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Relationship of Obesity with Abnormalities of Lipid Profile, Hba1c Level and Thyroid Profile in Children and Adolescents Aged 3-15 Years

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KEYWORDS
Obesity; Total Cholesterol; Triglyceride; LDL-C; HDL-C; HbA1c; fT4; TSH

ABSTRACT:

OBJECTIVE: To study the relationship of obesity with abnormalities of lipid profile, HbA1c levels and thyroid profile in children and adolescents aged 3-15 years and to find prevalence of metabolic syndrome in them.

METHODS: 70 obese children with BMI >95th percentile and 70 non-obese children in age group 3-15 years were included in our study. Each participant was subjected to anthropometric and biochemical assessment. Fasting blood lipid levels, fasting blood glucose levels, HbA1c levels, fT4 and TSH levels were performed. Measurements for waist circumference and blood pressure were taken.

RESULTS: Blood lipid levels including total serum cholesterol, triglycerides and serum LDL- cholesterol were significantly elevated in obese children and adolescents ($p < 0.001$) while serum HDL- cholesterol levels were significantly reduced ($p < 0.001$). FBS and HbA1c levels showed significant association of prediabetes and diabetes with obesity. Low fT4 and high TSH levels were significantly associated with obesity. Prevalence of hypertension was 24.29% in obese group compared to 5.71% in non-obese group. According to IDF consensus, prevalence of metabolic syndrome was 8.69% in obese group.

CONCLUSION: Obesity predispose children and adolescents to metabolic derangements including dyslipidaemia, prediabetes and diabetes, hypothyroidism and hypertension. Obesity poses a risk for children to develop metabolic syndrome at such a young age.

INTRODUCTION

Childhood obesity has reached epidemic levels in developed as well as in developing countries. Overweight and obesity in children are known to have significant impact on both physical and psychological health. Overweight and obese children are likely to develop non communicable diseases like diabetes, dyslipidaemia, thyroid disorders and cardiovascular diseases. Obesity also predispose them to hypertension and metabolic syndrome at much young age.

Overweight and obesity means an abnormal or excessive fat accumulation that may impair health. For children under 5 years of age[1]overweight is weight-for-height greater than 2 standard deviations and obesity is weight-for-height greater than 3 standard deviations above the WHO Child Growth Standards median. For children aged between 5–19 years[1]overweight is BMI-for-age greater than 1 standard deviation and obesity is greater than 2 standard deviations above the WHO Growth Reference median. The main cause of obesity and overweight is due to imbalance between calories consumed and calories utilized. Unhealthy dietary practices including fried and ready to eat foods, packed or canned foods, sedentary lifestyle, readily available various modes of transportation and more indoor activities all contribute to unhealthy weight gain and further health consequences.

Obesity has posed a major burden on healthcare system in India as well as around the globe. Implementation of lifestyle interventions and dietary counselling is required that would help keep the problem under control.

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In this study we aim to find association of lipid, HbA1c and thyroid derangements with obesity in children and adolescents.

MATERIAL AND METHODS:

This is a case control study which included 70 obese children and adolescents with body mass index (BMI) ≥95th percentile for age and sex, according to the standard growth references and 70 non-obese children (140 children in total) between 3 and 15 years old. Children were selected randomly who presented to Government Medical College, Amritsar in OPD and IPD.

Inclusion Criteria: Obese children aged 3-15 years with BMI >95th percentile for age and sex according growth references and equal number of non-obese in same age group.

Exclusion Criteria: All children reported by parents to be suffering from

1. Metabolic, endocrine, liver or kidney disorders
2. On long term use of corticosteroids and immunomodulators
3. On long term use of antiepileptic drugs.
4. Genetic syndromes of which obesity is a comorbid condition.

Anthropometric measurements of all the children were taken including weight, height, BMI and waist circumference. Blood pressure was noted. Fasting blood glucose levels (FBS), HbA1C levels, fasting blood lipid levels-including total serum cholesterol, triglycerides, LDL-cholesterol and HDL- cholesterol and fT4 and TSH levels were performed on each of the obese and non-obese participant.

Plasma glucose measurement was done with glucose dehydrogenase that catalyses the oxidation of glucose. The HbA1c analysis was performed using turbidimetric immunoassay method.

Total serum total cholesterol (TC) measurement was performed with an enzymatic, colorimetric assay. Antibodies against human lipoproteins were used to form antigen-antibody complexes with LDL, VLDL and chylomicrons in a way that only HDL cholesterol was selectively determined by an enzymatic cholesterol measurement. LDL was measured with homogeneous method without centrifugation steps for the direct measurement of LDL-cholesterol. In first step, LDL was selectively protected while non-LDL-lipoproteins were enzymatically processed. In second step, LDL was released and LDL-cholesterol selectively determined in a colour producing enzymatic reaction. Serum triglycerides were determined by colorimetric enzymatic test using glycerol-3-phosphate-oxidase (GPO).

FT4 and TSH tests were performed with Chemiluminescence immunoassay (CLIA) method.

Proper statistical analysis was done to compare abnormalities between lipid, thyroid and HbA1C levels and markers of metabolic syndrome between case and control group using t- test and ANOVA test. p value < 0.05 was taken as significant.

RESULTS: There were total 140 children (40 obese and 40 non-obese). The mean age of both groups was statistically insignificant. In obese children 16 cases (22.86%) had high cholesterol levels as compared to 1 (1.43%) in control group. Similarly 33 obese cases (47.14%) had high triglyceride levels compared to 2 (2.86%) in control group and 19 cases (27.14%) had high LDL-cholesterol levels compared to none in control group. Also 11 cases (15.71%) had low HDL-cholesterol levels compared to none in control group. All these findings were statistically significant (Table 1).

According to ADA classification,13 cases (18.57%) had HbA1c levels between 5.7-6.4%, thus belonging to prediabetes compared to 1 control (1.43%). 3 cases (4.29%) belonged to diabetes group with HbA1c levels >6.5% compared to none in the control group (‘p’<0.001). On the basis of fasting blood sugar levels,14 cases (20%) had prediabetes compared to 4 (5.71%) in control group and 3 children (4.29%) among cases were overt diabetic while none in control group were diabetic (‘p’ = 0.006) (Table 2).

In obese group 22 (31.43%) cases had low ft4 levels compared to 3 (4.29%) in control group. 1 (1.43 %) case had high fT4 levels compared to 1 (1.43%) in control group. Also 24 (34.29%) cases had high TSH levels compared to 2 (2.86%) in control group. None of the cases had low TSH levels while 1 (1.43%) in control group had low TSH levels. These results were also statistically significant. (Table3).

13 cases (18.57%) had high SBP levels compared to 3 (4.29%) in control group. Also 17 cases (24.29%) had high DBP levels compared to 4 (5.71%) in control group (Table 4).In our study, IDF consensus was used to diagnose metabolic syndrome in case and control group. As per IDF consensus, metabolic syndrome couldn’t be diagnosed in children aged less than 10 years. In case group, total number of children in between 10-15years of age were 46. In control group, there were 40 children between 10-15 years of age. So prevalence of metabolic syndrome in children between 10-15 years of age was evaluated. In case group it was present in 4 children (8.69%) while none of the children in control group was diagnosed with metabolic syndrome. The difference was not significant with p value=0.056

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TABLE 1: COMPARISON OF LIPID PROFILE IN CASES AND CONTROLS

LIPD PROFILE		Case group		Control group	
		No. of cases	%age	No. of cases	%age
Cholesterol (mg/dl)	< 200mg/dl	54	77.14	69	98.57
	> 200mg/dl	16	22.86	1	1.43
	Total	70	100.00	70	100.00
	'p' Value	'p'<0.001			
Triglyceride(mg/dl)	Normal	37	52.86	68	97.14
	High	33	47.14	2	2.57
	Total	70	100.00	70	99.71.00
	'p' Value	'p'<0.001			
LDL Cholesterol(mg/dl)	< 130 mg/dl	51	72.86	70	100.00
	≥130 mg/dl	19	27.14	0	0.00
	Total	70	100.00	70	100.00
	'p' Value	'p'<0.001			
HDL Cholesterol(mg/dl)	< 40mg/dl	11	15.71	0	0
	≥ 40mg/dl	59	84.29	70	100
	Total	70	100.00	70	100.00
	'p' Value	'p'<0.001			

TABLE 2:DISTRIBUTION OF HbA1c and FBS LEVELS IN CASES AND CONTROLS

		Case group (n=70)		Control Group(n=70)		Total	
		No. of cases	% age	No. of controls	% age	No. of cases	% age
HbA1c (mg/dl)	<5.7	54	77.14	69	98.57	123	87.85
	5.7-6.4	13	18.57	1	1.43	14	10
	>6.5	3	4.29	0	0.00	3	4.26

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	'p' value	<0.001, DF =2					
FBS(mg/dl)	<100	53	75.71	66	94.29	119	85.00
	100-125	14	20	4	5.71	18	12.85
	>126	3	4.29	0	0	3	02.14
	'p' value	<0.006, DF =2					

TABLE 3: COMPARISON OF fT4 and TSH LEVELS IN CASES AND CONTROLS

		Total Number of Cases		Control	
		No. of cases	Percentage	No. of cases	Percentage
fT4 (ng/ml)	Increased	1	1.43	1	1.43
	Decreased	22	31.43	3	4.29
	Normal	47	67.14	66	94.28
	Total	70	100.00	69	100.00
	'p' Value	p <0.001			
TSH (µIU/L)	Increased	24	34.29	2	2.86
	Decreased	0	0	1	1.43
	Normal	46	65.71	67	95.71
	Total	70	100.00	70	100.00
	'p' Value	p <0.001			

TABLE 4: COMPARISON OF SYSTOLIC BLOOD PRESSURE (mmHg) AND DIASTOLIC BLOOD PRESSURE (mmHg) IN CASES AND CONTROLS

BLOOD PRESSURE		Case group		Control group	
		No. of cases	% age	No. of cases	% age
Systolic Blood Pressure (mmHg)	<95th percentile	57	81.43%	67	95.71%
	>95th percentile	13	18.57%	3	4.29%
	Total	70	100.00%	70	100.00%
	'p' Value	'p' = 0.008, DF = 1			
Diastolic Blood Pressure (mmHg)	<95th percentile	53	75.71	66	94.29
	>95th percentile	17	24.29	4	5.71

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	Total	70	100.00%	70	100.00%
	'p' Value	'p' = 0.002, DF = 1			

DISCUSSION:

Obesity and overweight in the childhood represent a severe public health problem in children and adolescent life. This is a case control study conducted in Government Medical College, Amritsar to find abnormalities in lipid, thyroid profiles and HbA1c levels in obese children and compare it with healthy normal counterparts. It also aimed at finding prevalence of metabolic syndrome in such children.

In this study, as shown above, 16 (22.86%) obese children had high cholesterol levels compared to 1 (1.43%) in non-obese group. Mean serum cholesterol level in obese children was 190.44±57.29 mg/dl while in non-obese group was 145.97±15.40 mg/dl. The difference was significant with the p value <0.001. Serum triglyceride levels were significantly higher among obese children. 33 (47.14 %) children in case group with mean 141.28±62.48 mg/dl had high triglyceride levels compared to 2 (2.86%) in control group with mean 95.80±16.46 mg/dl ('p' value = <0.001). Serum LDL levels were high in 19 (27.14%) children in case group with mean 141.28±62.48 mg/dl ('p' value = <0.001). 11 (15.71%) cases had low HDL levels ('p' value = <0.001) with mean of 44.47±4.32 mg/dl which is an important component of metabolic syndrome. No one in control group had high LDL or low HDL levels. Our study showed statistical significance in both the groups. Similar observations were made in the study done by Friedland O et al[2] on obesity and lipid profiles in children and adolescents, 31% of the obese subjects had borderline and 21% had elevated cholesterol levels compared to only 12% and 4%, respectively, among the controls. Similarly, in study done by BerzazinskiM et al[3] regarding lipid disorders in children living with overweight and obesity, the most common lipid disorders were decreased high-density lipoprotein cholesterol (HDL-C) levels (present in 20.55% of the girls and 23.79% of the boys) and elevated low-density lipoprotein cholesterol (LDL-C) (present in 15.31% of the girls and 14.25% of the boys). Cizmecioglu FM et al[4], in a Turkish study showed 42.9% dyslipidaemia in school aged obese children. Another study done by HashemipourM et al[5]reported as 69.9% dyslipidaemia in 2064 obese Iranian children. Korsten-Reck U et al[6] in their study found 45.8% of the overweight children had an abnormal lipid profile. Jacob AS and Reetha G[7], in an Indian study reported dyslipidaemia in 63% of children and high LDL cholesterol being the most frequent lipid abnormality. In study by Khan MN and Khaleel M[8], significant higher cholesterol and triglycerides were observed in obese group compared to non-obese group. On the contrary, obese group had significant lower HDL-C concentration than the non-obese group.

As presented in this study, according to ADA classification based on HbA1c levels, 13 (18.57%) cases belonged to pre-diabetes group with HbA1c levels between 5.7-6.4% compared to 1 (1.43%) in control group and 3 cases (4.26%) belonged to diabetes group (>6.5%) compared to none in the control group. This was significant with 'p' value <0.001 (table no. 6) . Mean HbA1c levels in obese group was 5.48 ±0.55% while in non-obese group was 5.13±.026% ('p' value = 0.000). Findings of our study were similar to the study done byKisokanth G et al[9], nearly 20% and 3.3% of the HbA1c were in the pre-diabetes and diabetes category respectively. The mean HbA1c was significantly higher in male and obese compared to their counterparts (p<0.05). Study by Hovestadt I et al[10]showed that obesity was related to higher HbA1c values ($p < 0.001$).

In our study, as shoen in table no. 7, 14 cases (20%) had pre-diabetes on the basis of fasting blood sugar levels compared to 4 (5.71%) in control group and 3 children (4.29%) among cases were overt diabetic while none were diabetic in control group. The difference was significant with 'p' value 0.006. Obese group had higher mean FBS levels of being 96.40±18.15 mg/dl compared to control group with mean being 87.09±9.55 mg/dl ('p' value = 0.000).Similarly, in a cohort study conducted by Al Amiri E et al[11] in Emirati overweight/obese children and adolescents, the prevalence of pre-diabetes was found in a higher proportion of children (21.9 %). Also, study conducted by Nowicka P et al[12] carried out among a multi-ethnic cohort of 1,156 obese children and adolescents in New Haven, Connecticut found the similar findings with prevalence of pre-diabetes in 21% of children.

In this study, 22 (31.42%) cases had low fT4 levels compared to 3(4.29%) in control group while 1 (1.43%) case had high fT4 levels same as in control group (table no. 8 and 9). Mean fT4 levels in case group is 1.12±0.26 ng/dl and in control group is 1.22±0.21 ng/dl ('p' value = 0.013). As outlined in table no. 10 and 11, 24 (34.28%) cases had high TSH levels compared to 2 (2.86%) controls. None in obese group has low TSH levels while 1 (1.43%) in non-obese had low TSH levels. Mean TSH levels in case group is 4.07±3.93 µIU/ml and in control group is 2.57±2.21 µIU/ml ('p' value = 0.006). High TSH and low fT4 levels were statistically significant in obese

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group with p value <0.001. Thus, our study found hypothyroidism is significantly associated with obesity among children. This was similar to study done by Ghergherehchi R and Hazhir N[13],in which levels of TSH and total T4 were significantly higher in children with obesity compared with the control group. Subclinical hypothyroidism was significantly higher in children with obesity (14.7%) compared with normal subjects (‘*p’* = 0.02).Also in the study done byEmokpae MA and Obazelu PA[14], Triiodothyronine (‘p’ < 0.05), TSH (‘p’ < 0.02), and T3/T4 ratio (‘p’ < 0.05) correlated positively with BMI in obese children and adolescents. Serum T3, TSH, and T3/T4 ratio correlated positive with BMI in obese Nigerian children and adolescents. Findings of our study were in contrast to study done by LekhwaniS et al[15], in which thyroid stimulating hormone (TSH) remained unaltered in both obese and non-obese group. According to the data presented in their study there was no effect of obesity over the thyroid hormones level, though levels were on higher side in morbidly obese cases.

In this study, 13 (18.57%) children in obese group had high SBP levels compared to 3 (4.29%) in non-obese group (‘p’ value = 0.008) as given in table no. 12. Mean SBP in obese group was 106.43±15.28 mmHg while in control group was 98.26±9.82 mmHg (‘p’ value = 0.000). 17 (24.29%) obese children showed high DBP levels compared to 4 (5.71%) in non-obese group (‘p’ value = 0.002) (table no. 13). Mean DBP in case group 70.16±10.76 mmHg and in control group is 65.74±9.06 mmHg (‘p’ value = 0.010). Overall prevalence of hypertension in our study was 24.29% in case group compared to 5.71 % in control group. This was in accordance with study done by Mohan B et al[16], in which prevalence of hypertension was 4.6% in non- obese children, 12.5% in overweight and 28% in obese children. Similarly in study done by Jin Kwak Y et al[17], the prevalence of hypertension was 6% in non-obese children, 16.7% in overweight group and 29.8% in the obese group.

Our study used IDF consensus criteria to diagnose metabolic syndrome in case and control group. So, we were not able to diagnose prevalence of metabolic syndrome in children younger than 10 years of age.In our study 4 children in obese group between 10-15 years of age were diagnosed with metabolic syndrome with prevalence of metabolic syndrome being 8.69% in case group while none of the children in control group were diagnosed with it (table no. 14 and 15). This was comparable to a study in Turkey that adapted the ATP III criteria for metabolic syndrome for children and adolescents, 2.2 percent of adolescents had metabolic syndrom.[18] On the contrary, according to study by Atabek ME et al[19], metabolic syndrome was found in 27.2%, with a significantly higher rate among adolescents aged 12-18 years (37.6%) than among children aged 7-11 years (20%) (p < 0.001).

CONCLUSION:

To conclude, obesity in children and adolescents is associated with multitude of health problems such as dyslipidemia (most commonly hypertriglyceridemia), prediabetes, diabetes and hypothyroidsim. HbA1c can be used as an important diagnostic marker to assess insulin resistance and hence diabetes in children and adolescents. Obese children are more prone to cardiovascular problems like hypertension at an early age and obesity predisposes children to metabolic syndrome. Children who have obesity may experience bullying by their peers. This can lead to loss of self esteem, anxiety and depression.

Prevention at all means is better than cure. Screening for obesity in children should be introduced in all schools and colleges and parents should be guided to make sure their child sees the doctor for well child checkups at least once a year. Importance of balanced diet and exercise should be imparted to children at both school and at home. With this background, it is recommended that all efforts should be made by healthcare professionals to curb the menace of overweight and obesity and its complications in children and adolescents.

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