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Inflammatory Markers in Obese Children

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ABSTRACT

Background: Childhood obesity has become a crucial problem in both developed and developing countries. In 2018, the World Health Organization estimated 41 million infants and children were obese. This number is predicted to increase to 70 million by 2025.

Aim of the Work: To assess: Inflammatory markers: (tumor necrosis factor (TNF)-alpha- high sensitive CRP (HS- CRP) in obese children and the impact of obesity and inflammatory markers as risk factors for morbidity in obese children.

Patients and Methods: This study was a cross-sectional comparative study. The study group comprised forty obese and thirty control Egyptian children who were recruited from pediatric outpatient's clinic of Al-Zahra University Hospital and National Nutrition Institute. They were 24 females (60%) and 16 males (40%) obese children. Their ages ranged between 4-8 years.

Results: We found that there was statistically significant increase in high birth weight, decreased physical activity, formula feeding, junk food, high serum of tumor necrosis factor –alpha (TNF-alpha) and high sensitive CRP (hs-CRP) in obese children than control group.

Conclusion: Inflammatory mediators as hs-CRP and TNF –alpha are elevated in obese and overweight children more than healthy control group, which may indicate the presence of chronic inflammation.

Keywords: Tumor necrosis factor-alpha - High-sensitivity C-reactive protein - Lipid profile.

INTRODUCTION

Children are identified as a priority target group of obesity interventions worldwide. Without adequate intervention to prevent and manage childhood obesity, obese children will face chronic lifelong diseases, including cardiovascular disease, diabetes and cancer. Coping with childhood obesity is a cornerstone in preventing long-term complications and reducing premature deaths from chronic non-communicable diseases (NCDs) [(1)].

With the increase in adiposity that occurs with weight gain, a persistent low-grade inflammatory state is created. The most commonly studied inflammatory markers associated with obesity are the cytokines, tumor necrosis factor α and interleukin-6, and the acute-phase reactant, C-reactive protein [(2)].

Increased levels of inflammatory markers lead to physiological mechanisms that negatively affect health. Inflammatory markers have been shown to damage the innermost layers (intima media) and lining (endothelium) of blood vessels through the stimulation of atherosclerotic lesions that also cause hypertension and thrombosis [(3)].

In addition to cardiovascular dysfunction, inflammatory markers affect metabolic control by negatively influencing insulin sensitivity and glucose transport. Thus, obese individuals with elevated levels of inflammatory markers may experience physiological adaptations that negatively affect metabolic and cardiovascular health [(4)].

Early identification of inflammatory markers may provide another component to identifying those at risk of cardiovascular events and may even be stronger predictors of these events than are traditional risk factors (e.g., plasma total cholesterol, triglycerides, low-density lipoprotein, and high-density lipoprotein) [(5)].

Overall, these studies demonstrate that inflammatory markers are increased in obese children, leading to the development of risk factors for chronic diseases that are typically associated with adults [(6)].

AIM OF THE WORK

Was to assess:

1) Inflammatory markers: (tumor necrosis factor (TNF)-alpha and high sensitive CRP (HS- CRP) in obese children.
2) The impact of obesity and inflammatory markers as risk factors for morbidity in obese children.

PATIENTS AND METHODS

The current study was cross sectional descriptive comparative study. It was conducted on 70 children aged from 4-8 years. All Children were selected from outpatient clinic of Al-Zahraa University Hospital and National Nutrition Institute, Cairo, Egypt from October 2017 to February 2018. They were divided into two groups:

Patient group:

Included 40 obese children according to definition of Centers for Disease Control and Prevention (CDC) aged from 4-8 years of both sexes[(7)].

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Control group:

Included 30 apparently healthy children were taken as a control group. They were age and sex matched with patient group.

Inclusion criteria included **Obese children according to** Center of disease control and prevention growth charts (BMI at or > the 95th percentile). Boys and girls aged from 4-8 years.

Children were excluded from the study if their age < 4 yrs or > 8 years and obese children with medications causing weight gain as sulfonylureas, cortisol, tricyclic antidepressant and monoamine oxidase inhibitors. Hormonal disorders as growth hormone deficiency or resistance, hypothyroidism, or glucocorticoid excess. Any infectious disease. Genetic disorders as Prader-Willi syndrome, Down syndrome, Turner syndrome, or Laurence Moon Biedel syndrome). Children with skeletal abnormalities and congenital malformation. Children with chronic disease.

All studied children were subjected to full medical history taking with stress on: Personal History: Included name, age (date of birth), sex, birth weight, Medical History of any present or chronic illness (renal, hepatic, endocrinal). History of drug intake (steroids). A dietetic history including feeding during the first 6 months, taking fast food, consumption of nutritional food as vegetables and fruits and consumption of starchy and sweetie food. **Past history** diseases, operations, **Family history:** family history of obesity, diabetes, cardiovascular diseases eating disorders, gall-bladder diseases and hypertension.

- **Review of all systems:** The review of systems included asking about symptoms of potential co-morbidities of obesity as difficult breathing and asthma, sleep apnea syndrome, recurrent abdominal pain, joint pain, sleep disorders, polyuria, polydipsia and easy fatigability.

Complete physical examination was performed to all participants with focusing on signs of co-morbid conditions or any underlying conditions that may lead to excessive weight gain.

All patients were subjecetd to thorough clinical examination stressing on:

a- Blood pressure:

b- Skin examination: Acanthosis nigricans is a hyperpigmented area.

Anthropometric measures were taken from all the participants during their visit to the clinic including: Weight. Height. Body mass index (BMI). Waist Circumference. Hip circumference (HC). Waist/Hip Ratio (WHR). Triceps skin fold thickness.

Laboratory investigation:

These were done for both cases and control: After an overnight fast for at least 8 hours, 5 ml of venous blood were withdrawn from all participants. Blood was left to clot and serum was separated and stored frozen at -20° C for hormonal assay (high sensitive-C reactive protein and tumor Necrosis Factor –α). These samples were subjected for the following Bios ELISA Kit was used for quantitative determination of C - reactive protein concentration in human serum (Chemux Bioscience, Inc South San Francisco, USA). **Expected normal values: (68 -8200 ng/ml) [(7)].** TACE ELISA kits was used for quantitative detection of human TNF-alpha concentration in serum (catalog NO E1319gh, EIA WWW.eiaab.com). **Detection range: (0.31 - 20 ng/ml). Fasting blood glucose**: was measured by colorimetric enzymatic method GOD-POD by using a fully automated biochemistry device B T 1500 **(biotecnica instruments, Italy). Reference range:** 70-115 mg/dl [(7)]. **Lipid profile:** Total cholesterol, serum triglyceride and high-density lipoprotein (HDL) were measured by colorimetric enzymatic method CHOD- PAP by using a fully automated biochemistry device B T 1500 **(biotecnica instruments, Italy).** While low-density lipoprotein (LDL), was calculated by the equation: {total cholesterol – HDL – (triglyceride/5)} [(8)].

Ethical approval and written informed consent:

An approval of the study was obtained from Al-Azhar University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation.

Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD), median, and range. Qualitative data were expressed as frequency and percentage.

The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square (x^2) test of significance was used in order to compare proportions between two qualitative parameters.
- P-value <0.05 was considered significant.

RESULTS

This case control study was conducted on 40 obese children with BMI at or >95th percentile and 30 healthy children as control group who were matched for sex and age. Their age ranged between 4-8 years. Both groups included 35 females and 35 males. In this study, we found that the incidence of obesity was more in females than males. When we studied the birth weight as a contributing factor of childhood obesity, the percentage of high birth weight was (30% vs. 0%) between obese and control groups. there was a statistically significant decrease in physical activity in

obese children when compared to control group (Table 1)**.**

When we studied the level of education of mothers, we found that mothers of obese children had statistically lower level of education and positive family history of obesity than control children**.** Regarding the most common complaint of obese children, we found statistically significant more positive history of asthma in obese children than control group. There was a statistically significant more sleep disorder (obstructive sleep apnea) in obese than in control groups. As for the effect of fast food on obesity, we found that obese children consume statistically significant more junk food than control group**.** Artificial feeding was more common in obese children than in control group especially in the first 6 months of life**.** According to the presence of acanthosis nigricans, there was highly significant higher frequency of acanthosis nigricans in obese children than control group**.** Easily fatigability of obese children was more in the control group; there was statistically significant difference **(p=0.056) (Table 1)**.

The results of this study will be illustrated in the following tables and figures.

Table (1): Descriptive data of studied groups

		Obese cases (n=40)		Control (n=30)		P value
		No.	%	No.	%	
Sex	M	16	40.00%	19	63.30%	0.053
	F	24	60.00%	11	36.70%	
Birth weight	high	12	30.0%	0	0.0%	0.001
	normal	28	70.0%	30	100.0%	
Physical activity	yes	13	32.5%	24	80.0%	< 0.001
	no	27	67.5%	6	20.0%	
Education of mother	Low	29	72.50%	11	36.70%	0.003
	High	11	27.50%	19	63.30%	
Family history of obesity	yes	21	52.50%	0	0.00%	<0.001
	no	19	47.50%	30	100.00%	
History of asthma (difficulty of breathing)	yes	18	45.00%	3	10.00%	0.002
	no	22	55.00%	27	90.00%	
Taking junky food	yes	25	62.5%	7	23.3%	0.001
	no	15	37.5%	23	76.7%	
Feeding in first 6 months	AF	25	62.50%	4	13.30%	< 0.001
	BF	11	27.50%	25	83.30%	
	BF+AF	4	10.00%	1	3.30%	
Sleep disorder	yes	14	35.00%	2	6.70%	0.005
	no	26	65.00%	28	93.30%	
Acanthosis nigricans	yes	26	65.00%	0	0.00%	< 0.001
	no	14	35.00%	30	100.00%	
Easily fatigability	yes	15	37.50%	5	16.70%	0.056
	no	25	62.5%	25	83.3%	

Table (2): Anthropometric measurements and blood pressure of studied groups

	Obese Cases (n=40)				Control (n=30)				value
	Mean±SD	Median	Minimum	Maximum	Mean±SD	Median	Minimum	Maximum	
Weight (kg)	39.94±8.99	40.00	24.00	65.5	19.87±2.53	20	15	25	0.001
Height (cm)	113.54±11.13	115.00	90.00	138	113.68±7.46	113.5	102	131.5	0.924
BMI (kg/m^2)	30.55±1.86	30.35	25.40	35	15.34±1.05	15.35	13.6	17.3	0.001
Waist circumference (cm)	69.68±10.49	68.5	55	107	51.53±2.91	51	45	56	0.001
Hip circumference (cm)	79.1±11.2	78.5	62	117	62.77±3.22	62.5	56	69	0.001
W/H ratio	0.88±0.02	0.88	0.83	0.92	0.81±0.02	0.81	0.78	0.85	0.001
triceps skin fold(mm)	15.45±1.66	15.5	12	20	5±0.8	5	4	6	0.001
Systolic BP (mmgh)	106.88±10.66	110	90	140	97±6.51	100	90	110	0.001
Diastolic BP (mmgh)	68.5±7.7	70	60	85	65.67±4.87	70	60	70	0.133

BMI=weight (Kg)/height (m^2),

Table (2) showed highly significant difference increase of weight and body mass index, waist and hip circumferences, W/H ratio and triceps skin fold in obese group compared to control and no significant difference in height. There were highly statistically significant increased systolic blood pressure in obese than control group.

Table (3): Clinical evaluation of studied groups

	P value				
	Mean±SD	**Median**	**Mean±SD**	**Median**	
FBS (mg/dl)	**86.3±13.06**	**86**	**85.3±15.27**	**83**	**0.577**
s. cholesterol	**155.95±33.15**	**154**	**144.2±19.33**	**143.5**	**0.091**
s. triglyceride	**115.01±9.95**	**104.5**	**85.73±4.25**	**81.5**	**0.02**
HDL	**41.2±8.25**	**39**	**34.93±5.3**	**34**	**0.363**
LDL	**90.23±3.93**	**87.5**	**91.98±20.57**	**89.5**	**0.771**
TNF-alpha(ng/ml)	**35.56±2.95**	**30.5**	**11.1±2.33**	**12**	**<0.001**
hs-CRP(ng/ml)	**7346.25±294.07**	**9175**	**1616±341.86**	**1231**	**<0.001**

Table (3) shows that there were statistically significant differences between obese than control group as regard serum triglyceride and no significant differences with other lipid profile and fasting blood sugar.

There were highly statistically significant increase in TNF-alpha and hs-CRP in obese than control group as regard**.**

DISCUSSION

In this study, we found that the incidence of obesity was more in females (60%) than males (40%). There was statistically significant difference between obese cases and control.

This agrees with the studies done by **Mudur** [(8)]**,** in three major Indian cities who found that girls were more overweight and obese than boys. These studies therefore indicate that the sex of the child has an influence on the prevalence of overweight and obesity. Some authors stated that the onset of obesity and overweight occur around the ages of 5-6, especially among girls.

As regard the birth weight as a contributing factor of childhood obesity, there was statistically significant increased percentage of high birth weight in obese than in control group. Our result agrees with **Gillman *et al.*** [(9)]**,** who showed that a higher birth weight predicted increased risk of overweight in children and adolescence. On the other hand, **Strufaldi *et al.*** [(10)]**,** stated that the relationship between birth weight and childhood obesity is still controversial, suggesting that there was no association between birth weight and overweight or obesity in schoolchildren.

Our study showed that, there was a statistically significant decrease in physical activity in obese children when compared to control group. This agrees with **Güngör** [(11)]**,** who showed that low levels of physical activity, greater hours of TV/other screen time are associated with childhood obesity risk. On the other hand, **Bambra *et al.*** [(12)] found that there were no significant differences between the groups for physical activity on weight outcomes. This contradiction can be explained by the cultural difference among countries**.**

In the current study, regarding to family history of obesity, there was a statistically significant difference in obese children with positive family history of obesity than control children**.** This is in agreement with **Badawi *et al.*** [(13)] who revealed that positive family history of overweight and/or obesity were significantly associated with childhood obesity.

When we studied the most common complaint of obese children, we found positive history of asthma or difficulty of breathing was more frequent in obese children than in control group with statistically significant difference**.** These results agrees with **Dixon *et al.*** [(14)], who stated that obesity is a risk factor for breathing problems in people with and without asthma, however, the problems are worse in those with asthma. Along with the pro-inflammatory cytokines and factors secreted by adipose tissue, obese individuals have excess pressure on the chest, not from inflammation but from extra weight. **Sutherland** [(15)]**,** who revealed that functional residual capacity is reduced in obese individuals, which is associated with pressure on the lungs, and reduction of airway diameter. Airway diameter reduction can also disrupt smooth muscle function and lead to airway obstruction**.** Tidal volume, the volume of air in a normal breath, is also decreased in obese asthmatics.

In our study we found that there was a statistically significant higher frequency in sleep disorder (obstructive sleep apnea) in obese than in control groups. Supporting our findings **Hakim *et al.*** [(16)]**,** who stated that obesity seems to increase the risk of sleep related breathing disturbances in children and adolescents.

When we studied the effect of fast food on obesity, we found that obese children consumed junk food more than control group. There was a statistically significant difference between the two groups. Our finding was supported with **Talat and Shahat** [(17)]**,** who found that taking fast food is a risk factor for overweight and obesity in children. **Rosenheck** [(18)]**,** reported that, according to a systematic review of 16 studies conducted by the Harvard School of Public Health, strong evidence exists linking fast food consumption with increased caloric intake leading to weight gain. The most likely biological mechanism linking fast food and obesity is the high energy density of fast food**.**

In our study, according to the presence of acanthosis nigricans, there was highly significant increased frequency of acanthosis nigricans in obese

children than control group**.** Our result agrees with **Guran *et al.* [19],** who showed that acanthosis nigricans is an important predictor of the insulin resistance in childhood obesity, and this is in agreement with **Sivakumar and Banupriya [20],** who reported that acanthosis nigricans had a significant association with obesity. Acanthosis nigricans and skin tags presence had a strong correlation to the presence of metabolic syndrome.

In this study, the most common complaint of obese children was easily fatigability in obese children more than in the control group. There was statistically significant difference. Also **Fayed *et al.* [21]** found that the most frequent complaints in obese group was easy fatigability (85%). **Maloney *et al.* [22]** also found that a twofold increase in the likelihood of having the metabolic syndrome (including abdominal obesity) in those classified as chronic fatigue syndrome.

The present study demonstrated statistically significant increase of anthropometric measurements including body weight, body mass index, waist circumference, hip circumference, waist /hip ratio and triceps skinfold in obese group than control. Our findings agree with **Weiss *et al.* [23]** who reported that body mass index is a validated and widely accepted parameter to define the degree of obesity in children and adolescents. Because especially visceral obesity is associated with an increased risk for associated metabolic and cardiovascular diseases.

Our result is in agreement with **Hsieh *et al.* [24]** who reported that waist and hip circumferences, waist-to-hip ratio seem to be better predictors of cardiovascular risk factors in obese children than body mass index alone, and waist circumference may predict risk for obesity-related comorbidities, such as dyslipidemia and diabetes, beyond that predicted by BMI.

Our findings suggest that high body mass increase exerts greater influence on systolic blood pressure than diastolic blood pressure in obese and control group respectively**.** Our result agrees with **Li *et al.* [25]**, who found stronger correlation between body mass index and systolic blood pressure. This observation goes with other studies that have also demonstrated that systolic blood pressure is more affected by body mass index than diastolic blood pressure. Also **Burgos *et al.* [26]** found that some reports demonstrated an association between systolic blood pressure and body mass index, suggesting that obesity is a strong risk factor for high blood pressure development in childhood and adult life.

In the current study, we found that there was statistically significant higher value of serum triglyceride level measured in obese children than healthy children**.** We also found that there was no significant differences in other parameter of lipid profile and fasting blood sugar. **Laakso *et al.* [27],** showed that **i**n the dyslipidemia associated with obesity, triglyceride levels are usually between 100 and 400 mg/dL). **CDC [28]** also reported that data indicate this pattern is highly prevalent, present in 42.9% of children with BMI>95th%ile. Insulin resistance, another common feature in obese children and adolescents, contributes significantly to development of the combined dyslipidemia of obesity by enhancing hepatic delivery of non-esterified free fatty acids for triglyceride production and sequestration into triglyceride-rich lipoproteins.

In the present study, there was higher levels of hsCRP in the blood of obese children when compared to control group with highly significant difference**.** This indicates the presence of inflammatory state in obese children. This coincides with **Ebrahimi *et al.* [29],** who found that the increased levels of high-sensitivity C-reactive protein (hs-CRP), fibrinogen, amyloid-A, monocyte-chemo attractant protein-1 (MCP-1), plasminogen inhibitors (PAI-1), cytokines (TNF-a, IL-6, etc.) and other biological markers of inflammation in the blood of obese subjects confirmed the presence of chronic inflammation. The action of these inflammatory molecules may represent the molecular link between adipose tissue and the metabolic and cardiovascular complications in obese.

Our finding is supported by the results of **Toprak *et al.* [30],** who revealed that obese children experience increased levels of high sensitive C-reactive protein compared with children who are not obese. Recently, body fatness in childhood was found to be a major predictor of C- reactive protein in young adulthood.

We found high serum level of tumor necrosis factor –alpha (TNF-alpha) in obese children and there was statistically significant difference in TNF-alpha among the obese children compared with control group**.** Our result is in accordance with **Shengrong *et al.* [31]**, who revealed that obese children have a significant elevation in the serum levels of TNF compared with lean children.

Nakamura *et al.* [32], stated that although it was initially suggested that the main source of TNFα in obesity were adipocytes, it is now well recognized that macrophages infiltrated in adipose tissue are responsible for increased levels of this cytokine.

CONCLUSION

- Obesity is prevalent among primary school children, especially in female children than boys and it runes in families.
- High birth weight, decreased physical activity, formula feeding, junk food are more risk factors for obesity.
- Anthropometric measurements are simple, inexpensive and non-invasive methods to identify overweight and obesity.
- Inflammatory mediators as hs-CRP and TNF –alpha are elevated in obese and overweight children more than healthy control group, which may indicate the presence of chronic inflammation.
- Our observation adds to the hypothesis that the inflammatory state that occurs in obesity may

contribute to elevation of blood pressure and associated with an increased risk of cardiovascular disease.

REFERENCES

1. **Pamungkas RA and Chamroonsawasdi K (2019):** Home-Based Interventions to Treat and Prevent Childhood Obesity: A Systematic Review and Meta-Analysis. Behavioral Sciences, 9(4): 38.
2. **Esteghamati A, Morteza A, Khalilzadeh O *et al.* (2012):** Physical inactivity is correlated with levels of quantitative C-reactive protein in serum, independent of obesity: Results of the national surveillance of risk factors of non-communicable diseases in Iran. J Health Popul Nutr., 30: 66-72.
3. **Ogden CL, Carroll MD, Kit BK *et al.* (2012):** Prevalence of obesity and trends in body mass index among US children and adolescents, 1999-2010. JAMA., 307(5): 483-490.
4. **Arslan N, Erdur B and Aydin A (2010):** Hormones and cytokines in childhood obesity. Indian Pediatr., 47: 829-839.
5. **Skinner AC, Steiner MJ, Henderson FW *et al.* (2010):** Multiple markers of inflammation and weight status: Cross-sectional analyses throughout childhood. Pediatrics, 125(4): e801-9.
6. **Galcheva SV, Iotova VM, Yotov YT *et al.* (2011):** Circulating proinflammatory peptides related to abdominal adiposity and cardiometabolic risk factors in healthy prepubertal children. Eur J Endocrinol., 164: 553-558.
7. **Werner W, Rey HG and Wielinger H (1970):** Über die Eigenschaften eines neuen Chromogens für die Blutzuckerbestimmung nach der GOD/POD-MethodeOn the properties of a new chromogen for the determination of glucose in blood according to the GOD/POD-method. Fresenius' Zeitschrift Für Analytische Chemie., 252(2-3): 224-228.
8. **Mudur G (2003):** Asia grapples with obesity epidemics, World Health Organization. Obesity: preventing and managing the global epidemic. Geneva. BMJ., 326(7388): 515.
9. **Gillman MW, Rifas-Shiman S, Berkey CS *et al.* (2003):** Maternal gestational diabetes, birth weight, and adolescent obesity. Pediatrics, 111: e221-e226.
10. **Strufaldi MW, Silva EM and Puccini RF (2011):** Overweight and obesity in prepubertal schoolchildren: the association with low birth weight and family antecedents of cardiovascular disease. Embu-metropolitan region of São Paulo, 2006]. Cien Saude Colet., 16: 4465-4472.
11. **Güngör NK (2014):** Overweight and Obesity in Children and Adolescents. J Clin Res Pediatr Endocrinol., 6(3): 129-143.
12. **Bambra CL, Hillier FC, Cairns JM *et al.* (2015):** How effective are interventions at reducing socioeconomic inequalities in obesity among children and adults? Two systematic reviews. Public Health Res., 3(1).
13. **Badawi NE, Barakat AA, El Sherbini SA *et al.* (2013):** prevalence of overweight and obesity in primary school children in portsaid city. Egyptian pediatric Association Gazette, 61(1): 31-6.
14. **Dixon JB, Bhathal PS and O'Brien PE (2001):** Nonalcoholic fatty liver disease: predictors of nonalchoholic steatohepatitis and liver fibrosis in the severely obese. Gastroenterology, 121: 91-100.
15. **Sutherland ER (2014):** Linking obesity and asthma. Annals of the New York Academy of Sciences, 1311: 31-41.
16. **Hakim F, Kheirandish-Gozal L and Gozal D (2015):** Obesity and altered sleep: A pathway to metabolic derangements in children? Semin Pediatr Neurol., 22: 77-85.
17. **Talat MA and Shahat EE (2015):** Prevalence of overweight and obesity among preparatory school adolescents in Urban Sharkia Governorate, Egypt. Egyptian Pediatric Association Gazette, 64: 20-25.
18. **Rosenheck R (2008):** Fast food consumption and increased caloric intake: a systematic review of a trajectory towards weight gain and obesity risk. Obes Rev., 9: 535-547.
19. **Guran T, Turan S, Akcay T *et al.* (2008):** Significance of acanthosis nigricans in childhood obesity. J Paediatr Child Health, 44: 338-41.
20. **Sivakumar S and Banupriya K (2017):** A cross-sectional descriptive clinical study of dermatological manifestations in obesity. Int J Res Dermatol., 3: 337-41.
21. **Fayed SB, Ateya AA, Thorya HM *et al.* (2012):** Ultrasonographic assessment of Body fat Distribution in Obese Children. Nat Sci., 10(11): 182-187.
22. **Maloney EM, Boneva RS, Lin JMS *et al.* (2010):** Chronic fatigue syndrome is associated with metabolic syndrome: results from a case-control study in Georgia. Metab Clin Exp., 59: 1351–7.
23. **Weiss R, Dziura J, Burgert TS *et al.* (2004):** Obesity and the metabolic syndrome in children and adolescencents. N Engl J Med., 350: 2362-2374.
24. **Hsieh SD, Ashwell M, Muto T *et al.* (2010):** Urgency of reassessment of role of obesity indices for metabolic risks. Metabolism, 59: 834 – 840.
25. **Li L, Law C and Power C (2007):** Body mass index throughout the life-course and blood pressure in mid-adult life: a birth cohort study. J Hypertens., 25(6): 1215-23.
26. **Burgos MS, Reuter CP, Burgos LT *et al.* (2010):** Uma análise entre índices pressóricos, obesidade e capacidade cardiorrespiratória em escolares. Arq Bras Cardiol., 94(6): 739-44.
27. **Laakso M, Sarlund H and Mykkanen L (1990):** Insulin resistance is associated with lipid and lipoprotein abnormalities in subjects with varying degrees of glucose tolerance. Arteriosclerosis, 10: 223–31.
28. **Centers for Disease Control and Prevention (CDC) (2009):** Prevalence of abnormal lipid levels among youths. United States, 1999-2006. MMWR Morb Mortal Wkly Rep., 59: 29–33.
29. **Ebrahimi M, Heidari-Bakavoli AR, Shoeibi S *et al.* (2016):** Association of Serum hs-CRP Levels With the Presence of Obesity, Diabetes Mellitus, and Other Cardiovascular Risk Factors. J Clin Lab Anal., 30(5): 672–6.
30. **Toprak D, Toprak A, Chen W *et al.* (2011):** Adiposity in childhood is related to C-reactive protein and adiponectin in young adulthood: from the Bogalusa Heart Study. Obesity (Silver Spring), 19: 185–190.
31. **Shengrong O, Wei L, Zhuo L *et al.* (2016)**: Association between serum soluble tumor necrosis factor-α receptors and early childhood obesity. https://www.jstage.jst.go.jp/article/endocrj/63/6/63_EJ15-0628/_pdf
32. **Nakamura K, Fuster JJ and Walsh K (2014):** Adipokines: a link between obesity and cardiovascular disease. J. Cardiol., 63, 250–259.