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Serum C-peptide levels in Indian children and adolescents: Relation to clinical and biochemical parameters

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Abstract: The prevalence of obesity among the children has dramatically increased. The serum C-peptide and its correlation with biochemical, clinical and anthropometric parameters were evaluated in 296 children and adolescents(103 control, 96 obese, 97 overweight) of age group 10-17 years. The levels of serum C-peptide were measured by ELISA. Serum C-peptide levels were found to be significantly elevated in both overweight and obese children than controls. Serum C-peptide levels positively correlated with BMI, WHR, serum insulin, HOMA-IR, total cholesterol, triglycerides, LDL-c, systolic and diastolic blood pressure. Fasting glucose levels were found to be negatively correlated with serum C-peptide levels. HDL-c levels were non-significant among the study groups. Elevated serum C-peptide levels have been associated with atherogenic risk factors including increased triglycerides and high blood pressure.
Keywords: Serum C-peptide, Overweight, Obesity, Metabolic Syndrome, Cardiovascular Diseases.

INTRODUCTION

Reports from different parts from India suggested rising trend prevalence in childhood overweight and obesity. Several studies have reported the role of various biochemical parameters in the early detection of insulin resistance, dyslipidemia and cardiovascular diseases among obese children and adolescents. There is compelling evidence that, obesity is a risk factor for insulin resistance, metabolic syndrome and atherosclerotic coronary heart diseases in children [1].

Unfortunately, systemic data for children and adolescents for the early prediction of insulin resistance and cardiovascular diseases is scarce. There is now evidence that, atherosclerotic changes start pathologically in coronary arteries during childhood [2]. Several studies have mentioned that measurement of serum C-peptide levels predicts future risk of cardiovascular events and death regardless of the presence of diabetes [3-6]. C-peptide is the connecting peptide, which is made when proinsulin is split into insulin and C-peptide. Insulin and C-peptide are secreted equimolar amounts in both pancreas and circulation. Serum C-peptide test can be used to monitor beta cell activity. C-peptide stimulates Na^+- K^+ ATPase and endothelial nitric oxide synthase activities. C-peptide level does not affect the blood sugar level in the body. It influences the disaggregation of insulin, probably by binding to insulin oligomers with dissociation constants in the micromolar range [7]. Also, it has been found that C-peptide may have proatherogenic effects such as stimulation of monocytes and T-cell chemotaxis [8]. Unfortunately, the potential relationship between serum C-peptide, anthropometric and biochemical parameters has not been extensively reported in earlier studies especially in overweight and obese children in Indian population. Number of novel cardiovascular risk factors has recently been described in adults, only sparse information is available with regard to children and adolescents.

The study was undertaken to elucidate the relationship between serum C-peptide and biochemical, anthropometric parameters in overweight and obese children of Indian population and their risk of cardiovascular diseases. The focus of the paper is to identify children who are at risk of insulin resistance at an early stage to prevent future development of metabolic syndrome and cardiovascular diseases.

EXPERIMENTAL SECTION/ MATERIALS AND METHODS

The study group consists of 296 school going children with in the age group of 10-17 years from different schools in Chennai and Jabalpur were enrolled

as study participants. Informed written consent from the parents and children were obtained before the start of the study. A detailed questionnaire regarding medical history of the parents and children were recorded. This study was approved by institutional ethics committee. Overweight and obese children were included. Children with secondary causes of obesity, insulin dependent diabetes mellitus and insulin independent diabetes mellitus and children with relevant drug treatment were excluded. Anthropometric measurements such as height, weight, body mass index (BMI) and waist to hip ratio (WHR) were recorded. Weight was measured using a beam balance to the nearest centimeter using a tape stuck to the wall. Abdominal girth was measured at the level of umbilicus with the subject relaxed and in a standing posture. Hip girth was measured at the widest point of the hips at the level of the greater tronchanter with the patient standing with the both feet together. Waist to hip ratio was calculated from these measurements. Children with >85th percentile for age and gender were considered as overweight and children with >95th percentile for age and gender were considered as obese by using centers for disease control and prevention growth charts. Blood pressure levels were also recorded for all children using mercury sphygmomanometer.

12 hours fasting venous blood samples were collected from all the children, serum separated and the samples were stored at -20^{0}c until analysis. Serum C-peptide and serum insulin levels were measured using ELISA kit (Monobind Inc USA). Lipid profile which includes total cholesterol (TC), low density lipoprotein cholesterol (LDL-c), high density lipoprotein cholesterol (HDL-c) were analysed by enzymatic methods using auto analyzer. Serum triglycerides (TG) by GPO-PAP method and fasting glucose by GOD-POD method. Homeostasis model assessment (HOMA-IR) calculated by following formula.

HOMA-IR = fasting insulin (µU/mL) x fasting glucose (mmol/L) / 22.5

Statistical Analysis

Statistical analysis of the data was carried out using SPSS package 9.0. Results are expressed as Mean ± SD and p value of < 0.05 was considered to be statistically significant. Data of significance among the groups were analysed by one way ANOVA and Bonferroni comparison. Correlation analysis was done by Pearson's correlation at 5% level of significance. Since some of the parameters are slightly skewed, we have applied logarithmic transformations for all statistical analysis.

RESULTS

We studied 296 subjects (103 control, 96 obese and 97 overweight children and adolescents. The biochemical and anthropometric characterstics of study subjects are shown in table 1.

Table-1: Comparison between controls and overweight, obese children

Parameter	Group I	Group II	Group III
Age	14.45±1.36	13.93±1.47	14.07±1.56
BMI(Kg/m^2)	18.04±2.14	24.09±1.42**	28.35±2.56**
WHR	0.85±0.09	0.99±0.13**	1.02±0.13**
SystolicB.P(mmHg)	117.57±5.51	120.52±7.13†	124.48±8.81**
DiastolicB.P(mmHg)	75.44±6.68	77.94±9.01 ^{NS}	76.56±9.04 ^{NS}
TC(mg/dl)	140.93±18.22	151.93±21.76**	164.19±22.05**
TG(mg/dl)	75.72±26.85	90±32.31†	103.26±36.18**
LDL-C(mg/dl)	87.93±12.27	90.70±12.28 ^{NS}	92.57±12.34 ^{NS}
HDL-C(mg/dl)	39.46±4.83	38.99±4.03 ^{NS}	38.36±3.46 ^{NS}
Fasting glucose(mg/dl)	87.83±6.55	81.98±6.16**	80.97±6.5**
C-peptide(ng/mL)	1.39±0.85	3.34±1.29*	2.57±1.02*
Insulin(µU/mL)	3.43±2.78	20.13±8.37*	13.94±5.88*
HOMA-IR	0.74±0.59	4.02±1.68*	2.85±1.26*

**P<0.001; †P<0.05; NS-non - significant. < 0.05 (Control Vs Other Groups)

Group I – Healthy Children and Adolescents

Group II – Obese Children and Adolescents

Group III – Overweight Children and Adolescents

The mean serum C-peptide levels were significantly higher in obese (3.34 ± 1.29 ng/mL), overweight (2.57 ± 1.02 ng/mL) (p<0.001) than in control children (1.39 ± 0.85 ng/mL). Serum insulin, HOMA-IR were found to be significantly elevated in obese and overweight children than controls.

The mean levels of serum C-peptide, insulin and HOMA-IR in boys and girls of different groups are summarized in table 2.

Table-2: Mean levels of C-peptide, insulin and HOMA-IR in boys and girls of different groups

	Group I (N = 103)		Group II (N= 96)		Group III (N = 97)	
	Boys(55)	Girls(48)	Boys(54)	Girls(42)	Boys(47)	Girls(50)
C-peptide(ng/mL)	1.33±0.72	1.44±0.98	3.14±1.24	3.6±1.32	2.65±1.08	2.49±0.94
Insulin(µU/mL)	3.03±2.58	3.87±2.94	18±7.19*	22.86±9.05*	13.63±6.35*	14.22±5.45*
HOMA-IR	0.64±0.54	0.84±0.63	3.57±1.44	4.6±1.78	2.75±1.38	2.93±1.13

**P<0.001; †P<0.05; NS-non - significant. < 0.05 (Control Vs Other Groups)
Group I – Healthy Children and Adolescents
Group II – Obese Children and Adolescents
Group III – Overweight Children and Adolescents

Among the overweight and obese children and adolescents the parental history of obesity, hypertension, diabetes and heart diseases was 56%, 35%, 33% and 8.5% respectively.

The relationship between serum C-peptide, biochemical and anthropometric parameters for all the subjects are shown in table 3.

Table-3: Pearson's correlation analysis between Serum C-peptide and anthropometric, biochemical variables of the study subjects

	Overall (296) rho	pvalue	Boys(156) rho	pvalue	Girls (140) rho	pvalue
BMI(Kg/m^2)	0.64	0.001	0.60	0.001	0.69	0.001
WHR	0.37	0.001	0.42	0.001	0.34	0.001
Systolic B.P(mmHg)	0.34	0.001	0.38	0.001	0.30	0.001
Diastolic B.P(mmHg)	0.07	0.209	0.006	0.93	0.12	0.11
HOMA-IR	0.68	0.001	0.64	0.001	0.71	0.001
TC(mg/dl)	0.30	0.001	0.28	0.001	0.33	0.001
TG(mg/dl)	0.30	0.001	0.32	0.001	0.29	0.002
LDL-C(mg/dl)	0.21	0.001	0.15	0.004	0.27	0.001
HDL-C(mg/dl)	-0.08	0.11	-0.05	0.50	-0.13	0.11
Glucose(mg/dl)	-0.23	0.001	-0.23	0.001	-0.25	0.001
Insulin(µU/mL)	0.42	0.001	0.40	0.001	0.44	0.001

DISCUSSION

The prevalence of obesity is escalating at an alarming rate to epidemic propotions throughout the developing countries. There is a great deal of evidence that metabolic syndrome is increasing rapidly in both obese and overweight children. It is estimated that there is each half unit increase in BMI associated with a 50% increase risk of insulin resistance syndrome among overweight children and adolescents [9]. The present study aims to analyse the relationship between serum C-peptide and other biochemical, anthropometric parameters in obese and overweight children.

From this study we found significantly elevated serum C-peptide levels in both overweight and obese children. The available information suggests that both C-peptide and insulin secreted in equimolar quantities into the portal vein and also investigation data confirms the proatherogenic effects such as stimulation of monocytes and T-cell chemotaxis [8]. In our study we observed significantly elevated BMI, WHR in both obese and overweight children and adolescents than controls, this is natural as per the diagnostic criteria. Serum insulin, HOMA-IR levels significantly elevated in in both obese and overweight children and adolescents than controls. C-peptide levels positively correlated with insulin and HOMA-IR. Our observations raise the possibility that childhood obesity and overweight often precedes the hyperinsulinemic state and fasting insulin levels with elevated HOMA-IR determine insulin resistance and our data agree with those reported by others [10-12].

The results of our study show positive correlation between serum C-peptide and BMI, WHR. This finding implies that BMI plays an important role in variations of C-peptide levels and it is associated with abdominal obesity than with peripheral obesity and our results are in alignment with earlier studies [13,14]. However, the other author has not reported the significant effect of C-peptide in adipose tissue [15]. The results of our study are also consistent with other studies that have shown positive relationship between serum C-peptide and both systolic and diastolic blood pressure. Current data suggest that the pathophysiological role of C-peptide in obesity related hypertension [5].Total cholesterol, triglycerides, LDL-c was positively correlated with serum C-pepide levels. Whereas glucose levels negatively correlated. No significant correlation was observed between serum C-peptide levels and HDL-c levels. Collectively, these data suggest that the role of C-peptide in the

pathogenesis of dyslipidemia, cardiovascular and coronary artery disease related mortality and our results are in alignment with earlier reports [16,17].

On further comparison between boys and girls in all the groups, the higher levels of serum C-peptide were seen in girls than boys. The mechanism behind these apparent gender differences remains unclear, although the role of female sex hormones suspected. The observations are consistent with those reported by others [18]. Another interesting finding of the present study was, we identified 14 children (10 girls, 4 boys) and adolescents with features of metabolic syndrome according to international diabetes federation criteria [19]. Which were not identified in them earlier and the clinical reports were distributed to the school authorities. Most of these children showed BMI >30 with higher TG >150 mg/dl and lower HDL-c (<40mg/dl for females, <50 mg/dl for males). The potential limitation of our study was lack of puberty assessment in children, measurement of in detail dietary habits of children.

CONCLUSION

The present data confirm consistent positive correlation between serum C-peptide and anthropometric, clinical and biochemical parameters in all the groups. We observed negative correlation between serum C-peptide and fasting glucose levels. HDL-c levels were found to be non significant among all the groups. Our observations strongly suggest that obesity may be instrumental in bringing out symptoms of various metabolic disorders. Elevated serum C-peptide levels helps in predicting increased risk of cardiovascular events and death regardless of the presence of diabetes. Further studies are being planned on larger sample size to draw a healthy conclusion for clinical management of the patients.

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