SYNDROME COMPONENTS IN ADOLESCENTS OF PARENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Objectives: The objective of our study was to compare anthropometric and biochemical parameters in adolescents of one and both diabetic parents along with β cell function in both the groups.

Material and methods: It is an observational analytical study which had been carried out in the Department of Biochemistry, JNMC, DMIMS (DU), Sawangi (M), Wardha. In which 50 adolescents (17±2 years of age) participated. Out of them 42 were having one diabetic parent while 8 had both diabetic parents. All subjects were evaluated for WC, BMI, BP, FPG, Lipid profile, insulin level, insulin resistance and β-cell function by standard methods.

Observations and Result: Body Mass Index (BMI), serum triglyceride (TG) levels, serum insulin levels, insulin resistance and β-cell function was significantly high in adolescents of both diabetic parents as compared to one diabetic parent. These were 26.99 ± 6.67kg/m^2, 102.04 **±** 28.52 mg/dl, 22.7 **±** 4.96 μIU/ml, 4.97 **±** 1.37 and 211.74 ± 113.37 % respectively in adolescents of both diabetic parents as compared to 22.21 ± 3.94 kg/m^2, 74.59 **±** 27.73 mg/dl, 15.42 **±** 6.85 μIU/ml, 3.50 ± 1.66 and 348.2 **±** 105.8 % respectively in adolescents of one diabetic parent.

Conclusion: Insulin resistance syndrome (IRS) is a constant precursor for type-2 DM, which starts 10-20 years before the development of type-2 DM. So we can say that adolescents especially whose both parents are diabetic are on the edge of development of insulin resistant syndrome and later the Diabetes mellitus.

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Type-2 DM is caused by a combination of resistance to insulin action and an inadequate compensatory insulin secretary response. This form of DM, accounts for approximately 90 - 95% of total diabetics and was previously referred to as non-insulin dependent diabetes mellitus (NIDDM) or adult-onset DM [1].

Type-2 DM is a complex metabolic disorder of heterogeneous etiology with social, behavioral and environmental risk factors unmasking the effects of genetic susceptibility. It has become a global problem, both in developing countries that adopt the so called "westernized lifestyle" and in developed countries in which an association with overweight and obesity has been documented. Moreover, age at onset of Type-2 DM is decreasing worldwide and affected children and adolescents are on the rise. This trend is occurring too quickly to be the consequence of increased gene frequency, and the key role of environmental factors, like overeating and sedentary lifestyle, seems to be more realistic [2].

Type-2 DM has long been viewed as a disease with a substantial genetic contribution. Family history has been noted to double the risk of diabetes, equal to the risk of obesity, which is also heritable. Obesity and family history quadruple the diabetes risk [3].

Insulin resistant syndrome (IRS) 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 [4]. Despite abundant epidemiologic and experimental research that has been published on the IRS,

definitions of this syndrome and the various cutoffs for its components have varied widely [5]. Two definitions of IRS are widely accepted and considered [6]:

1. The presence of any three or more of hyperinsulinaemia, overweight, high systolic blood pressure, high triglycerides, low high density lipoprotein (HDL) cholesterol and impaired fasting glucose; and
2. The presence of hyperinsulinaemia and at least two of the other five risk factors.

Thus one definition is potentially exclusive of insulin resistance as defined in the first instance by high insulin levels.

In this study we compared anthropometric and biochemical parameters in adolescents of single and both diabetic parents with an aim to assess the influence of family history of type-2 DM on insulin resistance syndrome components.

Need of study:

Prevalence of insulin resistance is more in adolescents. Since insulin resistance syndrome begins in childhood we can add the preventive measures in early years of life, like-life style modification, eating habit, exercise etc. so that the onset of disease process can be prevented or extended in the children having insulin resistance syndrome.

MATERIAL AND METHODS:

Place and Type of Study: It is an institution based observational analytical study which was carried out in the Department of Biochemistry, JNMC Sawangi (meghe), Wardha from July 2012 to October 2014. Institutional ethical committee permission was taken.

Our study included 50 subjects which were divided into two groups:
1. Adolescents with one diabetic parent (ODP): (n=42)
2. Adolescents with both diabetic parent (BDP): (n=8)

Inclusion criteria:

All adolescents within the age group of 10-19 years, with single or both diabetic parents.

Exclusion criteria:

Adolescents having DM or any other major illness, which can directly or indirectly affect the result. Adolescents of non-diabetic parents.

Anthropometric Parameters:

Body mass index (BMI), waist circumference (WC) and blood pressure, were recorded for all subjects.

BMI was calculated by 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 by using a milli-metric non-extensible and non-elastic measuring tape (Sanny®) in midrespiration.

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

Sample Collection:

One day prior to sample collection, all the subjects were instructed not to take anything after dinner. On next morning after assuring 12 hours fasting, written consent was taken and then 5.0 ml of venous blood was drawn from the cubital vein for analytical purposes. In all cases blood was withdrawn between 08:00-09:00 am.

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° C until used for insulin estimation.

Analytical Determinations:

Following biochemical parameters were determined by using following standard procedures.

Sr. No.	Test	Method
1	FPG	GOD-POD method [7]
2	Glycosylated Hb	Latex agglutination inhibition assay [8]
3	TG	GPO-POD Enzymatic method [9,10]
4	Cholesterol	Enzymatic CHOD- POD method [10]
5	HDL	Enzymatic end point method [10,11]
6	VLDL	Indirect method- Friedewald Equation [12]
7	LDL	Indirect method- Friedewald Equation [12]
8	Insulin level	Sandwich ELISA [13]
9	Insulin Resistance	HOMA-IR [14]
10	β - cell function	HOMA-β [14]

Biochemical parameters were analysed as follows: fasting plasma glucose (FPG) (analysed by glucose oxidase and peroxidase method GOD-POD [7] with the help of Robonic autoanalyzer), HbA1c (by Latex agglutination inhibition assay) [8], serum fasting insulin (analysed by Sandwich ELISA [13]. kit from DRG International, USA), serum total Cholesterol (by Enzymatic CHOD- POD method [10]), high density lipoprotein (HDL) (by Enzymatic end point method [10,11]), serum triacylglycerols (TG) (by GPO-POD Enzymatic method [9,10]) low density lipoprotein (LDL) and very low density lipoprotein (VLDL) (by Indirect method- Friedewald Equation [12]). 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 (IR) (HOMA IR) and % beta cell functioning (HOMA β) [14].

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

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

(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. The statistical software was used SPSS 17.0 and Statecal.

RESULTS

Table- 1: Anthropometric and Biochemical parameters between adolescents of ODP & BDP

S. No.	Parameters	One diabetic parent (Mean ± SD)	Both diabetic parent (Mean ± SD)	P- value
1.	WC (cm)	82.51 ± 11.36	88.62 ± 10.47	0.165
2.	BMI (kg/m²)	22.21 ± 3.94	26.99 ± 6.67	*0.008
3.	SBP (mmHg)	113.57 ± 9.10	120.25 ± 9.65	0.065
4.	DBP (mmHg)	73.90 ± 8.45	77.50 ± 4.62	0.250
5.	FPG (mg/dl)	91.17 ± 7.78	88.10 ± 7.62	0.310
6.	HbA1c	5.70 ± 0.66	5.82 ± 0.70	0.656
7.	TG (mg/dl)	74.59 ± 27.73	102.04 ± 28.52	*0.01
8.	T. Cholesterol (mg/dl)	168.96 ± 30.30	185.50 ± 20.56	0.147
9.	HDL (mg/dl)	48.46 ± 11.05	48.05 ± 10.73	0.923
10.	LDL (mg/dl)	101.37 ± 31.70	116.99 ± 18.44	0.186
11.	VLDL (mg/dl)	16.48 ± 7.38	20.41 ± 5.70	0.162
12.	Insulin (μIU/ l)	15.42 ± 6.85	22.7 ± 4.96	*0.006
13.	IR	3.50 ± 1.66	4.97 ± 1.37	*0.023
14.	β- Cell function	348.2 ± 105.8	211.74 ± 113.37	*0.003

*p≤0.05 was considered significant.

Fig. 1: Comparison of anthropometric parameters between one & both diabetic parents
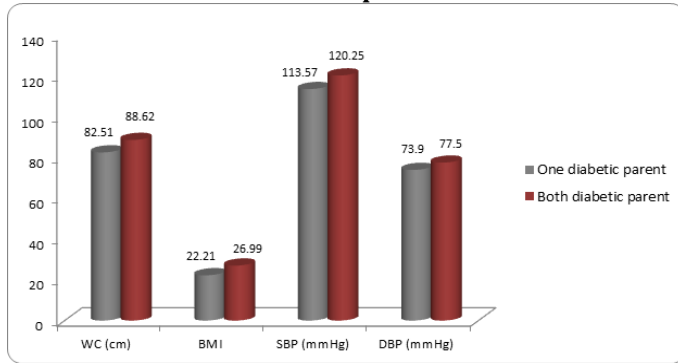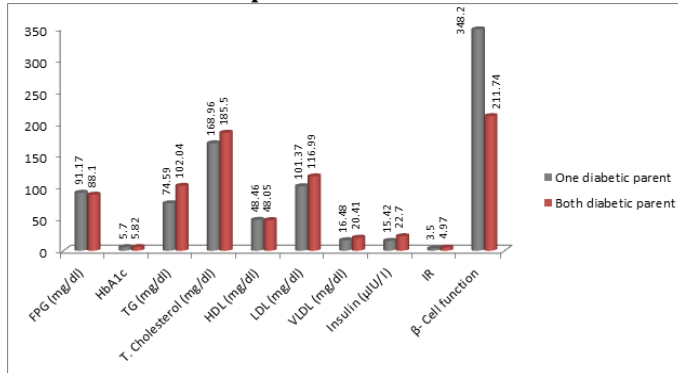

Fig. 2: Comparison of biochemical parameters between one & both diabetic parents

The BMI of adolescents with ODP was 22.21 (± 3.94) kg/m^2, which was significantly less as compared to BMI of BDP 26.99 (± 6.67) kg/m^2, as shown in table 1 and fig 1. Mean serum levels of TG, as shown in table 1 and fig 2, was 74.59 (±27.73) mg/dl in adolescents of ODP and was 102.04 (±28.52) mg/dl in adolescents of BDP, which is significantly high in BDP adolescents (P< 0.05). The serum insulin level, IR, and β- cell function were 15.42 (±6.85) μIU/ml, 3.50 (±1.66) and 348.2 (±105.8) % respectively in adolescents of ODP and were 22.7 (±4.96) μIU/ml, 4.97 (±1.37), and 211.74 (±113.37) % in adolescents of BDP, as shown in table 1 and fig 2. These all are significantly high in adolescents of BDP as compared to adolescents of ODP. p-value was < 0.05.

Rest other parameters like WC, SBP, DBP, HbA1c, total cholesterol; LDL and VLDL were high in adolescents of BDP but not statistically significant. p value > 0.05.

FPS and HDL levels were low in adolescents of BDP as compared to ODP, but not statistically significant. p value > 0.05. as shown in table 1 and fig 2.

DISCUSSION

In the present study various biochemical and anthropometric parameters were compared in adolescents of single diabetic parent (n=42) and both diabetic parent (n=8). The mean age of all subjects were 17 ± 2 years. β-cell function was also calculated and compared between both the groups.

Type-2 DM has a strong genetic component. Major genes that predispose to this disorder have yet to be identified, but it is clear that the disease is polygenic and multifactorial. Various genetic loci contribute to susceptibility, and environmental factors such as nutrition and physical activity further modulate phenotypic expression of the disease. The concordance of type- 2 DM in identical twins is between 70 - 90%. An individual with single diabetic (type-2 DM) parent have an increased risk

of diabetes; if both parents have type-2 DM, the risk approaches 40%. Insulin resistance, as demonstrated by reduced glucose utilization in skeletal muscles, is present in many nondiabetic, first-degree relatives of individuals with type 2 DM [15].

The incidence of the Insulin Resistant Syndrome 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 such as the high prevalence of excess body fat, abnormal body fat distribution, hypertriglyceridemia, and insulin resistance. The family history of type-2 DM contributes greatly for the onset of IRS [16].

When we compared BMI between adolescents of single and both diabetic parents, it was significantly high in adolescents of both diabetic parents as compared to one diabetic parent (p=**0.008)**. Supporting our results, Benigno et al reported highest proportion of BMI >95 of the entire group of offspring with both diabetic parents [17]. 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 [18]. Evidence also supports the association of FTO gene with high WC in genetically susceptible individuals [18].

In our study, we found significantly high level of serum TG in adolescents of BDP as compared to ODP (p=**0.01)**. In accordance with our results, Adeela Shahid et al. reported that the offspring with both diabetic parents shows significantly high serum triglyceride levels versus those with single diabetic parent [16]. 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 is usually present in subjects with family history of type 2 DM [19].

Our findings also showed significantly high levels of Insulin (p=**0.006)** and HOMA-IR (p=**0.023)** in adolescents of both diabetic parents than single diabetic parent. The study of Adeela Shahid et al [16] and Ten S et al [4] supports our study and states that genetic predisposition is responsible for development of hyperinsulinemia and IR in early childhood. Insulin resistance and a positive family history are both hypothesized to be significant risk factors in the development of type-2 DM. However, it is unclear whether these two factors serve as independent risk factors that may act through different pathways, or whether a positive family history increases risk through an effect on insulin resistance [20].

When we compare adolescents of one and both diabetic parents, β- cell function was significantly low in adolescents of BDP (p=**0.003)** as compared to adolescents of ODP. In adults, the progression of insulin resistance and the subsequent inability of the β-cell to adequately compensate through an increase in secretion is the basis for the development of type-2 DM. In children, this pathogenesis is likely to be similar but is exacerbated by transient insulin resistance that occurs during puberty and may further contribute to β-cell demand [21]; this may be the cause of decrease β-cell function in adolescents of BDP. Other parameters like WC, SBP, DBP, HbA1c, total cholesterol; LDL and VLDL were high in adolescents of BDP but not statistically significant. p value > 0.05.

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; specially the adolescents of BDP, as many IRS components were significantly high in them as compared to adolescents of ODP. IRS is a constant precursor for type-2 DM, which starts 10-20 years before development of type-2 DM. So we can say that adolescents whose parents are diabetic are on the edge of development of insulin resistant syndrome and later the Diabetes mellitus. Those having both diabetic parents are more prone to develop IRS. So 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.

RECOMMENDATION

Further such studies in adolescents of diabetic parents are needed with larger sample size.

REFERENCES

1. R Sharma, S Sharma, GG Kaushik. Gamma-glutamyltransferase (GGT) –a Novel Marker of Endothelial Dysfunction. Journal of Indian Academy of Clinical Medicine. 2010, January-March; 11(1): 27-30.

2. Giuseppe d'Annunzio1et al and the Diabetes Study Group of the Italian Society for Pediatric Endocrinology and Diabetes (ISPED). Insulin resistance and secretion indexes in healthy Italian children and adolescents: a multicentre study. ACTA BIOMED. 2009; 80: 21-28.

3. Steven C. Elbein, M.D. Genetics Factors Contributing to Type 2 Diabetes across Ethnicities. Journal of Diabetes Science and Technology. 2009, July; 3(4): 685-9 © Diabetes Technology Society.

4. Svetlana Ten and Noel Maclaren. Insulin Resistance Syndrome in Children. The Journal of Clinical Endocrinology & Metabolism. 2004; 89(6):2526–2539.

5. David E. Laaksonen, Hanna-Maaria Lakka, Leo K. Niskanen1, George A. Kaplan, Jukka T. Salonen, and Timo A. Lakka. Metabolic Syndrome and Development of Diabetes Mellitus: Application and Validation of Recently Suggested Definitions of the Metabolic Syndrome in a Prospective Cohort Study. American Journal of Epidemiology. 2002, June; 156 (11):1017-77.

6. K S Steinbeck. Insulin resistance syndrome in children and adolescents: clinical meaning and indication for action. International Journal of Obesity. 2004; 28: 829–832. doi:10.1038/sj.ijo.0802723.

7. David B. Sacks, M.B., Ch.B., F.R.C. Path. Carbohydrates. In: Burtis CA, Ashwood ER, Bruns DE, editors. Tietz textbook of clinical chemistry and molecular diagnostics. 4th ed. New Delhi: Saunders Elsevier; 2006. p. 837-901.

8. Cohen P.M. Perspective: measurement of Circulating Glycated Protein to Monitor Intermediate- Term Changes in Glycemic Control Eur J Clin. Biochem. 1992; 30 (12): 851-859.

9. Buccolo G et al. Quantitative determination of serum triglycerides by use of enzymes. Clin Chem. 1973; 19 (5): 476-482.

10. Rifai N, Warnick GR. Lipids, lipoproteins, apolipoproteins, and other cardiovascular risk factors. In: Burtis CA, Ashwood ER, Bruns DE, editors. Tietz textbook of clinical chemistry and molecular diagnostics. 4th ed. New Delhi: Saunders Elsevier; 2006. Page: 903-81.

11. Mary M Kimberly, Elizabeth T. Leary, Thomas G. Cole, and Parvin P. Waymack: Clin. Chem., 45, 1803 (1999).

12. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499-502.

13. Flier, J.S., Kahn. C.R. and Roth, J. (1979). Receptors, antireceptor antibodies and mechanism of insulin resistance; N. Engl. J. Med., 300, 8, 413-419.

14. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985; 28: 412-419.

15. Alvin C. Powers, Diabetes Mellitus. In : Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, et al, editors. Harrison's Principles of Internal Medicine.16th ed. New Delhi: Mc-Graw Hill; 2005. p. 2152-80.

16. Adeela Shahid, Khalid P. Lone, Sadia Saeed, Muhammad Arslan. Male offspring of both diabetic parents have higher insulin resistance and serum leptin levels compared to those with one diabetic parent. HORMONES. 2008; 7(4):313-319.

17. Benigno et al. Long-Term Consequences for Offspring of Paternal Diabetes and Metabolic Syndrome. Experimental Diabetes Research Volume 2012, Article ID 684562, 5 pages.

18. Frayling TM, Timpson NJ, Weedon MN, et al. A common variant in the FTO gene is associated with body mass index and predisposes to childhood and adult obesity. Science. 2007; 316: 889-894.

19. Edavan P. Praveen et al. Low HDL-cholesterol among normal weight, normoglycemic offspring of individuals with type 2 diabetes mellitus. HORMONES. 2011; 10(1):57-66.

20. Michael i. Goran, Kate Coronges, Richard N. Bergman, Martha L. cruz and Barbara a. Gower. Influence of Family History of Type 2 Diabetes on Insulin Sensitivity in Prepubertal Children. The Journal of Clinical Endocrinology & Metabolism. 2003; 88(1):192–195.

21. Louise A. Kelly, Christianne J. Lane, Marc J. Weigensberg, Corinna Koebnick, Christian K. Roberts. "Parental History and Risk of Type 2 Diabetes in Overweight Latino Adolescents": A longitudinal analysis. Diabetes Care. 2007, October; 30(10): 2700-5