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Serum adiponectin profile in obese Bangladeshi children attending an obesity clinic

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Abstract

Background and objective: Childhood obesity plays major role in the pathogenesis of various cardiovascular and metabolic diseases. Serum adiponectin has been found to be associated with several cardiometabolic risk factors. The study investigated the serum adiponectin levels and its relationship with obesity and cardiometabolic risk factors in Bangladeshi obese children.

Material and methods: Overweight or obese children, between 6-18 years of age, attending the obesity clinic of the Department of Endocrinology, BSMMU were enrolled. Waist circumference (WC) and blood pressure (BP) were measured and blood samples were taken for estimation of glucose, insulin, lipid profile and adiponectin. Fasting plasma glucose (FPG), serum insulin and lipid profile were estimated by automated analyzer. Insulin resistance (HOMA-IR) was calculated from fasting insulin and fasting plasma glucose values. Serum adiponectin (total) was measured by ELISA method using DRG ELISA kit, Germany.

Results: A total of 78 overweight or obese children of 6-18-year of age were enrolled. The mean (±SD) age of the study population was 12.22 ± 2.56 years and the mean BMI was 28.79 ± 4.54 kg/m^2. Mean (±SD) serum adiponectin was 36.93 ± 17.85 µg/ml in 78 overweight/obese children. One way ANOVA showed no significant (P= 0.582) difference of adiponectin levels among children with overweight and different grades of obesity. There was no significant correlation between adiponectin and measures of generalized (r=0.035, p=0.763) or central (r=0.098, p=0.392) obesity. Also, no significant correlation was found between serum adiponectin level and any of cardiovascular risk factors of obesity or metabolic health.

Conclusion: The study showed high serum adiponectin level in obese Bangladeshi children. Also, no association was found between serum adiponectin levels with grades of obesity and cardiometabolic risk factors among obese children of Bangladesh.

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Introduction

Obesity, a worldwide pandemic, affects not only adults, but also children [1]. According to report of WHO in 2018, over 381 million children and adolescents (5-19yrs) were overweight/obese [2]. A countrywide epidemiological study in Bangladesh reported that 3.5% and 9.5% of 6–15-year-old children were obese and overweight respectively [3]. Childhood obesity plays major role in the pathogenesis of various cardiovascular and metabolic diseases. It increases the risk of glucose intolerance, atherogenic dyslipidemia and atherosclerosis, hypertension, metabolic syndrome, non-alcoholic fatty liver disease, and polycystic ovarian syndrome, etc [4,5]. In obesity, adipose tissue has been proved to be the site of secretion of

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metabolically active mediators (adipokines) including adiponectin [6]. Adiponectin, having variety of protective roles: anti-inflammatory, anti-atherogenic, cardio-protective, vasculo-protective and insulin sensitizing properties, is dysregulated in expression in obesity [7].

Serum adiponectin has been observed to be decreased in childhood obesity [8-11]. Serum adiponectin has been found inversely correlated with insulin resistance, TC and TG, but positively correlated with HDL-C, insignificant or no association with LDL-C and blood pressure [9,11-17]. In Bangladesh, very few studies have been done to observe the association between adiponectin and obesity and its cardiometabolic risk factors. One recent study conducted in adults showed that serum adiponectin was decreased in metabolically unhealthy adults (both normal weight and overweight/obese) [18]. However, correlation was not significant between obesity phenotypes and adiponectin. Serum adiponectin has not yet been investigated adequately on children in Bangladesh. So, the present study was conducted to find out the profile of serum adiponectin and its relationship with obesity and cardiometabolic risk factors in overweight/obese children.

Material and Methods

This cross-sectional study was conducted at the Department of Endocrinology, BSMMU from March 2019 to August 2020. The protocol was duly approved by the Institutional Review Board (IRB) of BSMMU before the initiation of the study. Informed written consent or assent was obtained from the participants and their guardians prior to the enrollment in the study.

Study population and anthropometry: Overweight or obese children between 6-18 years of age attending obesity clinic of the department were enrolled. Overweight and obese children having secondary causes of obesity were excluded. Standing height was measured by using a portable stadiometer in standing upright position on a flat surface without shoes. Weight was measured using a digital weighing machine. Height and weight were recorded to the nearest 0.1kg. Waist circumference (WC) for central obesity and blood pressure (BP) of each participant were measured. WC was measured by using a non-extensible and non-elastic measuring tape in mid respiration. BMI (kilograms per square meter) was calculated from height and weight measurements and was plotted on the CDC age and sex specific growth chart to determine the BMI-per-age percentile.

Collection of blood samples and biochemical analysis: About 5 ml of fasting blood sample was collected aseptically from each child by venipuncture for estimation of adiponectin and other biochemical investigations. Serum was immediately separated and preserved in -70^{0}C freezer until tested. Blood glucose, insulin and lipid profile were analyzed by automated analyzer using glucose oxidase, chemiluminescent immunoassay and glycerol phosphate oxidase methods respectively. Serum adiponectin (total) was measured by sandwich ELISA method using DRG ELISA kit, Germany.

Categorization of study population: Based on BMI percentile, children were classified into normal, overweight, grade-I, grade-II and grade-III obese as follows: normal - < 85th percentile, overweight - 85th to less than 95th, obese – equal to or greater than 95th, Grade I obesity - ≥ 95th percentile to < 120% of the 95th percentile, Grade II obesity - ≥ 120% to < 140% of the 95th percentile and Grade III obesity - ≥ 140% of the 95th percentile [19].

Central obesity was classified by waist circumference into: normal - 5th to < 90th percentile and increased (central obesity present) - equal to or greater than the 95th percentile [20].

Systolic and/or diastolic blood pressure was categorized into normal, pre-hypertension (elevated blood pressure), and stage 1 and 2 hypertension) for age (1-13 and ≥ 13 years), gender and height according to the “Fourth Report on Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents” (Table-1) [21,22].

Homeostasis model assessment for insulin resistance (HOMA-IR) was employed to measure the insulin resistance [23]. Formula used was - HOMA-IR = Fasting plasma insulin (μU/ml) × fasting plasma glucose (mmol/L)/22.5. HOMA-IR value above 3 was considered to be insulin resistance in children (corresponds to the 95th percentile healthy reference children) [24].

Table-1: *Categories of systolic and/or diastolic blood pressure for children aged 1-13 and ≥ 13 years*

Category/stage	Children aged 1-13 yrs	Children aged ≥ 13 yrs
	Systolic and/or diastolic BP	**Systolic and/or diastolic BP**
Normal BP	< 90th percentile	<120/<80 mm Hg
Elevated BP/Prehypertension	≥90th percentile to < 95th percentile, or 120/80 mm Hg to < 95th percentile (whichever is lower)	120/<80 to 129/<80 mm Hg
Stage 1 Hypertension	> 95th percentile to ≤ 99th percentile + 5 mm Hg, or 130/80 to 139/89 mm Hg (whichever is lower)	130/80 to 139/89 mm Hg
Stage 2 Hypertension	≥99th percentile + 5 mm Hg, or ≥ 140/90 mm Hg (whichever is lower)	≥140/90 mm Hg

Impaired fasting glycemia (IFG) and diabetes mellitus (DM) were defined as fasting plasma glucose (FPG) levels between 5.6 to 6.9 mmol/l and FPG ≥7 mmol/l respectively [25].

Dyslipidemia in children and adolescents was defined as at least one abnormal value for HDL, LDL, total cholesterol, or triglyceride [26,27]. Abnormal cutoffs value of individual blood lipids in children is shown in Table-2.

Table-2: *Plasma lipid ranges for children and adolescents [27]*

Category	Lipid range (mg/dl)		
	Acceptable	**Borderline**	**High/Low**
TC	<170	170-199	≥200
LDL-C	<110	110-129	≥130
HDL-C	>45	45-40	<40
TG			
For 0-9 year	<75	75-99	≥100
For 10-19 yrs	<90	90-129	≥130

Note: TC: total cholesterol, LDL-C: low-density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol, TG: triglycerides.

According to the International Diabetes Federation (IDF) metabolic syndrome was defined as abdominal obesity (waist circumference ≥ 90th percentile for age and sex) plus at least two of the following parameters: high triglyceride (TG) and/or low HDL-cholesterol, elevated blood pressure or hypertension, and impaired glucose tolerance or type 2 diabetes mellitus [28].

Data analysis

Data obtained from the study were analyzed using computer-based IBM SPSS Statistics software program version 26. The data distribution was assessed by Shapiro–Wilk test. Skewed continuous variables were log-transformed when necessary. Results were described in frequencies or percentages for qualitative values and mean (± SD/SE) for quantitative values with normal distribution. Subgroups made based on obesity and metabolic findings were compared by one way ANOVA or, unpaired independent t-test as applicable. Correlation between variables was analyzed by Pearson correlation coefficient test or Spearman rho correlation coefficient test as appropriate. P values ≤ 0.05 was considered statistically significant.

Results

A total of 78 overweight or obese children of 6-18-year of age were enrolled. The mean (±SD) age of the study population was 12.22 ± 2.56 years and the mean BMI was 28.79 ± 4.54 kg/m^2.The characteristics of the study population are depicted in Table-3.

Of the total participants, 53 (67.9%) were male and 71 (91%) were obese of which 51.3% and 32.1% had grade I and II obesity respectively. Majority (92.3%) had high waist circumference. Though the majority was normotensive (62.8%) and normoglycemic (87.2%), 97.5% of the population had dyslipidemia. The frequencies of baseline characteristics of study population are depicted in Table-4.

Table-3: *Characteristics of the study population (n=78)*

Variables	Mean ± SD
Age (yrs)	12.22 ± 2.56
BMI (kg/m^2)	28.79 ± 4.54
WC (cm)	93.12 ± 12.56
SBP (mm of Hg)	103.55 ± 15.36
DBP (mm of Hg)	68.17 ± 9.56
FPG (mmol/L)	5± 0.6
FPI (mmol/L)	17.36 ± 28.54
HOMA-IR	3.80 ± 6.08
TC (mg/dl)	182.64 ± 47.64
LDL-C (mg/dl)	110.24 ± 35.78
HDL-C (mg/dl)	40.03 ± 8.43
TG (mg/dl)	160.04 ± 94.45

Note: BMI=Body Mass Index, WC= Waist circumference, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, FPG=Fasting plasma glucose, FPI=Fasting plasma insulin, HOMA-IR= Insulin resistance by Homeostasis Model Assessment, TC=Total cholesterol, LDL-C=Low-density lipoprotein cholesterol, HDL-C=High-density lipoprotein cholesterol, TG=Triglyceride.

Table-4: *Baseline clinical characteristics of the study population (n=78)*

Variable		Number (%)
Gender	Male	53 (67.9)
	Female	25 (32.1)
BMI	Overweight	7 (8.9)
	Grade I obese	40 (51.3)
	Grade II obese	25 (32.1)
	Grade III obese	6 (7.7)
WC	Normal	6 (7.7)
	High	72 (92.3)
BP	Normal	49 (62.8)
	HTN/PreHTN	29 (37.2)
FPG	Normal	68 (87.2)
	IFG/Diabetes	10 (12.8)
HOMA-IR	Normal	56 (71.8)
	High	22 (28.2)
Dyslipidemia	None	2 (2.6)
	Borderline	12 (15.4)
	Present	64 (82.1)
MetS	Absent	51 (65.4)
	Present	16 (20.5)
	*Not applicable	11 (14.1)

*Note: MetS = Metabolic syndrome; *Below 10 years of age, cut-offs of metabolic and blood pressure variables are not well defined for metabolic syndrome.*

More than half (51/65.4%) of the study population was metabolically healthy obese whereas only 20.5% of the study population was metabolically unhealthy obese. The frequency of metabolic health categories is shown in Table-5.

Table-5: *Distribution of study population according to the different metabolic health categories (n=78)*

Metabolic health group	Number (%)
Metabolically healthy overweight	6 (7.7)
Metabolically healthy obese	45 (57.7)
Metabolically unhealthy overweight	0
Metabolically unhealthy obese	16 (20.5)
*Not applicable	11 (14.1)

*Note: *Below 10 years of age, metabolic health categories are not applicable as cut-offs of metabolic and blood pressure variables are not well defined for metabolic syndrome.*

The mean (±SD) serum adiponectin level in children and adolescents with overweight and obesity was 36.93 ± 17.85 µg/ml. Details of the distribution of serum adiponectin are shown in Table-6. There was no significant (p=0.676) difference of serum adiponectin between male (36.34 ± 16.55 µg/ml) and female (38.17 ± 20.65 µg/ml) children.

Table-6: *Statistical measures of serum adiponectin (n=78)*

Measures	Adiponectin (µg/ml)		
	Male (n=53)	Female (n=25)	Total
Central tendency			
Mean	36.34*	38.17*	36.93
Median	34.4	35.7	35.5
Mode	50.3	7.49	50.3
Dispersion/spread			
5th percentile	12.05	7.95	9.65
95th percentile	68.86	85.87	72.52
Minimum	6.8	7.49	6.8
Maximum	82.7	87.7	87.7
SD	16.55	20.65	17.85

Note: p value = 0.676 by independent t test for adiponectin level between male and female; SD = standard deviation*

One way ANOVA showed no significant (P= 0.582) difference of adiponectin levels among children

with different grades of overweight and obesity (Table-7). Although serum adiponectin level was higher in those with high waist circumference, the difference was not statistically significant (P=0.408) There was also no significant difference of serum adiponectin level between children with and without cardiometabolic risk factors or metabolic syndrome (Table-8). There was also no significant difference of adiponectin levels among various metabolic health categories.

No significant correlation between adiponectin level and measures of generalized or central obesity was observed (Table-9). Similarly, there was no significant correlation between adiponectin level and cardiovascular risk factors of obesity or metabolic health status.

Table-7: *Serum adiponectin levels of study population with different grades of obesity (n=78)*

Obesity category	Number	Serum adiponectin (Mean ± SE) µg/ml	P value
Grades of obesity			
Overweight	7	31.74±7.13	
Grade 1	25	37.53±1.71	0.582*
Grade 2	40	35.77±2.28	
Grade 3	6	45.16±4.55	
WC category			
Normal	6	31.17±5.54	0.408**
High	72	37.52±1.39	

*Note: *One way ANOVA was done; **Independent t test was done.*

Table-8: *Comparison of serum adiponectin levels between patients with and without cardiometabolic risk factors (n=78)*

CM risk factors	Category	Serum adiponectin (µg/ml) (Mean ± SD)	P value
SBP	Normal	37.47±16.94	0.792
	PreHTN/HTN	36.11±22.56	
DBP	Normal	35.15±16.62	0.12
	PreHTN/HTN	42.40±21.04	
FPG	Normal	36.39±17.69	0.493
	IFG/Diabetes	40.57±19.43	
HOMA-IR	Normal	35.93±16.98	0.437
	High	39.45±20.09	
TC	Acceptable	38.23±20.61	0.585
	Borderline/high	35.97±15.70	
LDL	Acceptable	37.07±18.87	0.935
	Borderline/high	36.74±16.71	
HDL	Acceptable	39.28±17.32	0.483
	Borderline/low	36.06±18.11	
TG	Normal	36.76±19.86	0.974
	Borderline/high	36.95±17.66	
MetS	Absent	37.24±17.09	0.975
	Present	37.41±22.62	
Metabolic health group	Metabolically healthy overweight	33.73±19.83	
	Metabolically healthy obese	37.71±16.88	*0.886
	Metabolically unhealthy obese	37.41±22.62	

*Note: *one way ANOVA was done; Independent t test was employed for the remaining parameters.*

Table-9: *Relationship of serum adiponectin with measures of obesity (generalized and central), cardiometabolic risk factors and metabolic health (n=78)*

Determinants of 'r'	r	P value
WC vs. adiponectin	0.098	0.392
BMI Z score vs. adiponectin	0.035	0.763
SBP vs. adiponectin	0.122	0.292
DBP vs. adiponectin	0.191	0.098
FPG vs. adiponectin	0.047	0.682
HOMA-IR vs. adiponectin	0.021	0.854
TC vs. adiponectin	0.017	0.881
LDL vs. adiponectin	-0.014	0.903
HDL vs. adiponectin	0.017	0.882
TG vs. adiponectin	-0.065	0.574
*Met health vs. adiponectin	-0.031	0.806

*Note: Pearson correlation coefficient test was done. *Spearman rho correlation coefficient was done; Met health = Metabolic health*

Discussion

This cross-sectional study was designed to study the serum adiponectin levels and its relationship with obesity and cardiometabolic risk factors among Bangladeshi obese children and adolescents. There was no association between serum adiponectin level and obesity (generalized and central) or cardiometabolic risk factors.

In the present study, serum adiponectin was paradoxically high, instead of low, irrespective of metabolic health status in comparison to reference range of adiponectin i.e. 4.58–8.30 µg/ml [29]. However, in most previous studies, serum adiponectin was found to be decreased in overweight/obese children compared to normal weight children [8-11]. A recent study conducted in Bangladeshi individuals less than 30 years of age with diabetes mellitus also found high adiponectin levels compared to healthy individuals [30]. High serum adiponectin, as found in this study, might be due to inherent high adiponectin in Bangladeshi children, which however may be confirmed by further studies. Other plausible causes of high adiponectin in this study could be due to calorie restriction and physical exercise undertaken by the study children prior to enrollment in study. In addition, most of the study population were healthy obese, as only 20.5% had metabolic syndrome. A higher percentage of metabolically healthy obese children might have contributed to observed higher adiponectin concentration.

In this study, there was no significant association found between adiponectin and generalized or central obesity. Most previous studies found a negative association between serum adiponectin and obesity (generalized and central) in children [8-11]. There were only few studies that contradicted these findings. In a study in non-diabetic Asian Indian teenagers, no correlation was found between adiponectin level and BMI and WC [31]. Plausible causes might be ethnic variation, unreported weight loss, and use of indirect and less sensitive measures of adiposity (BMI and WC).

In this study, no significant correlation was found between serum adiponectin and cardiometabolic risk factors or metabolic health status. Similar insignificant or no association of serum adiponectin with LDL-C was reported earlier [17]. Also, no correlation between adiponectin and HDL-C, TC or TG was found in children [21]. Numerous studies were thoroughly reviewed to find out the association of serum adiponectin with insulin resistance. Many studies reported inverse correlation between serum adiponectin with insulin resistance [9,11-14]. However, similar to this study only a few studies found no association between adiponectin and insulin resistance in children [10,15,31]. Relation of adiponectin with blood pressure is yet conflicting and unresolved. Similar to this study, no correlation between plasma adiponectin and blood pressure was observed in most studies in children [14,15,31]. In contrast to this study, in majority of studies adiponectin was positively correlated with HDL-C and inversely correlated with TC and TG in children [15-17]. Findings in the present study about adiponectin levels related to cardiometabolic risk factors could also be due to less number of children with metabolic syndrome and more metabolically healthy obese children.

However, the present study had some limitations. We did not measure the serum adiponectin levels of healthy age and sex matched non-obese children. In conclusion, the study has provided a profile of serum adiponectin levels in obese

children of Bangladesh. Also, the study has demonstrated no association between serum adiponectin levels and obesity or cardiometabolic risk factors in obese children.

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Conflict of interests

None of the author has conflict of interest.

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