Annals of Clinical Case Reports

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Could High-Sensitivity C-Reactive Protein Considered as a Biomarker for the Detection Metabolic Syndrome in **Iranian Girls?**

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Accepted Date: 10 Jul 2023 Published Date: 14 Jul 2023

Citation:

Fazeli M, Mohammad-Zadeh M, Tabatabaeizadeh SA. Meshkat Z. Ferns G, Bahrami-Taghanaki H, et al. Could High-Sensitivity C-Reactive Protein Considered as a Biomarker for the Detection Metabolic Syndrome in Iranian Girls?. Ann Clin Case Rep. 2023; 8: 2439.

ISSN: 2474-1655.

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Abstract

Background: The prevalence of Metabolic Syndrome (MetS) is increasing globally and is associated with an increased risk of Cardiovascular Disease (CVD) and Type 2 Diabetes Mellitus (T2DM). The increased risk of CVD and T2D in an individual with MetS is proposed to be at least partially related to chronic low-grade inflammation that is reflected by increased serum High-sensitivity C-Reactive Protein (Hs-CRP) level. We aimed to investigate the relationship between serum hs-CRP and MetS.

Methods: Nine hundred eighty-eight school girls (mean age 14.56 ± 1.53 years) were recruited using random cluster sampling. Demographic information was collected by questionnaire. Biochemical and anthropometric measures were estimated by standard routine procedures. The IDF, NCEP-ATPIII, and two modified NCEP (Cook and DeFerranti) were used for metabolic syndrome diagnosis.

Results and Conclusion: Our findings show that hs-CRP was associated with WC, elevated serum triglyceride and low HDL in adolescent school girls; but the association with serum HDL was weak. We found no correlation between hs-CRP and blood pressure and FBG. For all definitions of MetS, the prevalence of MetS in a high-risk group of hs-CRP (>3 mg/L) was higher than other groups except when using the DeFerrant definition. Logistic regression revealed that the highest and lowest ORs (CI 95%) were in the Cook (1.410 (1.22-1.63)) and DeFerranti (1.228 (1.14-1.43)) definitions of MetS, respectively. The sensitivity and specificity were: 68.29% to 82.61% and 64.68% to 65.90% for serum hs-CRP using the different definitions, respectively. In ROC analysis, the AUC for different definitions varied between 0.649 to 0.788 and serum hs-CRP cutoff value for all definitions was >1.33 mg/L. In conclusion, serum hs-CRP, an inflammatory marker, may be of useful in the diagnosis of MetS in girls; but not reliable.

Keywords: Metabolic syndrome; Pediatrics; Hs-CRP; Low-grade chronic Inflammation; **Biomarker; Pro-inflammatory factors**

Introduction

Cardiovascular Disease (CVD) is a major cause of mortality globally. The increasing prevalence of obesity and obesity-related condition such as Metabolic Syndrome (MetS) is associated with a high risk of CVD mortality and morbidity. Hypertension, life style, smoking, obesity and obesityrelated disorder including hyperlipidemia, Type 2 Diabetes (T2D) and MetS are identified as a risk factor for CVD [1-4]. MetS comprises a cluster of several metabolic risk factors including central obesity, dyslipidemia, elevated blood pressure, high fasting blood glucose and insulin resistance that are associated with increased susceptibility to CVD and all-cause mortality [5-9]. The high risk of CVD and T2D in individuals with MetS, may be associated with a chronic low-grade state of inflammation that is reflected in an increased serum high sensitivity C Reactive Protein (Hs-CRP). Serum hs-CRP is a biomarker of low-grade inflammation. Increased serum hs-CRP is observed in individuals with MetS patients, and is also associated with CVD and T2D risk [10-17].

Examinations of several features that comprise MetS in screening and monitoring procedures, or measuring the prognosis are very problematic especially in adolescent because of pubertal and developmental changes in this period [18]. Therefore, it may be useful, in screening and monitoring in large scale studies, a single reproducible and reliable marker is identified that can replace the assessment of each of the separate MetS criteria.

Based on the association of hs-CRP with MetS and insulin resistance, some investigators have suggested that serum hs-CRP could be used as a marker for the prediction of CVD and T2D and should be included as one of the diagnostic criteria for MetS [1,3,19,20].

According to findings of the large-scale population cohort of the Women Health Survey (WHS), there is a relationship between serum hs-CRP, MetS and CVD [21]. For the prediction of future risk of coronary heart disease and stroke, serum hs-CRP values have been classified into three categories: <1 (low risk), 1-3 (moderate risk) and >3 mg/L (high risk) respectively [22]. We aimed to investigate the association between serum hs-CRP and definitions for the MetS adjusted for children and adolescents, and its constituent components.

Subjects and Methods

Schoolgirls [mean age of 14.56 ± 1.53 years (ranging from 12 to 18 years)], resident in the cities of Mashhad and Sabzevar, in northeastern Iran, were recruited using a random cluster sampling method, as part of a vitamin D supplementation study. The study was approved by the local institutional Ethics Committee, as well all participants gave written informed consent. Demographic information collected by using research made questionnaires.

After an overnight fast, blood samples were taken from all participants, for estimation of fasting blood glucose, lipid profile and high sensitivity C-reactive protein levels. The high sensitivity C-reactive protein was measured using particle enhanced turbidimetric assay (Bioscience, Germany), and the enzymatic assay was applied to measuring the fasting blood glucose, lipid profile as manufacturer manual (Pars AzmoonTeb, Iran).

Waist circumference was measured at a point midway between 12th rib and top of the iliac crest, at the end of normal expiration.

The IDF, NCEP-ATPIII, Cook's and De Ferranti's definitions were used for the diagnosis of MetS as indicated in Table 1.

Prevalence was reported as a percentage. Normality of data was examined by Kolmogorov-Smirnov test. Results represent median and first and third interquartile because of the abnormal distribution of data. Statistical significance was determined by the paired t-test, as well, one-way ANOVA test was used for comparison of means in groups. ROC curves were drawn for estimation of area under curves, and the optimal cutoff value was computed by Yandex index and Delong method applied for determining sensitivity and specificity of serum hs-CRP for MetS definitions. Pearson's test was used for computing of association between variables, also the point-biserial correlation test was performed for estimation of the correlation between quantitative and dichotomous variables. Binary logistic regression was used for computing of odd ratios (CI 95%). All statistical analysis was performed using SPSS software version 11.0 (Chicago. IL.)/MedCalc software version 15.8 was applied for ROC analysis. P-value <0.05 was considered as significant.

Results

Table 1 showed the serum Hs-CRP values in subjects with and without MetS and each MetS components separately, and the associations of serum Hs-CRP with each component of MetS based on four different definitions of MetS adapted for children and adolescents represented in this table. In regard to subjects with WC measure that met the criterion of MetS in Cook's, NCEP-ATPIII and IDF, serum hs-CRP was significantly higher in girls with MetS (1.92 (1.16-3.86)) as compared to those without MetS (0.9 (0.46-1.68)). Also, similar differences were observed in the WC based on DeFerranti's criterion (75th percentile) with 1.60 (1.00-3.17) vs. 0.86 (0.43-1.61) of hs-CRP in MetS and non-MetS, respectively. In participants with FBG that met the cutoff values for IDF definition, serum hs-CRP was higher than in healthy girls (1.02 (0.51-2.00) vs. 0.95 (0.5-1.8)) but these differences were not significant (P=0.462), in the other definitions of MetS a cutoff for FBG ($\geq 110 \text{ mg/dL}$), similar results were observed (hs-CRP in MetS: 1.01 (0.48- 1.47 vs. non-MetS: 0.96 (0.50-1.83); P=0.994). There were no significant differences between subjects that met the SBP criterion with healthy individuals, while the hs-CRP values were higher in who met the IDF (1.38 (0.71-3.54) vs. 0.96 (0.50-1.83) P=0.122), ATP III and Cook's (0.98 (0.51-2.95) vs. 0.97 (0.50-1.84) P=0.644) and DeFerranti's (1.24 (0.63-3.37) vs. 0.98 (0.52-1.91) P=0.376) criteria. In DBP, two different cutoffs were investigated in the studied definitions, in spite of higher values of hs-CRP in individuals with DBP criterion for IDF 1.12 (0.49-3.02) vs. 0.96 (0.50-1.83) and other definitions 1.10 (0.58-1.78) vs. 0.95 (0.50-1.85) contributed to healthy subjects; but again, these differences were not significant (P>0.05). There are three different cutoffs for hypertriglyceridemia among the studied definitions, Hs-CRP concentration in subjects who met the criterion, was significantly higher in each of the three different cutoffs, according to IDF (≥ 150 mg/dL), ATPIII and Cook's (\geq 110 mg/dL) and DeFerrant's (\geq 100 mg/dL) criteria cutoffs, positive individuals with these cutoff, have serum hs-CRP of 2.09 (1.24-3.34), 1.47 (0.75-2.67) and, 1.34 (0.75-2.37) mg/L, while the negative subjects showed a median serum hs-CRP of 0.92 (0.48-1.75), 0.88 (0.45-1.61) and, 0.86 (0.42-1.60) mg/L, respectively. Decreased HDL criterion was also defined by three different cutoffs in used definitions, and IDF and Cook's definitions have the same cutoff (<40 mg/dL). Based on these cutoffs, positive participants have significant higher hs-CRP concentration than those who were negative. Serum hs-CRP values for subjects with HDL below cutoffs were 1.20 (0.59-2.58), 1.16 (0.58-2.28), and 1.07 (0.58-1.93) as compared with participants with HDL values more than cutoffs who have Hs-CRP concentrations 0.93 (0.49-1.72), 0.91 (0.47-1.75), and 0.85 (0.40-1.60) for IDF and Cook's, NCEP-ATP III and finally DeFerranti's definition, respectively. Hs-CRP median to be higher in individuals with MetS than without in all comparisons, but these differences were not significant for fasting blood glucose and systolic and diastolic blood pressures.

Often individual components of MetS have been associated with serum hs-CRP but this association is especially weak for HDL using the IDF and Cook definitions; r=0.095 (P=0.009), NCEPT-ATPIII

Onitonia	*M-40	Serum hs-CRF	P median (IQ ₃ -IQ ₁)	_		
Criteria	^MetS criteria cu	MetS	Non-MetS	р	correlation test	
WC (cm)	IDF, NCEP-ATPIII and Cook et al., 2003 α	>90 th (for Cook et al) and ≥ 90 th percentile	1.92 (3.86-1.16)	0.9 (1.68-0.46)	0.0001	0.244 (0.0001)
	De Ferranti et al. 2004	>75 th percentile	1.60 (3.17-1.00)	0.86 (1.61-0.43)	0.0001	0.246 (0.0001)
	IDF	≥ 100 mg/dL	1.02 (2.00-0.51)	0.95 (1.8-0.5)	0.462	0.026 (0.463)
FBG (mg/dL)	NCEP-ATPIII, Cook et al. 2003 and De Ferranti et al. 2004 β	≥ 110 mg/dL	1.01 (1.47-0.48)	0.96 (1.83-0.50)	0.994	0.0001 (0.992)
	IDF	≥ 130 mmHg	1.38 (3.54-0.71)	0.96 (1.83-0.50)	0.122	0.057 (0.123)
SBP (mmHg)	NCEP-ATPIII and Cook et al. 2003 μ	≥ 90 th percentile	0.98 (2.95-0.51)	0.97 (1.84-0.50)	0.644	0.017 (0.645)
	De Ferranti et al., 2004	>90 th percentile	1.24 (3.37-0.63)	0.98 (1.91-0.52)	0.376	0.048 (0.377)
DBP (mmHg)	IDF	≥ 85 mmHg	1.12 (3.02-0.49)	0.96 (1.83-0.50)	0.467	0.027 (0.468)
	NCEP-ATPIII, Cook et al. 2003 and De Ferranti et al. 2004 Ω	≥ 90 th percentile	1.10 (1.78-0.58)	0.95 (1.85-0.50)	0.531	0.023 (0.532)
	IDF	≥ 150 mg/dL	2.09 (3.34-1.24)	0.92 (1.75-0.48)	0.0001	0.182 (0.0001)
TG (mg/dL)	NCEP-ATPIII and Cook et al. 2003 π	≥ 110 mg/dL	1.47 (2.67-0.75)	0.88 (1.61-0.45)	0.0001	0.194 (0.0001)
	De Ferranti et al. 2004 ≥ 100 mg/dl		1.34 (2.37-0.75)	0.86 (1.60-0.42)	0.0001	0.199 (0.0001)
HDL (mg/dL)	IDF and Cook et al. 2003 Σ	<40 mg/dL	1.20 (2.58-0.59)	0.93 (1.72-0.49)	0.009	0.095 (0.009)
	NCEP-ATPIII	≤ 40 mg/dL	1.16 (2.28-0.58)	0.91 (1.75-0.47)	0.019	0.085 (0.019)
	De Ferranti et al. 2004 <50 mg/dL		1.07 (1.93-0.58)	0.85 (1.60-0.40)	0.005	0.102 (0.005)
MetS**	IDF	IDF Obesity +2 or more		0.96 (1.83-0.50)	0.0001	0.142 (0.0001)**
	NCEP-ATPIII		3.52 (5.47-1.34)	0.95 (1.81-0.49)	0.0001	0.149 (0.0001)**
	Cook et al., 2003	3 or more	4.58 (5.86-1.54)	0.96 (1.83-0.50)	0.0001	0.138 (0.0001)**
	DeFerranti et al., 2004		1.73 (5.15-1.15)	0.93 (1.80-0.49)	0.0001	0.156 (0.0001)**

Table 1: Hs-CRP values in MetS and its components based on different definitions.

IDF: International Diabetes Federation; NCEP-ATPIII: National Cholesterol Education Program-Adult Treatment Panel; WC: Waist Circumference; FBG: Fasting Blood Glucose; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; TG: Triglyceride; HDL: High-Density Lipoprotein; MetS: METABOLIC SYNDROME *In these two columns used criteria, and their cutoffs have been showed, some cutoffs are same in those criteria that marked by Greek letters. **The point- biserial correlation test was performed for determining of association between dichotomous and quantitative variables

 Table 2: Age-adjusted prevalence of metabolic syndrome and median serum hs-CRP values.

			Metabolic s			
Age (years)	n	IDF	NCEP-ATPIII	Cook's	De Feranti's	hs-CRP median (IQR ₃ -IQR ₁)
12	57	7	8.8	8.8	15.8	0.9 (2.00-0.45)
13	236	1.3	2.5	1.3	5.1	1.09 (1.93-0.49)
14	232	0.9	1.7	0.4	1.7	0.89 (1.79-0.47)
15	170	0.6	1.2	0.6	3.5	0.83 (1.6-0.4)
16	147	0	2.7	2	4.1	1.12 (1.92-0.56)
17	123	0.8	2.4	0.8	4.1	0.96 (1.84-0.59)
18	16	6.3	0	0	6.3	1.45 (6.42-0.57)
Total	981	1.2	2.4	1.4	4.3	0.97 (1.85-0.5)

IDF: International Diabetes Federation; NCEP-ATPIII: National Cholesterol Education Program-Adult Treatment Panel; hs-CRP; Highly Sensitive C- Reactive Protein

r=0.085 (P=0.019), and in DeFerranti's definition r=0.102 (P=0.005). Also, no significant association was observed with fasting blood glucose and blood pressure. The strongest association was observed between WC and hs-CRP values, in WC cutoff for DeFerranti's r=0.246 (P=0.0001) and for other studied definitions r=0.244 (P=0.0001).

There were statistically significant associations between serum hs-CRP and different MetS definitions. The strongest and weakest correlations were observed for the DeFerranti's (r=0.156 (P=0.0001)) and Cook's (r=0.138 (P=0.0001)) definitions, respectively (Table 1).

The prevalence of MetS according to age and using the different definitions are shown in Table 2. The median value for serum hs-CRP in each age group with MetS showed that highest and lowest
 Table 3: Ddistribution of subjects with MetS in Hs-CRP risk groups-based percentage.

Mote definition	Hs-CRP risk groups						
wets demition	Low (%)	Moderate (%)	High (%)				
IDF	9.1	27.3	63.6				
NCEP-ATP III	13	34.8	52.2				
Cook's	14.3	21.4	64.3				
De Ferranti's	22	43.9	34.1				

IDF: International Diabetes Federation; NCEP-ATPIII: National Cholesterol Education Program-Adult Treatment Panel; hs-CRP; Highly Sensitive C-Reactive Protein; MetS: Metabolic Syndrome

values were present in 18- and 15-years old adolescents, respectively. The highest prevalence of MetS was found in the 12 years old girls

Table 4: Binary logistic regression analysis to the prediction of pediatric MetS by hs-CRP	among Iranian school girl children.
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Definition	Bota	Constant	Wald	P value	Likelihood	Cox and Snell R2	Nagelkerke R2	CI 05%
Demition	Dela	Constant	waiu	r. value	statistics	statistics	statistics	01 95 /0
IDF	1 367	-4 99	13 732	0 0001	105 94	0.012	0.09	1 16- 1 61
NOED	4.050	4.40	04 400	0.0004	404.44	0.004	0.00	4 40 4 54
NCEP	1.356	-4.18	21.423	0.0001	191.11	0.021	0.09	1.19- 1.54
Que et la la	4.44	4.05	00 700	0.0004	405.04	0.00	0.110	4 00 4 00
COOKS	1.41	-4.85	20.796	0.0001	125.01	0.02	0.119	1.22- 1.63
DeFermentile	4 000	0.00	40.400	0.0004	207.00	0.010	0.055	4 4 4 4 4 9
DeFerranti's	1.228	-3.38	18.109	0.0001	307.06	0.019	0.055	1.14- 1.43

IDF: International Diabetes Federation; NCEP-ATPIII: National Cholesterol Education Program-Adult Treatment Panel

Table 5: AUC, specificity, and sensitivity of hs-CRP in four different definitions.

Definition	hs-CRP						
Definition	Specificity (%)	Sensitivity (%)	AUC (95% CI)	Cutoff value (mg/L)			
IDF	64.72	75	0.682 (0.536-0.828)	>1.33			
NCEP-ATP III	65.53	82.61	0.788 (0.673-0.864)	>1.33			
Cook et al. 2003	64.68	69.23	0.649 (0.514-0.784)	>1.33			
De Ferranti et al. 2004	65.9	68.29	0.700 (0.622-0.779)	>1.33			

AUC: Area Under the Curve; IDF: International Diabetes Federation; NCEP-ATPIII: National Cholesterol Education Program-Adult Treatment Panel; MetS: Metabolic Syndrome



Figure 1: Receiver Operating Characteristic (ROC) curve of hs-CRP for a different definition of pediatric MetS. As illustrated in charts, highest AUC (0.788 (0.673- 0.864)) belonged to NCEP-ATPIII and Cook's definition showed the lowest (0.649 (0.514- 0.784)). Hallow circle showed the optimal cutoff point.

and using the DeFerranti's definition of MetS was used to estimate highest prevalence of MetS. Except in 12 years old girls, highest values for hs-CRP concentrations 1.45 mg/L, 1.12 mg/L, and 1.09 mg/L approximately contributed to high prevalence based on DeFerranti's definition 6.3%, 4.1% and 5.1% in different age groups, respectively. In general, the lowest prevalence also related to a lower median serum hs-CRP. While there was no clear relationship between prevalence and median serum hs-CR in other MetS definitions in this population.

Girls with MetS were in a high-risk group as defined by serum hs-CRP, apart from when using the DeFerranti's definition (Table 3), with the highest prevalence of MetS in all the definitions of MetS investigated. Often subjects with MetS are classified into a high-risk group of hs-CRP with values more than 3 mg/L. Data on the odd ratios indicate that serum hs-CRP is a risk factor for MetS in female adolescents. The highest and lowest odd ratios were found when using the Cook's or DeFerranti's definitions of MetS, respectively (Table 4). ROC analysis showed that serum hs-CRP had the greatest AUC using the NCEP-ATPIII definition, and the smallest for Cook et al. (Table 5, Figure 1). The highest specificity of hs-CRP as a biomarker was observed for the DeFerranti's definition (65.90%), followed by the NCEP-ATPIII definition (65.53%). However, hs-CRP showed 82.61% sensitivity as a marker for NCEP-ATPIII, while DeFerranti's definition has the lowest sensitivity of hs-CRP (68.29%).

In general, hs-CRP showed the highest sensitivity (82.61%) and second highest specificity (65.53%) for NCEP-ATPIII definition. The threshold value for serum hs-CRP value for all studied definitions was similar for all of definitions of MetS, and was approximately a value of 1.33 mg/L.

The subjects classified based on some MetS components who met its cutoffs and participants with three or four components integrated into one group because it was often the case that for any definition only one subject meet four criteria together, also no one met all five criteria. Results presented in Table 6 show that with an increasing number of components of MetS, the median serum hs-CRP increased for all the studied criteria except in IDF definition. In the latter definition, in contrast with median values for hs-CRP, most frequent value in 3 or more and two components group was 5.47 mg/L and 0.20 mg/L, respectively; but due to different subject numbers in each group, median value in group with two component showed higher amount than 3 or more group.

Discussion

In this study, we aimed to investigate the potential use of serum hs-CRP as a biomarker for pediatric MetS in schoolgirls. MetS was defined using four different criteria: The IDF, NCEP, Cook's and DeFerranti's definitions. In general, the prevalence of MetS based on studied definitions was very low and ranged from 1.2% to 4.3% for IDF and DeFerrani's definition, respectively. According to our findings, the highest prevalence was observed in 12 years old and then in 18year age group. Based on often used definitions of MetS, the 14 years age group showed the lowest prevalence of MetS in this population. Kelishadi et al. reviewed the prevalence of MetS among Iranian children and adolescents; they are reported the prevalence of pediatric MetS ranged between 1% to 22% based on different definitions, such as NCEP-ATPIII: 3% to 16%, IDF: 0% to 8% and, DeFerranti's: 0% to 22% [4]. In meta-analysis study by Ostovar et al. [23] showed that

Number of features of MetS	hs-CRP median (IQR3-IQR1)						
	IDF	NCEP-ATPIII	Cook et al. 2003	De Frranti et al. 2004			
0	0.83 (1.4542)	0.80 (1.5139)	0.82 (1.4640)	0.75 (1.3535)			
1	1.04 (1.9058)	1.06 (1.8257)	1.12 (1.9358)	0.89 (1.6445)			
2	3.05 (5.91-1.33)	1.41 (2.6278)	1.46 (3.0393)	1.27 (2.4077)			
*3 or more	2.89 (5.33-1.54)	3.52 (5.47-1.34)	4.58 (5.87-1.54)	1.73 (5.15-1.15)			

Table 6: The hs- CRP median based on a number of criteria in four different definitions.

IDF: International Diabetes Federation; NCEP-ATPIII: National Cholesterol Education Program-Adult Treatment Panel

*in often definition only one subject meet four criteria together, also no one meets five criteria together, so this subject integrates into one group named 3 or more.

prevalence of pediatric MetS among girls was 7.6%, 3.9% and, 15.5% for ATPIII, IDF and DeFerranti's definition, respectively. In the east of Iran, some reports showed the low prevalence of MetS in children and adolescents [24,25].

Obesity as a major component of MetS is associated with insulin resistance possibly due to the increased production of inflammatory cytokines, and some researchers believed to inflammation as an important mechanism in the etiology of MetS [26]. Serum hs-CRP could be useful for the prediction of CVD risk and diabetes development in the future; as well as prognostic information from the Framingham risk score is available [27]. Therefore, in the present study, we measured the association of each definition and their components with hs-CRP values. A significant association was found between serum hs-CRP and WC, TG and, HDL; but this association with HDL was weak. Similar to the present study, many studies showed an association between high hs-CRP and MetS [3,11,13,16,28-30]. Among the MetS components, obesity has the highest correlation with hs-CRP, this finding has been confirmed by other research which that found association between high hs-CRP and BMI or WC as a measure of obesity [1,13,14,17,20,28,31-33].

In adults, serum hs-CRP levels are significantly associated with body fat and also with some components of MetS [19]. This suggests that a high serum hs-CRP in MetS might be related to chronic systemic inflammation. In some studies, there is relationship between lipid profile abnormalities and hs-CRP values [3,11,13,17,28,29,31,34], relation between hs-CRP and lipid profile disorders might be proposed that this condition affected normal function of liver and high hs-CRP levels lead to liver dysfunction, there are evidence for that adolescent with NAFLD have high-level hs-CRP in comparison of no NAFLD ones [14], also Oda et al. [29] showed a correlation between hs-CRP levels and ALT.

We did observe no statistically significant association between hs-CRP and FBG and BPs in any of the studied definitions, the relationship between hs-CRP and BP was not significant. Some studies have reported a significant association between a high serum hs-CRP and systolic BP [3,11,29], diastolic BP [1,34]; also, some studies like our study did not observe any correlation between hs-CRP and BP [20,27,31]. However, Abdullah et al. [28] did find serum hs-CRP was associated with BPs only in obese individuals with MetS. They found no significant correlation between hs-CRP and BP in overweight and normal individuals [28]. This complicated relationship may be attributed to sampling size, gender, and ethnicity and may need more investigation.

We found no significant association between FBG and serum hs-CRP in our study. Similar findings reported by Oliveira et al. [17] which that may be related to increasing of hs-CRP influenced by obesity before the disturbance of glucose metabolism. Many studies have shown that serum hs-CRP is related to the number of MetS components [11,17,27,29,30]. This suggests MetS components clustering may be accompanied by an increasing proinflammatory status that is closely related to adipose tissue dysfunction. Also, these findings point to a higher the risk of cardiovascular being a consequence of a higher number of components of MetS.

ROC analysis was performed for computing sensitivity and specificity of serum hs-CRP for pediatric MetS definition. We found sensitivity and specificity, 68.29% to 82.61% and 64.68% to 65.90% for serum hs-CRP for the different definitions of MetS, respectively. AUC for different definitions varied 0.649 to 0.788 and cutoff value for all studied definitions have been determined more than 1.33 mg/L hs-CRP. As similar to these findings, Oda and Kawai reported that AUC of hs-CRP was 0.74 and sensitivity 67% and specificity 72% in Japanese women [29]. In another report, the cutoff value for serum hs-CRP was 1.04 mg/L with sensitivity and specificity, 58% and 92%, respectively [1]. Also, Han et al. resulted that AUC of hs-CRP for prediction of MetS development was 0.684 [3]. This similarity in different ethnic groups with MetS might be suggested hs-CRP as a potential inflammatory marker for MetS which that reproducible, easy access results; but low values for specificity make it unreliable.

Conclusion

MetS is recognized as a cluster of risk factors including obesity, lipid profile abnormalities, glucose metabolism disorders, and hypertension. MetS is also characterized by a chronic lowgrade inflammation condition. Current definitions of MetS lack a component that measures inflammatory status. Serum hs-CRP has been suggested as a sensitive marker that is predictive of MetS as well as the development of cardiovascular problems. The present study investigated the relationship of hs-CRP and MetS in pediatrics. In conclusion, we found an association between hs-CRP and pediatric MetS and some of its components, by certain definitions. We also show that hs-CRP values can predict MetS in pediatrics and suggest measurements of hs-CRP as a risk factor for MetS in large scale screening due to easy access and cost-effective measures, but more studies are required to clarify the clinical application of hs-CRP, particularly in boys, and in girls who are defined by menarche status.

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