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High Sensitive C-reactive Protein for Prediction of Cardiovascular Risk Level in Patients with Metabolic Syndrome in Sulaimania-Iraq

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Abstract
Background and objective: Metabolic syndrome is a group of characteristics, which include obesity, high blood pressure, elevated blood sugar levels, and high triglycerides (fat-like substances in the blood). Having a combination of these characteristics increases the risk of developing type 2 diabetes and heart disease. People with central obesity have an increased risk for developing metabolic syndrome, type 2 diabetes, and cardiovascular disease. However, a substantial number of obese individuals have no other cardiovascular risk factors, besides their obesity. C-reactive protein (CRP) is an acute phase protein produced predominantly by hepatocytes under the influence of cytokines such as IL -6 and TNF-α. Determination of hs-CRP was carried out in this study to discriminate between centrally obese people with and without metabolic syndrome. **Patients and Methods:** One hundred and forty subject with central obesity aged 20-70 years underwent a physical examination and laboratory assays to determine the presence of metabolic syndrome (NCEP ATP III criteria). The subjects were categorized into metabolic syndrome and non -metabolic syndrome group to decide whether CRP has an impact on the development of metabolic syndrome, and further subdivision have made to sub classify them to five sub-groups according to the existence of components of metabolic syndrome. **Results:** Mean hs-CRP levels were significantly higher in individuals with central obesity with metabolic syndrome (n = 101; 72.1%) compared to individuals with central obesity without metabolic syndrome (3.64 mg/L versus 1.75 mg/L (IQR 1.25-2.24); $p < 0.0001$). Mean hs-CRP levels increased with increasing number of metabolic syndrome components present. In univariable linear regression analyses, hs-CRP was significantly correlated positively with body mass index, waist circumference, and atherogenic index, while a significant negative correlations was found with HDL-C level. All the obese participants were at risk of cardiovascular events. **Conclusions:** The degree of central obesity (waist circumference) and BMI seemed to be the main determinant of an increased hs-CRP level. Serum hs-CRP was significantly correlated with the presence of metabolic syndrome; strong relationship between serum hs-CRP and various features of metabolic syndrome. The addition of serum hs-CRP to the present definition of the metabolic syndrome may help to identify patients at high risk for future cardiovascular disease.
Keywords: Abdominal obesity, Metabolic syndrome, High sensitive C-reactive protein.

Introduction

It is well known that obesity is detrimental to health. The abdominal obesity (also known as central obesity, central adiposity) means that most of the excess fat is located in the abdominal area. It is the most serious form of obesity and is strongly associated with cardiovascular disease (Pérez *et al*., 2007; Gelber *et al*., 2008; Zalesin *et al*., 2008), diabetes mellitus (Wang *et al*., 2005), some types of cancer (Folsom *et al*., 2000), psoriasis (Setty *et al*., 2007), adverse pregnancy outcomes (Wendland *et al*., 2007), earlier mortality in old age (Price *et al*., 2006) and many other health conditions. Furthermore, it is also a component of the metabolic syndrome for most definitions (Grundy *et al*., 2005).

Adipose tissue produces and releases a variety of proinflammatory and anti-inflammatory factors, including the adipokines; leptin, adiponectin, resistin, and visfatin, as well as cytokines and chemokines such as TNF-α, IL-6 (that stimulates the liver to produce and release C-reactive protein [CRP]), monocyte chemo attractant protein-1, and others. Proinflammatory molecules produced by adipose tissue have been implicated as active participants in the development of insulin resistance and the increased risk of cardiovascular disease associated with obesity.

Metabolic syndrome is defined as the clustering of multiple metabolic risk factors that increase the risk of cardiovascular diseases, type 2 diabetes and all-cause mortality (Meigs, 2000; Laaksonen *et al*., 2002; Lakka *et al*., 2002). However, currently, there is no accepted criterion for the diagnosis of metabolic syndrome. The National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) identifies various components of metabolic syndrome in adults and defines it as having three or more of the following: abdominal

obesity (waist circumference ≥102 cm for men and ≥88 cm for women), triglyceride levels ≥150 mg/dl, high-density lipoprotein (HDL) cholesterol ≤ 40 mg/dl for men and ≤ 50 mg/dl for women, blood pressure ≥130/ 85 mm Hg, and fasting plasma glucose ≥100 mg/dl (Grundy *et al*., 2004). Other organizations, such as the World Health Organization (Alberti and Zimmet , 1998), the European Group for the Study of Insulin Resistance (Balkau and Charles, 1999) the American College of Endocrinology (Einhorn *et al*., 2003) , and the International Diabetes Federation (Alberti *et al*., 2005) have also proposed a criteria for the diagnosis of the metabolic syndrome, keeping in common the general features of a combination of central obesity, elevated blood pressure, dyslipidemia, and impaired glucose metabolism.

Findings from the Hispanic Health and Nutrition, metabolic syndrome is also considered as a proinflammatory state (Grundy *et al*.,2004), and measurement of inflammatory markers like high-sensitivity C-reactive protein (hs-CRP) (Ridker *et al*., 2004) might improve the prediction of cardiovascular disease and diabetes in patients with metabolic syndrome. Previous studies showed that CRP is associated with components of metabolic syndrome (Festa *et al*., 2000), and including abdominal obesity (Dandona *et al*., 2005). Cytokine production by adipocytes might mediate the elevation of CRP levels.

The aim of this study is to:

1- Evaluate the application of hs-CRP to discriminate those with metabolic syndrome from those without metabolic syndrome in a population with central obesity.

2- Evaluate the association between serum hs-CRP level and number of components of metabolic syndrome.

3- Evaluate the role of High sensitive C-reactive Protein for prediction of Cardiovascular risk level in Metabolic Syndrome patients In Sulaimania.

Materials and Methods

2.1. Subjects and sample collection

2.1.1. Subjects

This randomized cross sectional based study was approved by the Scientific Committee of the Hawler Medical University at the College of Pharmacy. The patients were recruited from Endocrinology Centre of Sulaimani at Sulaimania governorate-Kurdistan Region-Iraq over a period from May to September 2012. A verbal consent form was obtained from each participant prior to admission into the study.

2.1.2. Criteria of inclusion

Every centrally obese people from both genders (male and female) aged between twenty to eighty years. Central obesity is defined as measured waist circumference (≥ 88 cm in women; ≥ 102 cm in men). Obese peoples already on drug treatment for diabetes and hypertension were considered as diabetic and hypertensive respectively.

2.1.3. Criteria of exclusion

Patients with evidence of acute infections, chronic inflammatory disorders and autoimmune diseases were excluded from the study. Also patients with serum hsCRP >10 mg/L have been excluded.

A total number of one hundred and forty patients were admitted into the study and fulfill the above criteria of inclusion and exclusion. Each Patient was subjected to physical examination, determination of blood pressure and anthropometric measurements. Three measurements of blood pressure (systolic and diastolic) were obtained from the right arm of the patient in sitting position after 30 minutes of resting at five minutes intervals and their average values were calculated. The anthropometric measurements included weight (kg), height (m), waist circumference (cm) and calculated body mass index. The waist circumference (cm) was measured with a soft tape measurement on standing position, midway between the lowest rib and the iliac crest. Body mass index (BMI) was calculated using Quetlett's equation:

$$\text{BMI (kg/m}^2\text{)} = \frac{\text{weight}}{\text{squared height}}$$

Then the patients were subjected to the laboratory investigations including the determination of fasting serum glucose and lipid profile, and hs-CRP.

Metabolic syndrome (MetS) was defined by the criteria of the NCEP ATP III. The diagnosis was made when at least three of the five following criteria were present: waist circumference ≥ 88 cm (women) or ≥ 102 cm (men); triglycerides ≥ 150 mg/dl; HDL cholesterol < 50 mg/dl (women) or < 40 mg/dl (men); blood pressure ≥ 130/≥ 85 mmHg; fasting glucose ≥ 100 mg/dl. (individuals on antihypertensive, hypoglycemic agents expected as hypertensive & diabetic respectively).

Then the patients were classified into two groups; metabolic group and non-metabolic group.

3. Results

3.1. Distribution of participants according to the number of MetS components:

A total number of 140 patients fulfilling the criteria of inclusion were admitted in the study. From these 140 obese peoples; 8 (5.7%) have one MetS component ; 31(22.1) have two MetS components; 38(27.1) have three

MetS components; 51(36.4) have four MetS components; and 12(8.6%) have five MetS components (Figure 3.1).

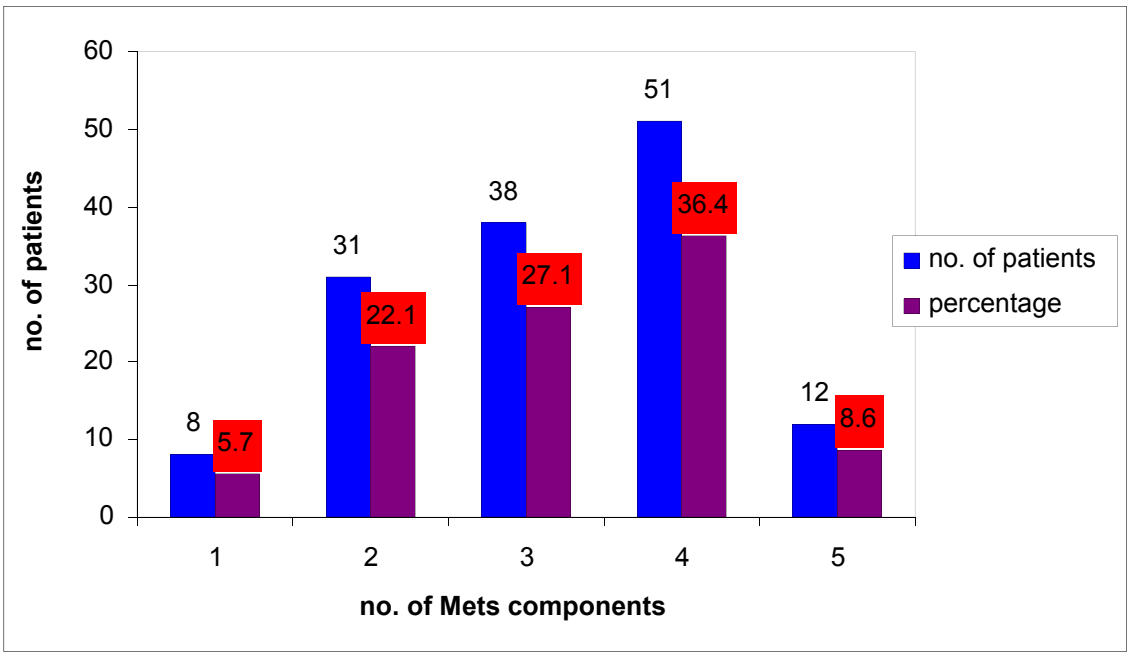

Figure 3.1. Distribution of participants according to the number of Metabolic Syndrome components.

3.2. Distribution of cases according to the evidence of MetS:

metabolic syndrome was evident in 72.1% (101 out of 140) with the existence of 3 or more MetS components whereas 27.9% (39 out of 140) were non metabolic (Figure 3.2).

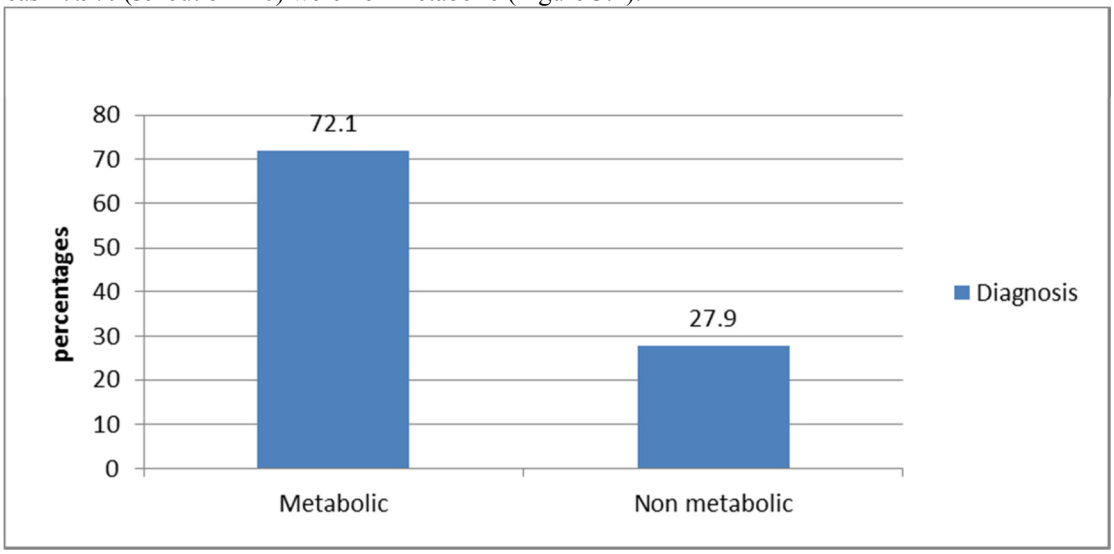

Figure 3.2. Distribution of cases according to the evidence of Metabolic Syndrome.

3.3. Distribution of participants according to the gender:

Female gender comprised 70.7% (99 out of 140) of total participants and 70.7% of them (70 out of 99) were MetS while 29.3% (41 out of 140) were men and 75.6% of them (31 out of 41) were MetS (Table 3.1).

Sex	Frequencies	Percentages	Non Mets N (%)	MetS N(%)	P values
Male	41	29.3	10(24.4)	31(75.6)	
Female	99	70.7	29(29.3)	70(70.7)	0,55
Total	140	100	39 (27.9)	101(72.1)	

The results are expressed as number (%)

Table 3.1 Distribution of participants according to the gender

3.4. Serum hs CRP level in both (metabolic & non metabolic) groups:

The mean±SD hs-CRP value of the participants without MetS was 1.75±1.530 mg/L compared with 3.64±2.760 mg/L in the group with MetS, and there is a significant differences between them (p= 0.0001) (Table 3.2).

	Mean Mg/L	±S D Mg/L	95% Confidence Interval for Mean		P values
			Lower limit	Upper limit	
HsCRP					
Non MetS	1.75	1.530	1.25	2.24	0.0001
MetS	3.64	2.760	3.10	4.19	

Table 3.2 Serum high sensitive C-reactive protein level in both (metabolic & non metabolic) groups

3.5. The mean age of patients in respect of the number of metabolic syndrome components:

The mean age of patients tended to be increased as the number of MetS component increased up to four and five (Figure 3.3).

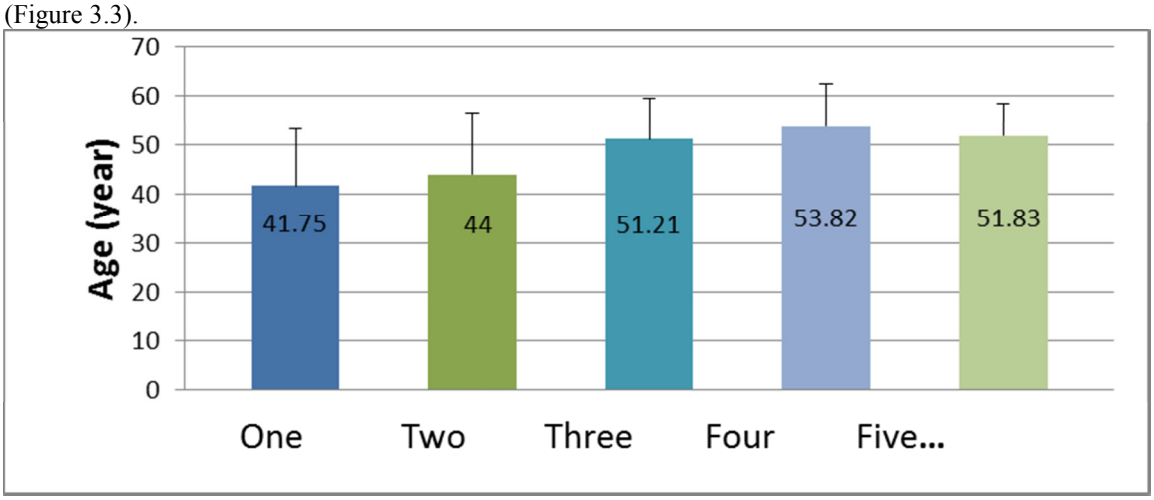

Figure 3.3 The mean age of patients in respect of the number of metabolic syndrome components

3.6. Anthropometric measurements:

Table3.3 showed the anthropometric measurement of patients enrolled in the study. The mean values of BMI showed that all the patients were overweight (one component MetS) or obese (Two, three, four and five components MetS). Central obesity assessed by measuring the waist circumference was observed in all patients.

	One Component (n=8)	Two Component (n=31)	Three Component (n=38)	Four Component (n=51)	Five Component (n=12)
Weight (kg)	76.62±4.43	76.32±12.06	81.73±14.20	86.27±16.36	87.75±15.51
Height (m)	1.606±0.108	1.587±0.085	1.592±0.094	1.616±0.092	1.604±1.105
BMI (kg/m^2)	29.88±2.704	30.28±4.14	32.24±5.358	32.92±5.23	33.92±3.64
Waist circumference(cm)	97.37±5.90	98.74±7.65	104.68±9.63	106.94±10.29	107.0±9.72

The results are expressed as mean ± SD

Table 3.3 Anthropometric measurements

3.7. Correlations between waist circumference and number of MetS components:

The mean value of waist circumference tended to be increased with increasing the number of MetS components This increment tended to be significantly ($p<0.001$) positively correlated ($r=0.945$)(Figure 3.4).

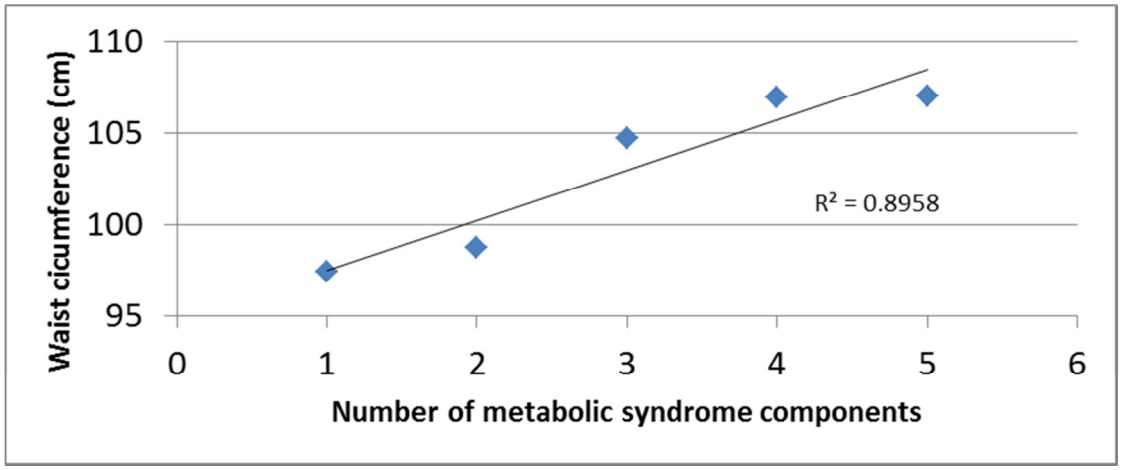

Figure 3.4 Correlations between mean value of waist circumference and number of metabolic syndrome components. Each point represents the mean value of number of patients.

3.8. Blood pressure measurements

The means of systolic and diastolic blood pressures were within normal range. This indicates that the presence of high blood pressure as a component of metS was sporadically distributed.

	Component (1) (n=8)	Component (2) (n=31)	Component (3) (n=38)	Component (4) (n=51)	Component (5) (n=12)
Blood pressure (mmHg)					
Systolic	118.75±3.535	108.38±12.13	117.36±17.19	118.43±13.61	120.0 ±17.58
Diastolic	78.75±3.535	73.70±11.39	76.84±12.32	76.56±10.83	80.83±11.64

The results are expressed as mean ± SD

Table 3.4 Blood pressure measurements

3.9. Fasting serum Lipid profile measurements:

Table 3.5 shows the mean values of lipid profile in centrally obese patients presented with evidence of metabolic syndrome.

	Component (1) (n=8)	Component (2) (n=31)	Component (3) (n=38)	Component (4) (n=51)	Component (5) (n=12)
Cholesterol	173.75±32.5	151.67±28.55	156.1±36.55	159.66±37.47	153.08±23.73
Triglycerides	112.25±29.21	106.77±26.35	153.65±87.10	211.54±100.25	229.33±60.09
HDL	45.25±4.13	43.45±10.51	40.10±9.59	34.39±8.13	28.66±6.154
LDL	106.05±33.13	86.87±26.36	85.34±33.87	82.96±41.68	78.55±23.37
VLDL	22.45±5.84	21.35±5.27	30.73±17.42	42.30±20.05	45.86±13.81
TG/HDL ratio	2.483±0.644	2.564±0.796	4.004±2.322	6.440±3.900	8.234±2.581

The results are expressed as mean ± SD. HDL; high density lipoprotein, LDL; low density lipoprotein, VLDL; very low density lipoprotein

Table 3.5 Fasting serum Lipid profile measurements

3.10. Correlations between number of MetS components and HDL:

The fasting serum HDL tended to be significantly and negatively correlated with number of components of MetS (Figures.3.5).

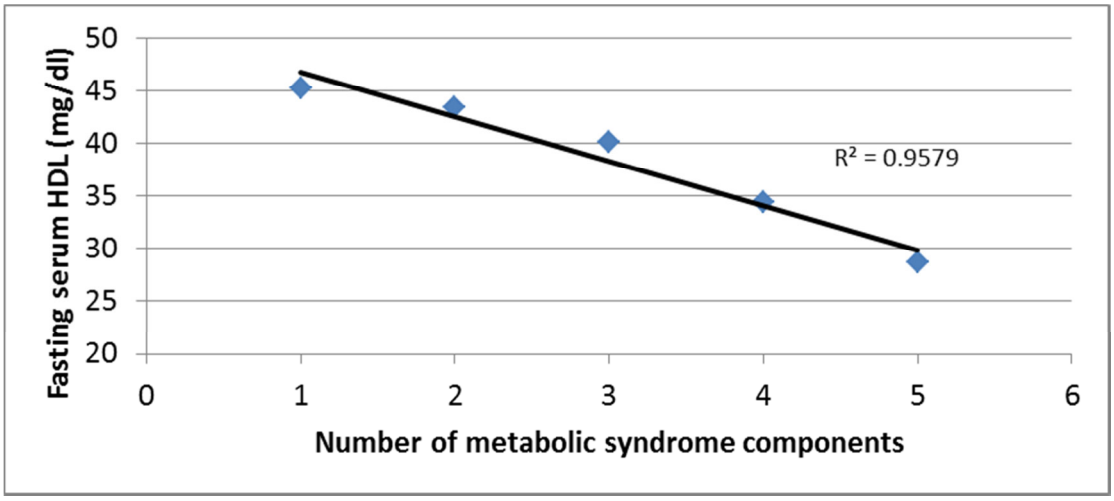

Figure 3.5 Correlations between number of metabolic syndrome components and mean value of HDL. Each point represents the mean value of number of patients.

3.11. Correlations between number of Mets components and LDL:

The fasting serum LDL tended to be significantly and negatively correlated with number of components of MetS (Figures.3.6).

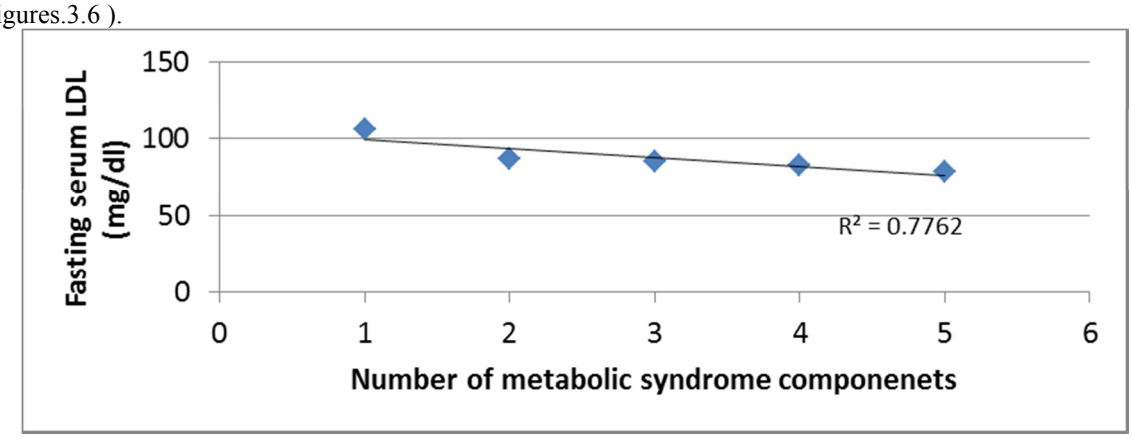

Figure 3.6 Correlations between number of metabolic syndrome components and mean value of LDL . Each point represents the mean value of number of patients.

3.12. Correlations between number of MetS components and atherogenic index:

Significant positive (direct) correlation between fasting serum triglycerides and atherogenic index with the number of MetS components were observed (Figures 3.7).

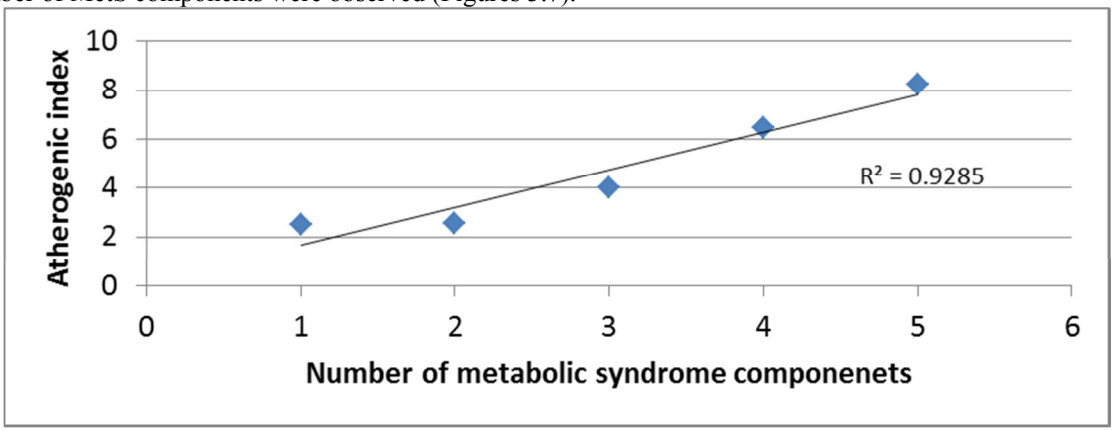

Figure 3.7 Correlations between number of metabolic syndrome components and mean value of atherogenic index. Each point represents the mean value of number of patients.

3.13. Correlations between number of MetS components and Triglyceride:

Significant positive (direct) correlation between fasting serum triglycerides and atherogenic index with the number of MetS components were observed (Figures 3.8).

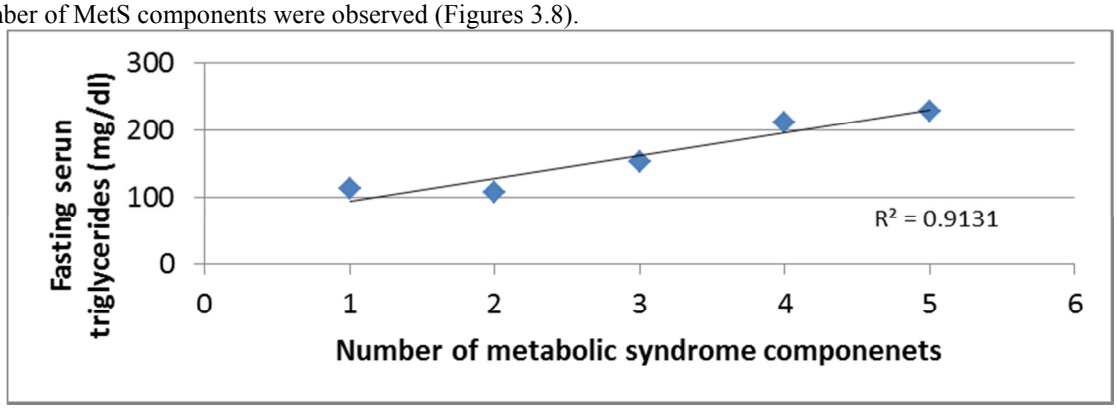

Figure 3.8 Correlations between number of metabolic syndrome components and mean value of triglycerides . Each point represents the mean value of number of patients.

3.14. Correlations between number of MetS components and fasting blood glucose:

The mean value of fasting blood sugar increased with an increase in the number of MetS components to reach a diabetic level values (Figure 3.9).

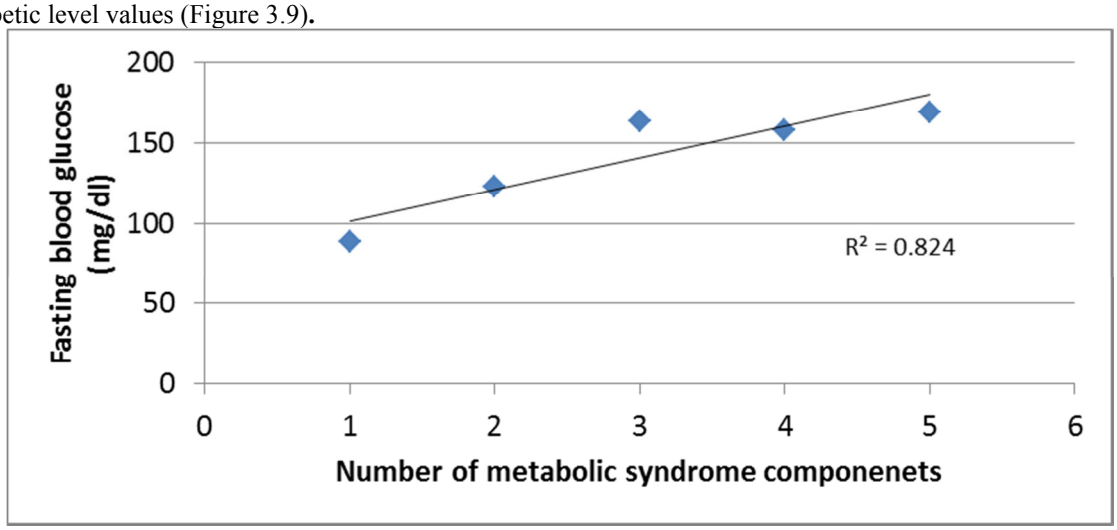

Figure 3.9 Correlations between number of metabolic syndrome components and fasting blood glucose

3.15. Correlations between the mean serum level of hs-CRP level of each component number and the component numbers of MetS:

Serum level of hs-CRP increased significantly with a rise in the number of MetS components and it amounts 0.987±0.438, 1.943±1.651, 3.083±2.774, 3.934±2.713, 4.180±2.842 mg/L for one, two, three, four and five components of metabolic syndrome respectively. Taking in consideration the regression equation of best fit line, for each one component increment there is an increase of 0.821 mg/L hs-CRP (Figure 3.10).

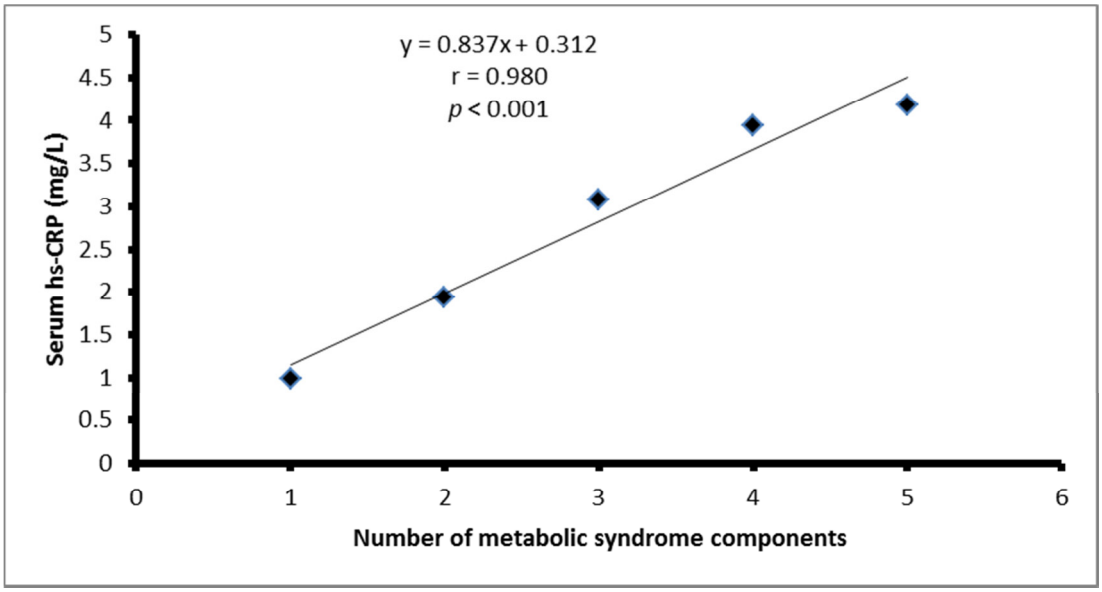

Figure 3.10 Correlations between the mean serum level of hs-CRP level of each component number and the component numbers of metabolic syndrome

3.16. Correlations between body mass index and serum hs-CRP level:

Significant positive correlation between hs-CRP and anthropometric measurements related to the obesity. We observed that the hs-CRP was significantly correlated with body mass index (Figure 3.11).

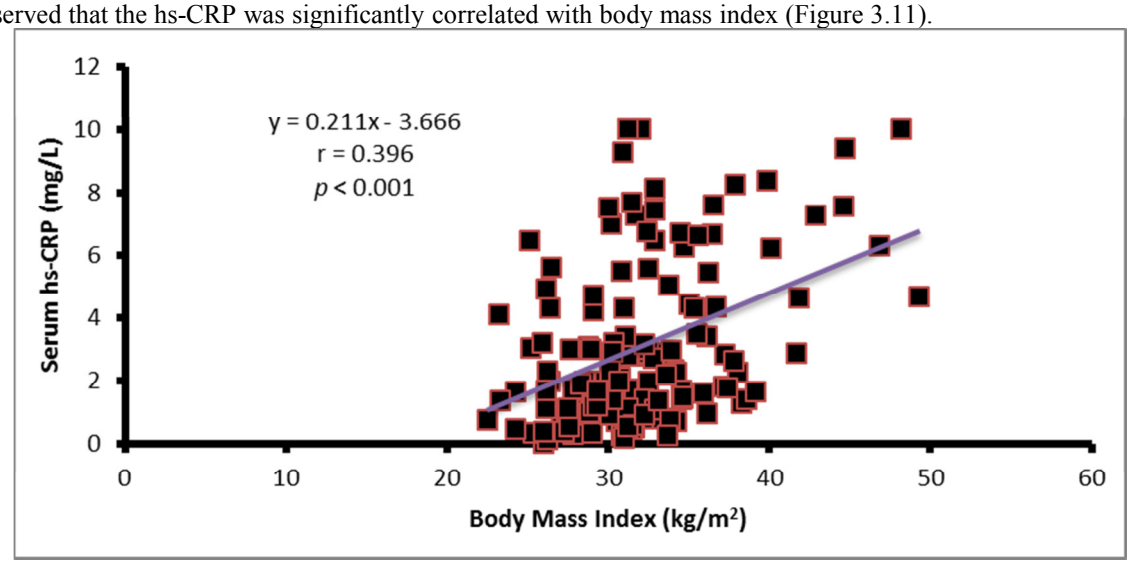

Figure 3.11 Correlations between body mass index and serum hs-CRP level.

3.17. Correlations between waist circumference and serum hs-CRP level:

Hs-CRP significantly directly correlated with waist circumference (Figure 3.12).

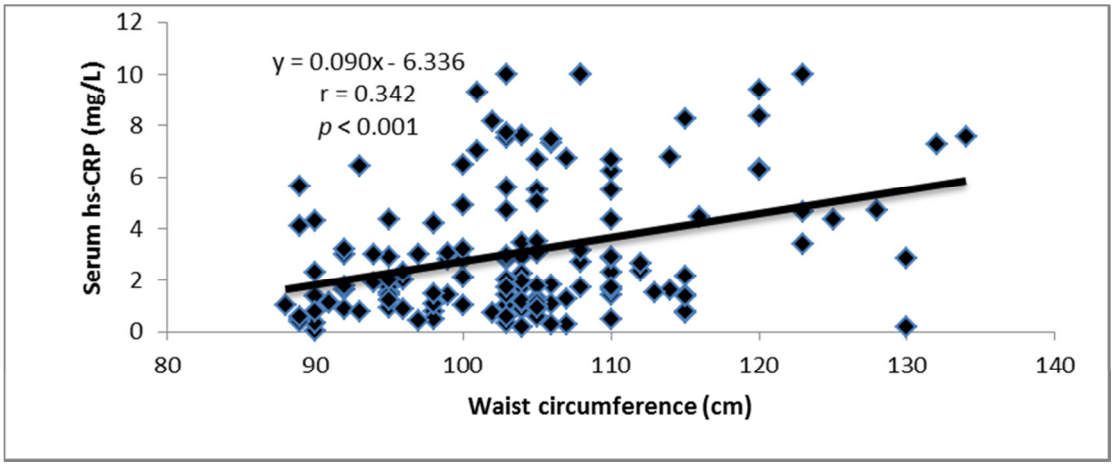

Figure 3.12 Correlations between waist circumference and serum hs-CRP level.

3.18. Correlations between mean arterial blood pressure and serum hs-CRP level:

Figure 3.13 shows non significant negative correlation between the serum level of hs-CRP and the mean arterial blood pressure (mean arterial blood pressure= diastolic blood pressure $+\frac{1}{3}$ (systolic blood pressure –diastolic blood pressure).

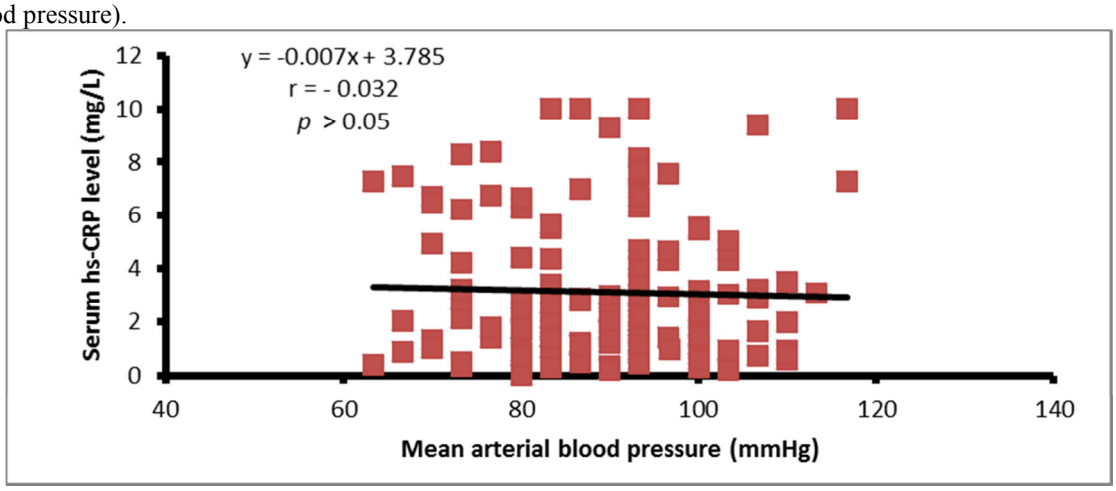

Figure 3.13 Correlations between mean arterial blood pressure and serum hs-CRP level

3.19. Correlations between serum high density lipoprotein level and serum hs-CRP level:

The serum level of hs-CRP is significantly and negatively correlated with high density lipoprotein level (Figure 3.14).

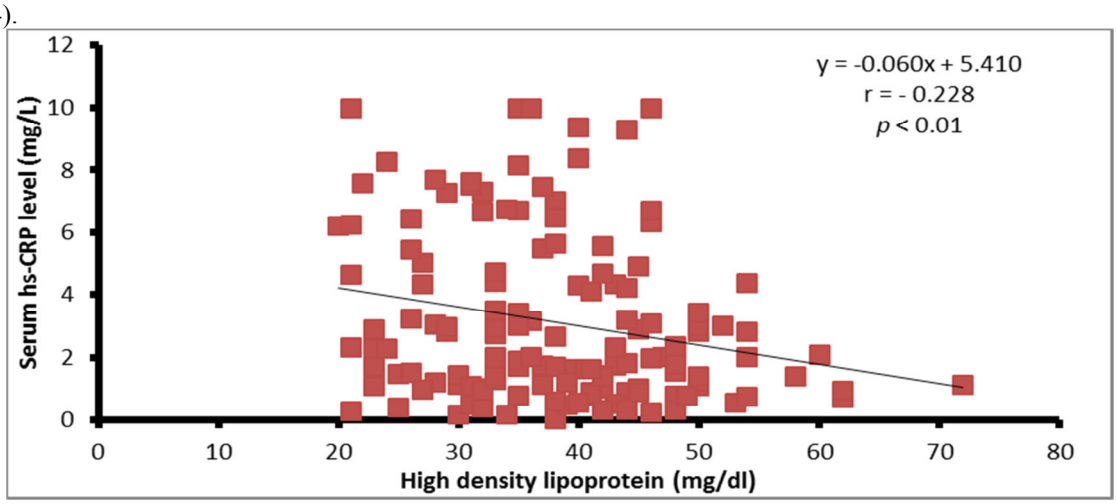

Figure 3.14 Correlations between serum high density lipoprotein level and serum hs-CRP level.

3.20. Correlations between serum triglycerides level and serum hs-CRP level:
Non-significant positive correlation between serum triglycerides level and hs-CRP (Figure 3.15).

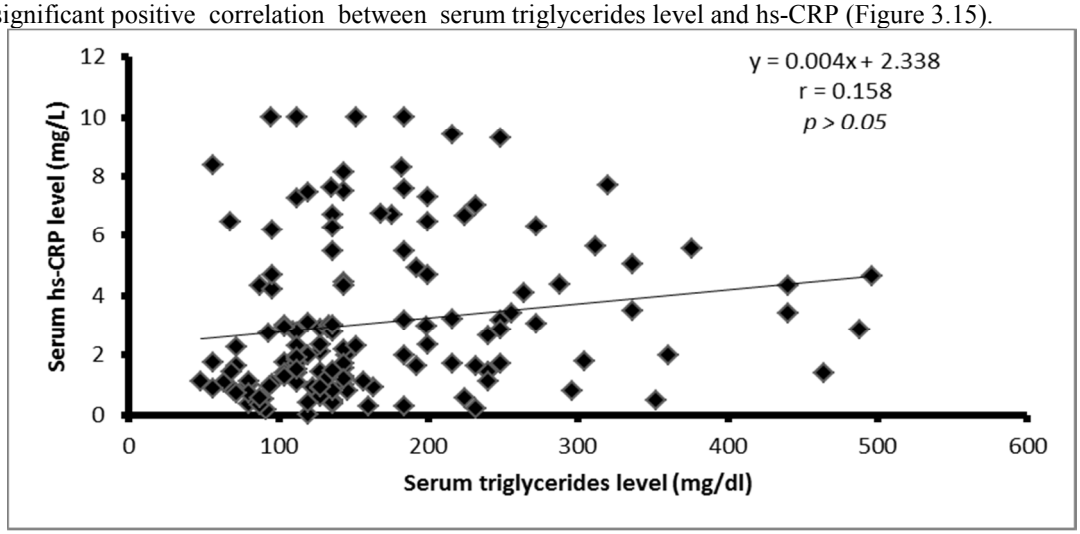

Figure 3.15 Correlations between serum triglycerides level and serum hs-CRP level

3.21. Correlations between atherogenic index and serum hs-CRP level:
Atherogenic index as a marker of cardiovascular risk factor is directly and significantly correlated with hs-CRP (Figure 3.16).

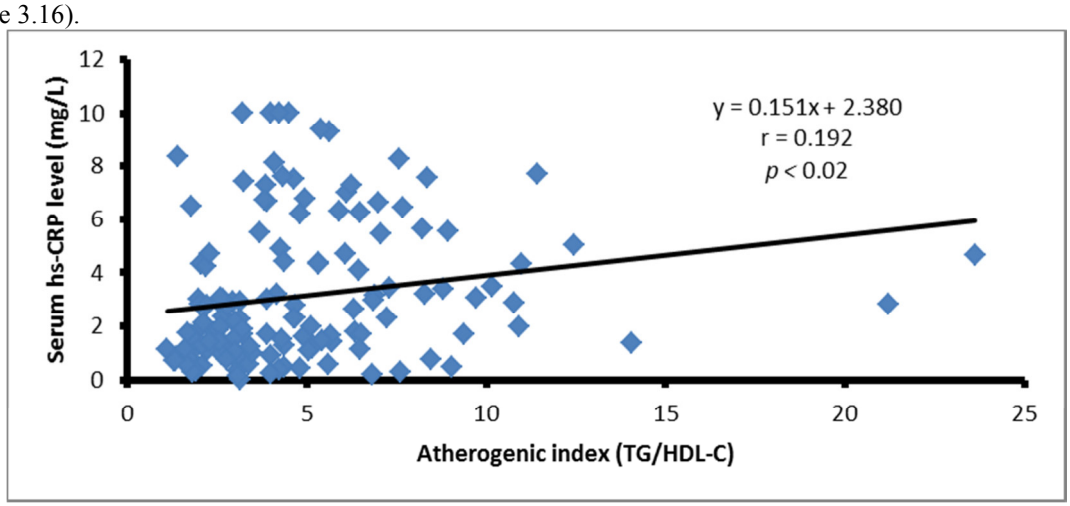

Figure 3.16 Correlations between atherogenic index and serum hs-CRP level

3.22. Patients at cardiovascular events risk with respect to high sensitive C-reactive protein and number of components of metabolic syndrome:
Table 3.6 shows the importance of measurement of serum hs-CRP in obese subjects. All the obese participants were at risk of cardiovascular events; 20.7% were at low risk; 41.4% were at average risk; and 37.86% were at high risk. On the other hand, as the number of components of metabolic syndrome increased the level of hs-CRP increased and the risk status also increased.

Hs CRP level	Number of components of metabolic syndrome					Total
	1	2	3	4	5	
Low risk 0-1.0 mg/L	5	8	8	7	1	29 (20.7%)
Moderate risk 1.0–3.0 mg/L	3	18	17	15	5	58 (41.4%)
High risk 3.0–10.0 mg/L	0	5	13	29	6	53 (37.86%)
Total	8	31	38	51	12	140 (100%)

The results are expressed as number (percent)

Table 3.6 Shows the patients at cardiovascular events risk in respect to high sensitive C-reactive protein and number of components of metabolic syndrome

4. Discussion

The results of this study demonstrate the importance of measuring the level of hs-CRP in metabolic syndrome as well as its significant association with the other components of metabolic syndrome.

The close relationship between abdominal obesity, metabolic disturbances and cardiovascular disease is apparent for clinicians (Santos *et al.*, 2005; Gonzalez *et al.*, 2006; Dupuy *et al.*, 2007; Zuliani *et al.*, 2009; Kressel *et al.*, 2009;) .

Adipose tissue is not just a storage facility for fatty acids. It is an active endocrine organ, producing bioactive proteins named adipokines (Winkler *et al.*, 2003; Trayhurn, 2005). Adipokines include interleukin-6, adiponectin, resistin, adipsin, tumor necrosis factor-alpha, plasminogen activator-inhibitor-1 and many more.

Adipokines involved in a multitude of processes like inflammation, insulin resistance, lipid metabolism, blood pressure, macrophage infiltration, fibrinolysis, food intake, fat mass regulation and more (Hajer *et al.*, 2008).

Cytokines/Adipokines associated with low-grade inflammation were interleukin-6 and tumor necrosis factor-alpha, and these are shown to be up-regulated in obese patients (Winkler *et al.*, 2003).

Studies showed that levels of CRP are significantly related to levels of IL-6 and TNF-apha (Yudkin *et al.*, 1999). Interleukin-6 is the chief stimulator of CRP production. Abdominal adipose tissue, with its increased production of cytokines from both immune cells and adipocytes, is drained directly to the portal circulation. It could be that this direct route to the liver, where CRP is produced, is partly responsible for the increased production of CRP in abdominally obese people (Hajer *et al.*, 2008).

Metabolic syndrome is a clustering of risk factors for diabetes and cardiovascular disease, and abdominal obesity is a central feature in this syndrome. The syndrome is recognized as both a proinflammatory and prothrombotic state, but the cause of this is not yet fully understood (Reaven , 1988; Imayama *et al.*, 2012; Illán-Gómez *et al.*, 2012).

High sensitive -CRP is the most extensively studied inflammatory biomarker in cardiovascular disease. MetS seems to be a proinflammatory state characterized by increased concentrations of CRP. Several earlier studies have shown that high CRP concentrations predict the development of diabetes. CRP is shown to impair insulin signaling (D'Alessandris *et al.*, 2007). Although increased CRP concentrations correlate most strongly with adiposity and insulin resistance, CRP also correlates significantly with the other features of MetS (Yudkin *et al.*, 1999; Hak *et al.*, 1999; Festa *et al.*, 2000). Furthermore, CRP concentrations anticipate increased cardiovascular events in MetS and in diabetes (Ridker *et al.*, 2003; Rutter *et al.*, 2004; Aguilar *et al.,* 2006; Linnemann *et al.,* 2006).

In this study metabolic syndrome was detected in 101 patients (72.1%) with respect to NCEP ATP III definition.

4.1. Effect of Metabolic syndrome on the level of serum hs-CRP:

The mean of hs-CRP levels were significantly higher in individuals with central obesity with the MetS compared to individuals with central
obesity without the MetS.

The Results of this study are in line with several studies demonstrating higher hs-CRP levels in individuals with the MetS (Hak *et al.*, 1999; Festa *et al.*, 2000; Ridker *et al.*, 2003; Rutter *et al.*, 2004; Lee *et al.*, 2004; Santos *et al.*, 2005; Gonzalez *et al.*, 2006; Dupuy *et al.*, 2007; Zuliani *et al.*, 2009; Kressel *et al.*, 2009; Mahajan *et al.*, 2012).

4.2. Correlations between components of MetS and serum hs-CRP:

The means of hs-CRP levels increased with the increasing number of MetS components and our results are concordant with other studies which displayed a linear increase in hs-CRP levels with the rising number of components of the MetS described previously (Hak *et al.*, 1999; Festa *et al.*, 2000; Frohlich *et al.*, 2000; Ridker *et al.*, 2003; Rutter *et al.*, 2004; Lee *et al.*, 2004; Aronson *et al.*, 2004; Santos *et al.*, 2005; Gonzalez *et al.*, 2006; Zuliani *et al.*, 2009; Mahajan *et al.*, 2012) .

As the metabolic syndrome has several components, it could be stated that hs-CRP elevation is related to just one or some of these components. Several studies assessed the relation between hs-CRP and different MetS components; the results of our study is in a covenant with a number of univariable analyses showing significant associations for the individual MetS components(Festa et al., 2000;

Ridker et al., 2003; Rutter et al., 2004; Lee et al., 2004; Santos et al., 2005; Gonzalez et al., 2006; Dupuy et al., 2007; Zuliani et al., 2009).

Further multivariable analyses; adjusting for other MetS components, reported that central obesity was the major determinant of elevated hs-CRP levels in individuals with the MetS. The other MetS components do not, or only marginally, increase hs-CRP level (Aronson et al., 2004; Santos et al., 2005; Florez et al., 2006; Dupuy et al., 2007; Zuliani et al., 2009; Lu et al., 2010). This might explain why hs-CRP cannot be used to

predict the presence of the MetS. Nevertheless, researchers have proposed to add hs-CRP biomarker as a clinical criterion for the metabolic syndrome (Ridker et al., 2004). The reasons could be that it is shown to be a consistent prognosticator of cardiovascular and diabetes risk, and is practical in clinical settings.

The relationship between central obesity and increased levels of hs-CRP is well studied. Adipose tissue is known to secrete cytokines that stimulate the production of hs-CRP in the liver, but adipose tissue itself may also secrete hs-CRP and thereby raise hs-CRP levels (Ouchi *et al.*, 2003). Genetic polymorphisms could partially explain the inter-individual variability observed in the inflammatory profile of obese patients and the inter-individual variability in metabolic perturbations associated with obesity (Bouchard *et al.*, 2007; Faucher *et al.*, 2012).

Strong associations between CRP and measures of body fat (BMI and waist circumference) and measures of insulin resistance (insulin sensitivity index, fasting insulin, and proinsulin) were reported (Yudkin *et al.*, 1999; Festa *et al.*, 2000; Ridker *et al.*, 2003; Rutter *et al.*, 2004).

Although central obesity (waist circumference) and BMI seem to be the major determinant of elevated hs-CRP levels in the MetS, significant independent associations between hs-CRP and other components were found . Aronson *et al*., 2004 found an independent association between triglyceride level and hs-CRP (however, in our study we have found a non significant relation between hs-CRP and serum triglyceride) . In addition, they found associations between hs-CRP and glucose level and HDL cholesterol (our results have showed agreements with this results). However, this only accounted for ~1% of the variability in CRP levels (Aronson *et al.*, 2004).

Weight loss is shown to decrease CRP levels in obese subjects (Illán-Gómez *et al.*, 2012; Imayama *et al.*, 2012), which could support the theory that the adipose tissue is actively involved in the low-grade inflammatory state seen in abdominally obese people. Increased levels of CRP is found in obese people.

A cross sectional study on nondiabetic subjects done by (Yudkin *et al.*, 1999) showed that levels of CRP were correlated with all measures of obesity. CRP-levels were also related to insulin resistance, blood pressure, HDL, and triglycerides and markers of endothelial dysfunction. Yudkin *et al* (1999) suggested that adipose tissue is an important determinant of low-grade chronic inflammation, and that chronic low-grade inflammation may induce insulin resistance and endothelial dysfunction. They also stated that this could be a possible link between insulin resistance and endothelial dysfunction and obesity & cardiovascular disease (Yudkin *et al.*, 1999).

A Tunisian case control study found that waist circumference was a significant independent predictor of elevated CRP levels in both men and women with metabolic syndrome (Belfki *et al.*, 2012). Also, HDL-C was another significant predictor of elevated CRP levels in women only.

Further cross sectional study found that hs-CRP correlated significantly with all the components of the syndrome in both men and women, but the highest correlation was between waist circumference and hs-CRP (Rogowski *et al.*, 2010). These findings suggested that waist circumference is the Metabolic component of the syndrome that influences the low-grade inflammatory response. They also pointed out that overweight and obese individuals without the syndrome were at an increased risk for cardiovascular disease.

A cross-sectional study done in the Netherlands evaluated the use of hs-CRP to discriminate between centrally obese people with and without the syndrome (Engelsen *et al.*, 2012). They found that hs-CRP has limited capacity to predict the presence of the metabolic syndrome in people with central obesity. The mean hs-CRP levels were significantly higher in people with abdominal obesity with the metabolic syndrome than without it. As the numbers of components of the syndrome increased, so did the mean hs-CRP levels. Only waist circumference and triglyceride levels showed a significant independent association with hs-CRP. They concluded that the degree of central obesity seemed to be the main determinant of increased hs-CRP levels. The levels of hs-CRP were higher in centrally obese people with the syndrome than those without it, but it could not be used to diagnose centrally obese people with the metabolic syndrome in this study. Moreover, further studies found an independent association between hs-CRP and fasting glucose (Gonzalez *et al.*, 2006; Niehoff *et al.*, 2007).

Other Studies have also concluded that hs - CRP positively correlated with atherogenic index (Altan *et al.,* 2010; Idemudia and Idogun , 2012) and this is in agreement with the results of and supports the current study

Atherogenic index can be easily calculated from standard lipid profile. As a marker of lipoprotein particle size it adds predictive value beyond that of the individual lipids, and/or TG/HDL-C ratio (Dobiásová, 2006).

4.3. Hs-CRP as a predictor of risk level for future CVD:

All the obese participants were at risk of cardiovascular events;. On the other hand, as the number of components of metabolic syndrome increased the level of hs-CRP increased and the risk status also increased and this is in concordance with the results of German population-based study found that there was a positive trend in levels of CRP with increasing numbers of components of the metabolic syndrome using BMI and not waist circumference,. The age-adjusted geometric means (rather than arithmetic) mean of CRP concentrations in

subjects grouped according to the presence of 0-1,1- 3 and > 3 features of the metabolic syndrome were 1.11, 1.27, and 2.16 mg/L, respectively, (Frölich *et al.*, 2000).

Conclusions

Emerging laboratory and clinical evidence in participants with central obesity which were involved in this study have provided:

1. The degree of central obesity (waist circumference) and BMI seemed to be the main determinant of an increased hs-CRP level.
2. The serum hs-CRP was significantly correlated with the presence of metabolic syndrome, meaning that there is a strong relationship between serum hs-CRP and various features of metabolic syndrome
3. The addition of serum hs-CRP to the present definition of the Mets may help identify patients at high risk for future CVD.
4. According to the serum level of hs-CRP that was demonstrated in this study, all the patients are at risk of cardiovascular events.

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