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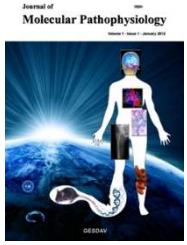

Original Research

CRP Marker Adds a Risk Factor for Lebanese Obese Children and Adolescents

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Abstract

Objectives: Obesity in children and adolescents is increasingly recognized as a major health concern. It is actually a pandemic disease by itself. Several cytokines and inflammatory mediators are induced in obesity and they may trigger atherosclerosis, coronary disease and heart failure. It is reported that increased high sensitivity C-reactive protein (CRP) was an independent predictor of cardiovascular events in adults and this relation is less clear in pediatrics age group.

1) To Measure the high sensitivity CRP level in children and adolescents who are obese or normal weight (control group) with no known history of associated co morbidities and to define the abnormality in CRP level among obese children and adolescent in Lebanese population. 2) To prove that the increase in CRP among obese children could be as early as 2 years of age. 3) Follow up the obese children and adolescents who had positive CRP with scheduled diet regimen by help of the nutritionist and seek the effect of diet on CRP level.

Method: This is a prospective case control study, collecting children and adolescents between 2 and 15 years of age and determining the obese group according to definition of obesity which refers to BMI that vary with age and sex. Obese group selected if BMI > 95th percentile and normal weight (control group) selected if BMI < 85th percentile for age and sex respectively. This was achieved by using document analysis, paper based questionnaire, interviews, complete physical examination, direct measurement of weight and height. Then after justification for the inclusion criteria, CRP level was drawn and tested in Makassed General Hospital laboratory.

Results: CRP level was significantly different between obese and control group (normal weight). All subjects of control group had negative CRP value with mean result of 0.08, while 33 subjects (57.9%) of obese group had positive CRP value with a mean of 0.83 that has statistically significant P value of 0.003.

This relation was observed among obese children as young as 2 years of age. For All members who had weight reduction the CRP decreased, while only one subject who lost the dietary control had elevation in CRP level.

Conclusions: We conclude that obesity in children and adolescents with no comorbidities is strongly associated with elevated CRP level (a high sensitivity inflammatory marker) which may reflect a future increase in the risk of developing atherosclerosis process. This relation was observed among obese children as young as 2 years of age. Changing life style according to diet regimen lowered CRP level in direct correlation to the weight reduction.

INTRODUCTION

Obesity in children and adolescents is increasingly recognized as a major health concern [1]. It is actually a pandemic disease by itself especially by its numerous associated complications and it is considered among the most important cause of morbidity and mortality throughout the world [2].

Evidence from several studies indicates that obesity substantially increases the risk of hypertension, heart disease, diabetes and impairs the quality of life [3, 4].

Obesity in children and adolescents from age 2 to 20 years is defined according to the body mass index which varies with age and sex [5-7]. The center for disease control (CDC) defines obesity as BMI greater than 95th percentile, overweight between 85th and 95th percentile, and normal weight below 85th percentile [6].

Exposure to cardiovascular risks factors in childhood contributes to the development of atherosclerosis later in life. Guidelines for the primary prevention in children and adolescents recommend early assessment of conventional cardiovascular risk factors such as obesity, serum lipids, and blood pressure to identify children at high risks for early development of cardiovascular disease [8].

Clustering of multiple risk factors and their persistence throughout childhood and adulthood are particularly prevalent among those with increased body adiposity [8, 9]. Several cytokines and inflammatory mediators are induced in obesity and they may trigger atherosclerosis, coronary disease and heart failure [10, 11]. The pathophysiology of atherosclerosis includes local inflammation as a promoter for the atherosclerotic plaque formation [8].

Several prospective epidemiological studies have reported that increased high sensitivity CRP was an independent predictor of cardiovascular events in adults [8]. There is lack of longitudinal control studies directly related to the abnormalities in CRP level that can predispose obese children and adolescents with no metabolic syndrome or associated comorbidities to develop cardiovascular disease.

Metabolic syndrome is a cluster of risk factors that raise the risk of developing heart disease; one must have 3 of the following: High blood pressure, low HDL, increase triglyceride and high blood sugar.

Objectives

1. Measure the high sensitivity CRP level in children and adolescents who are obese or normal weight (control group) with no known history of associated comorbidities and define the abnormality in CRP level among obese children and adolescents.
2. To prove that the increase in CRP among obese children could be as early as 2 years of age.
3. Follow up the obese children and adolescents who had positive CRP with scheduled diet regimen by help of the nutritionist and seek the effect of diet on CRP level.

MATERIAL AND METHODS

This is a prospective case control study, collecting children and adolescents between 2 and 15 years of age and determining the obese group according to definition of obesity which refers to BMI that vary with age and sex [5]. Obese group selected if BMI > 95th percentile for age and sex, and normal weight (control group) selected if BMI < 85th percentile for age and sex.

This was achieved by using document analysis, paper based questionnaire, interviews, complete physical examination, vital signs with blood pressure, and direct measurement of weight and height. Then after justification for the inclusion criteria, CRP level done at Makassed General Hospital laboratory. Questionnaires were distributed during well care visit in OPD involving the selected group for the study at pediatric faculty practice.

Multiple questions concerning the following: name, age, date of birth, phone number, height, weight, past medical history (high blood pressure, diabetes, sleep apnea, day time sleepiness, reflux, known to have dyslipidemia, dietary history and exercise history, pop and juice drink, parental past medical history, and their weight and height).

This study was approved by the IRB committee.

Inclusion Criteria

1. Obese group between ages 2 and 15 yrs
2. Normal weight group between ages 2 and 15 yrs
3. One month post cold infection.

Exclusion Criteria

1. Recent infection
2. Known to have anemia
3. Use of diet regimen
4. History of trauma
5. Asthmatic patients
6. Patients with chronic diseases
7. Known to have diabetes
8. Known to have dyslipidemia.

Statistical Analysis

Data analysis was performed using statistical package of social science (SPSS) version 16.0 for windows. Numerical variables were reported in terms of mean and standard deviation. Categorical variables were reported in terms of numbers and percentages. Association of each of the categorical variable with response variable was assessed by Chi-square test. Variables showing statistically significant association in univariate analysis with the outcome variable were considered as risk factor. Only those variables were subjected to multivariate analysis. In multivariate

analysis, variables showing P-value less than 0.05 were considered to be statistically significant.

RESULTS

This is a prospective and case control study collected 150 children and adolescents between 2 and 15 years of age.

Sixty (42.9%) were excluded, 25 (41.7%) lost of follow up, 30 (50%) had acute infection, 5 (8.3%) obese members on diet regimen. The remaining 90 (57.1%) were enrolled in the study after adjustment to the inclusion criteria, 57 (63.3%) obese and 33 (36.7%) had normal weight (control group) (Figure 1).

The variable percentages of obese and control group among children and adolescents were as follows: 22 (24.4) subjects collected from age (2-5 yrs), half of them were obese, while 34 (37.8%) subjects was collected between (6- 9yrs), 21 (23.3%) were obese. From age 10 and 15 yrs, 34 (37.8) members were collected and 25(27.7%) were obese. For gender of obese group was 32 (56.1%) male and 25 (43.9%) female while control group were 17 (51.5%) male and 16 (48.5%) female with no significant P-value 0.671. 29 (50.9%) of obese members had positive exercise history where all control group members had positive exercise history with statistically significant P-value of 0.0001. Concerning the dietary history 50 (87.7%) of obese members had excessive snacking in comparison to control group 29 (87.9 %) had regular normal diet with statistically significant P-value of 0.0001. Forty nine (86%) of obese subjects drink pop in comparison to control group with statistically significant P-value of 0.014; However, there is no significant difference in the juice drink between both groups (Table 1).

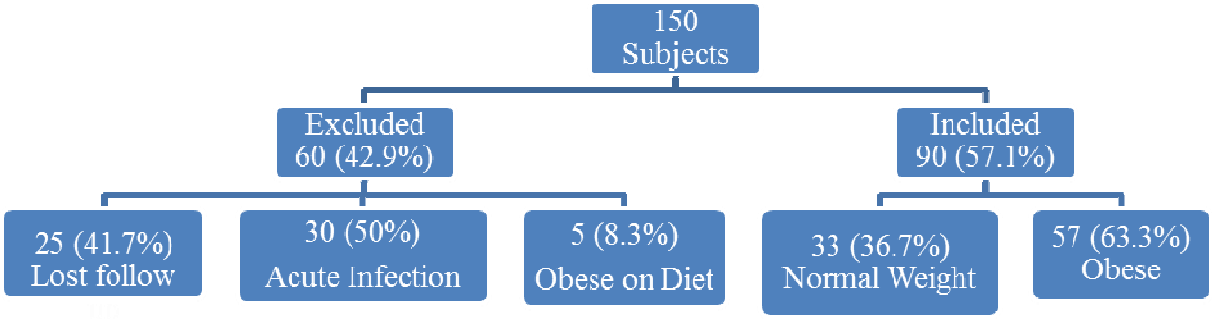


Figure 1. Number of volunteers who were enrolled in the study

Table 1. Obese and control group characteristics

	Obese	Control Group	P-Value
Age			
(2yrs- 5yrs)	11 (12.2%)	11 (12.2%)	
(6yrs- 9yrs)	21 (23.3%)	13 (14.4%)	
(10yrs- 15yrs)	25 (27.7%)	9 (10%)	
Gender			
Female	25 (43.9%)	16 (48.5%)	0.6
Male	32 (56.1%)	17 (51.5%)	NS
Exercise History			
Yes	29 (50.9%)	33(100%)	0.0001
No	28 (49.1%)	0 (0%)	
Dietary History			
Excessive Snaking	50 (87.7%)	2 (6.1%)	
Normal Diet	7 (12.3%)	29 (87.9%)	0.0001
Less than Normal	0	2 (6.1%)	
Pop	49 (86.0%)	21 (63.6%)	0.014
Juice	52 (91.2%)	29 (87.9%)	0.610

None of our cases including both group of obese and control group had by history high blood pressure, diabetes, sleep apnea, day time sleepiness, reflux, or dyslipidemia.

Regarding the parental weight status in relation to both groups was as follows: 20 (69%) obese from total of 29 members had maternal overweight, however this percentage increased to 24 (75%) obese from total of 32 members had maternal obesity with statistically significant P-value of 0.01. Moreover, 27 (61.4%) obese from a total of 44 members had paternal overweight and this percentage increased to 22 (81.5%) from total of 27 members if they had paternal obesity with statistically significant P-value of 0.008. None of both groups had significant differences in relation to parental co morbidities.

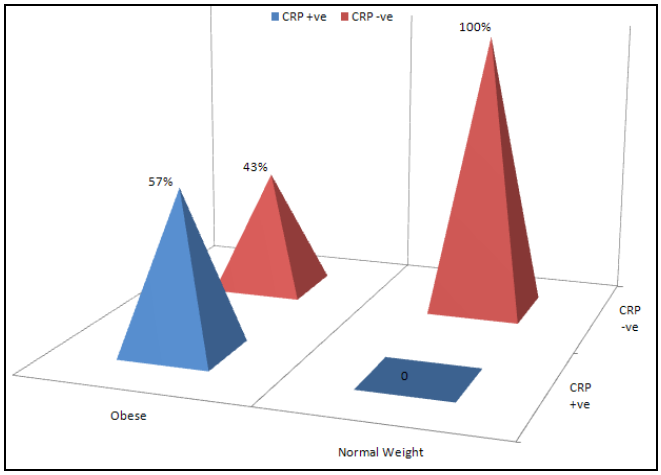
The relation between both group and one or both of parental overweight or obesity was as follow: 2 (33.3%) of obese group had parental BMI < 25 (normal weight), while 13 (40.6%) of obese group had one of the parents with BMI > 25(obese or overweight), and 38 (79.2%) of obese group had both parents with BMI > 25 (obese or overweight) (Table 3).

Table 2. Parental weight status and characteristics in comparison to control and obese groups

	Obese	Control Group	P-Value
Parental Weight Status			
Maternal Normal Weight	10 (38.5%)	16 (61.5%)	
Maternal Overweight	20 (69.0%)	9 (31.0%)	0.011
Maternal Obesity	24 (75.0%)	8 (25.0%)	
Paternal Normal Weight	6 (35.3%)	11 (64.7%)	
Paternal Overweight	27 (61.4%)	17 (38.6%)	0.008
Paternal Obesity	22 (81.5%)	5 (64.7%)	
Parental co Morbidities			
Maternal DM	25 (45.5%)	9 (27.3%)	0.09
Maternal Heart Disease	28 (50.9%)	14 (42.4%)	0.44 NS
Paternal DM	23 (41.8%)	12 (36.4%)	0.61 NS
Paternal Heart Disease	25 (45.5%)	13 (39.4%)	0.57 NS

Table 3. The effect of parental weight status among both groups

Parental BMI	Normal Weight	Obese	Total	P-Value
Both with BMI < 25	4 (66.7%)	2 (33.3%)	6	
Only one with BMI > 25	19 (59.4%)	13 (40.6%)	32	0.001
Both are with BMI > 25	10 (20.8%)	38 (79.2%)	48	



Graph 1. Results of CRP among obese and normal weight groups

CRP value was defined as positive if it was more than 0.3 mg/dl among all studied age groups. All subjects of control group (normal weight) had negative CRP value with mean result of 0.08, while 33 subjects (57.9%) of obese group had positive CRP value with a mean of 0.83 that has highly significant P-value of 0.003 (Table 4). The CRP mean among obese group was rising with age (graph 2). It was 0.628 for obese between 2 and 5yrs increased to 1.052 in obese subjects between 6 and 9yrs, moreover CRP mean was 1.7 in obese members between 10 to 15yrs. Concerning the effect of exercise history, dietary history, parental weight status on the positivity of CRP among obese group was as follows:

For the exercise history; the obese group whom were not exercising had CRP mean 1.29, while those who were exercising had CRP mean 0.24 which is negative that had highly significant P-value of 0.007 (Table 5).

The CRP mean in obese group with maternal obesity was 1.02, while the CRP mean in those with normal maternal weight was negative (0.16) with a statistically significant P-value of 0.02 (Table 5). About the dietary history; CRP mean in obese group with excessive snacking was 0.95 while it was negative in those with normal diet but the P-value was not significant 0.16 (Table 5). No difference was found for the effect of paternal weight status and pop drink on CRP mean among obese group.

Then we instructed all parents of obese children and adolescents with positive CRP value to follow a diet regimen according to scheduled program which was done by the help of two expert nutritionists, but unfortunately only some of them accepted and for those we repeated the CRP level after one month from the special diet. Of 33 obese members only 20 (60%) underwent dietary regimen from which 10 (30%) had no repeated CRP because of study time limit, while 10 (30%) who still on diet regimen repeated CRP after one month (Figure 2).

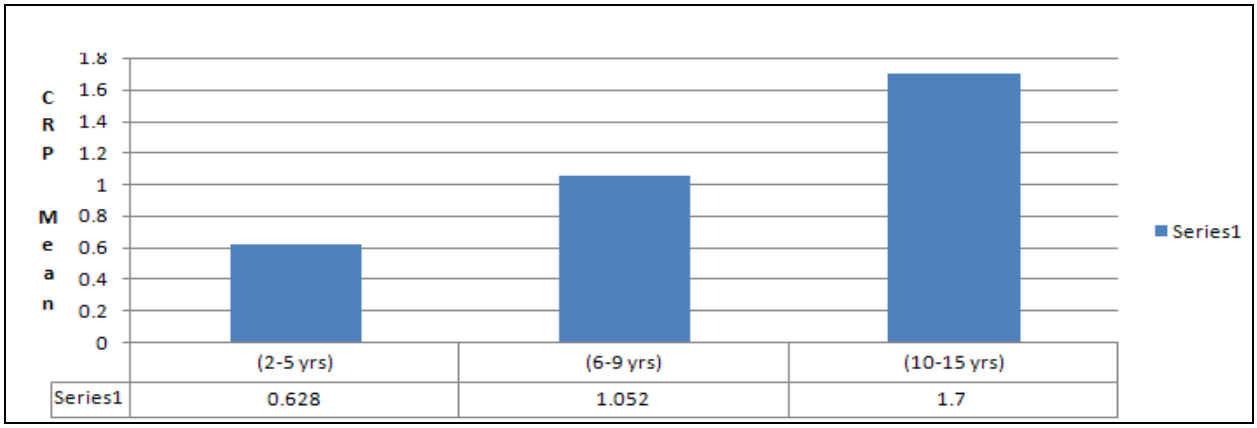
The good dietary control was achieved if weight reduction was about 2 kilo per month and the mild weight reduction was defined if less 0.5 kilo of weight reduction per week.

For All members who had weight reduction 8 (80%); the CRP decreased, while only two subjects (20%) who lost the dietary control had elevation in CRP level. According to the nutritionist references good weight reduction was defined if there was 0.5 kilo loss per week.

The mildly weight reduction group (one kilo loss) 2 subjects (20%) controlled on diet regimen had mild decrease in CRP level with mean of 0.1. However, 6 subjects (60%) had markedly decreased of the repeat CRP with a mean of 0.4 mg/dl due to a good weight reduction on diet regimen with a mean of 4 kilos in a period of one month. To mention that 2 of these subjects normalized their CRP level (Figure 3) (Table 6) (Graph3).

Table 4. CRP means result among normal weight and obese groups

	Obese	Normal Weight	P-Value
CRP Mean(SD)	0.851(1.43)	0.083(0.083)	0.003



Graph 2. CRP mean in obese group regarding the age

Table 5. CRP mean result in comparison to exercise history, dietary history, and maternal weight status among obese group

	CRP Mean (SD)	P-Value
Exercise History		
Yes	0.24 (0.38)	0.007
No	1.29 (1.89)	
Dietary History		
Excessive Snacking	0.95 (1.50)	0.001
Normal Weight	0.14 (0.17)	
Maternal Weight Status		
Obese	1.02 (1.61)	
Overweight	0.46 (1.09)	0.02
Normal	0.16 (0.17)	

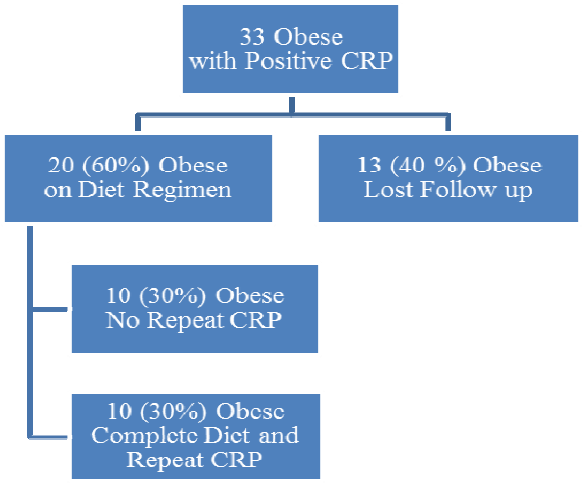


Figure 2. Follow up group with dietary regime

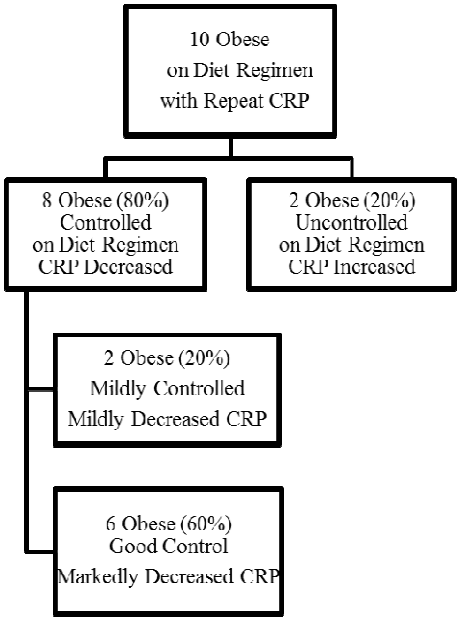
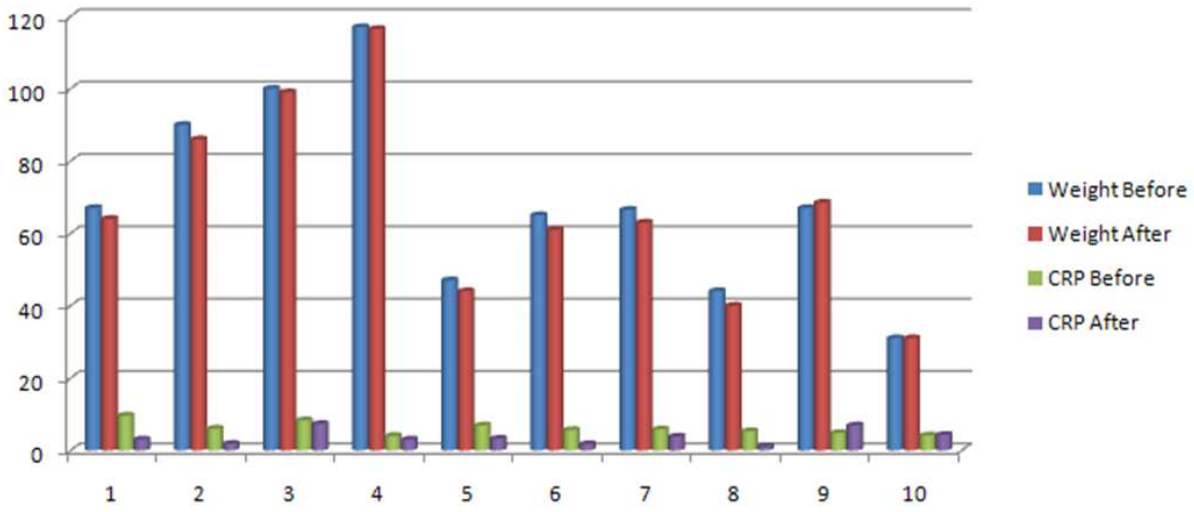


Figure 3. Follow up group with dietary regimen and its effect on CRP

Table 6. Follow up obese group with diet and diet effect on CRP

	Weight Before	Weight After	CRP Before	CRP After
1	67	64	0.96	0.3
2	90	86	0.6	0.18
3	100	99	0.83	0.73
4	117	116.5	0.4	0.3
5	47	44	0.69	0.32
6	65	61	0.56	0.17
7	66.5	63	0.58	0.38
8	44	40	5.3	1.11
9	67	68.5	0.48	0.69
10	31	31	0.41	0.43



Graph 3. Follow up obese group with diet and diet effect on CRP

DISCUSSION

To our knowledge this is the first study in Lebanon and (middle East Zone) to demonstrate a strong association between CRP as an inflammatory marker and obesity, this relation was observed among obese children as young as 2 years of age, 3 members were obese ages 2 years had positive CRP with a mean of 0.4.

All subjects of control group (normal weight) had negative CRP value with mean result of 0.08, while 33 subjects (57.9%) of obese group had positive CRP value with a mean of 0.83 that has statistically significant P-value of 0.003 (Table 3).

In a previous research used ultrasound techniques to show that increased CRP value seems to be related to vascular intima media thickness in children and early atherosclerotic changes related to inflammation [7]. Together with these pathophysiologic findings, the results of our work raise concerns about the entire population of obese children's risk for long term cardiovascular disease.

In 2 studies were done, one of them by Shin JY et al. in Korea University, on 2008 measuring CRP and tissue necrotic factor between obese group with co-morbidities and non obese children [12], and other by Marie Lambert et al. in Canada on 2004 about CRP and features of the metabolic syndrome in a population-based sample of children and adolescents [13], both studies concluded a metabolic correlates of excess weight, including a state of low grade systemic inflammation, are detectable early in life.

In our study the collected obese group had no clinical metabolic syndrome or associated comorbidities, there were positive findings for increment of CRP level

among obese group in comparison to all members of control group (normal weight) who had negative CRP level with significant P-value of 0.003. This adds to literature that CRP value in children is an independent marker to be a risk factor for atherosclerosis and cardiovascular disease in pediatric age group. A study in Japan done by Guran O et al. on 2003 about elevation of serum CRP level in obese boys with average age of 11 years and the finding was CRP is one of the useful indices of childhood obesity that would affect the progression to future atherosclerotic disease [14]. Collected subjects in this study were as early as 2 years of age. Another study done by Wasilewska A et al. at medical university of Bialystok, Poland on 2010 about the high sensitivity CRP and mean platelet volume in pediatric hypertension and concluded a parallel increase in CRP and platelets with the mean platelet volume in pediatric hypertension [15].

In our study we chose the obese and normal weight group with no hypertension or associated co morbidities and this made our results more specific toward the effect of CRP in healthy children and adolescents. Also another study done by Tauman R et al. at university of Louisville, Kentucky on 2004 assuming the CRP levels were increased among some children with sleep disordered breathing [16], for this reason we excluded all children who had sleep breathing disorder.

To our knowledge no studies measured the effect of diet regimen on CRP level in obese children, this study add an important role of diet as a control and therapeutic measure for the rise of CRP level (Table 4).

In an epidemiological study was done at AUB-MC Lebanon on 2003 provides the first national data addressing overweight and obesity are associated covariates among the Lebanese population resulting in a prevalence rate of overweight and obesity for boys higher than for girls (22.5% versus 16.1% and 7.5 versus 3.2%) (3). Another study was done by Chakar H et al. on 2007 about Growth charts and obesity prevalence among Lebanese private schools adolescents concluding that 7.4% of obese individuals and 24.4% of individuals at risk of obesity and obesity prevalence is 2.5 times higher in boys (10.1%) than in girls (4.2%). Boys at risk of obesity (28.8%) are almost 1.5 times more numerous than girls (19.0%) [17]. In our study the percentage of obese group according to gender was for boys 32 (56.1%) which is higher than for girls 25 (43.9%) (Table1).

In the present era of obesity epidemics, our analysis provides a significant rise in number of obese children, obese members were easily collected as compared to the normal weight members whom were hard to find and study (Table 1). We suggest further epidemiological studies to define a new prevalence of pediatric obesity in Lebanon.

For the exercise and dietary history as a comparison between both groups in our study, our result showed a significant association between absence of exercise and excessive snacking with obesity (Table 1). Only exercise history and maternal obesity had an important effect on CRP secondary to increased body adiposity [8] (Table 5). Concerning the effect of parental weight status on obesity in children, it is well known that maternal obesity had positive correlation to obesity in their children.

Our data suggest both parental obesity and overweight had correlations to obesity of their children with significant P-value of 0.001 (Table 2). Whereas our study has important strengths, there are also limitations. First we were unable to compare other inflammatory marker with CRP among the studied groups due to financial causes. Second issue we based on questionnaire and not laboratory studies to diagnose diabetes, dyslipidemia of the subjects. Third issue about time limited for the follow up group to repeat CRP. More importantly, although the relationship between inflammation and adiposity is evident in very young children [7], the case control design does not permit us to comment on whether the relationship is maintained for individual children across time or certainly into adulthood.

We applied a multivariate analysis to all our data and as a result we found that dietary history has a high specificity of 88.7% to identify obesity and also multivariate analysis done for CRP and were found that exercise history has high specificity of 80% to decrease weight and CRP level.

CONCLUSION

We conclude that obesity in children and adolescents with no co morbidities is strongly associated with elevated CRP level a high sensitivity inflammatory marker which may reflect a future increase in the risk of developing atherosclerosis process.

This study also showed childhood obesity associated with low exercise, excessive snaking and parental obesity. Another important point that was demonstrated in our study is that changing life style according to diet regimen lowered CRP level in direct correlation to the weight reduction.

Further justifying early obesity prevention efforts with diet regimen is recommended. We recommend appliance of multivariate analysis in a further study from which we can identify children at risk for obesity and cumulative vascular disease.

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