Metabolic syndrome and risk of Coronary Artery Disease in west of Iran

Shila Berenjy [1,2], Asmah Bt Rahmat [3], Zaitun Bt Yassin [4], Lye Munn Sann [5], Farzad Sahebjamee [6], Parichehr Hanachi [7]

1. PhD. Candidate, Department of Nutrition and Dietetics, Faculty of Medicine and Health Sciences Universiti Putra Malaysia, 43400 UPM Serdang, Selangor D. E., Malaysia
2. Faculty of Food Sciences and Technology, Varamin-Pishva Branch, Islamic Azad University, Varamin, Iran
3. Professor, Department of Nutrition and Dietetics, Faculty of Medicine and Health Sciences Universiti Putra Malaysia, 43400 UPM Serdang, Selangor D. E., Malaysia
4. Associate Professor, Department of Nutrition and Dietetics, Faculty of Medicine and Health Sciences Universiti Putra Malaysia, 43400 UPM Serdang, Selangor D. E., Malaysia
5. Professor, Department of Community Health, Faculty of Medicine and Health Sciences Universiti Putra Malaysia, 43400 UPM Serdang, Selangor D. E., Malaysia
6. Associate Professor Department of cardiology, Kermanshah University of Medical Sciences Kermanshah, Iran
7. Associate Professor Biochemistry unit, Biology Department, Faculty of Science Alzahra University, Tehran-Iran

shila135071@yahoo.com

Abstract: A major concern about MS (Metabolic Syndrome) and CAD (Coronary Artery Disease) is that patients with these defects are at higher risks of mortality and morbidity due to a combination of MS risk factors. The purpose of study was to examine the differences between CAD and non-CAD patients regarding their MS components and selected lifestyle behaviors (i.e., dietary intake, physical activity patterns, and smoking habits) and there was an attempt to determine whether MS was an independent risk factor for CAD among the patients. The study used case-control methodology for collection and analysis of the data. 600 participants recruited for study. CLR was applied to quantify the odds Ratio (OR) of CAD associated with MS and its components and other life style risk factors of CAD. MS increased the risk of CAD 4.19 times significantly (OR=4.19, 95%CI=2.603-6.47, P= 0.0001). Multivariate analysis showed that MS conveyed no additional predictive information beyond its components (odds Ratio=0.81, p=0.6). The focus of physicians should be treatment of individual CAD risk factors, using the metabolic syndrome will not improve prediction of CAD as compared with detailed information on individual CAD risk factors.

[Shila Berenjy, Asmah Bt Rahmat, Zaitun Bt Yassin, Lye Munn Sann, Farzad Sahebjamee, Parichehr Hanachi. **Metabolic syndrome and risk of Coronary Artery Disease in west of Iran**. Life Sci J 2012;9(2):706-717] (ISSN: 1097 – 8135). http://www.lifesciencesite.com. 106

Keywords: Metabolic syndrome; Coronary artery disease; Risk factor; Iran

1. Introduction

Metabolic Syndrome (MS) also known as syndrome X, is comprised of hypertension, glucose intolerance, high triglycerides, and decreased level of high density lipoproteins (HDL). These defects in the body are considered as risk factors of cardiovascular diseases (Reaven, 1988). MS is also at time referred to as the Deadly Quartet, the Dysmetabolic Syndrome, and Insulin Resistance Syndrome. The above mentioned MS risk factors are considered as the main causes of development and progression of atherosclerosis, which eventually results in a higher risk for coronary artery diseases. MS components have also been associated with a higher risk for diabetes type 2. Generally, there is no single cause for MS; however, abdominal obesity and insulin resistance are the most important risk factors for this disease. Other underlying risk factors that can increase the risk of MS include physical inactivity, aging, hormonal imbalance, and race (Grundy, 2005). Previous research has shown that the MS confers an approximately twofold increase in relative risk for coronary vascular events. This implies that MS brings a relatively high risk for both CVD and diabetes (Stern et al., 1995). For the sake of brevity and clarity, I have classified the previous studies on MS into five categories. The first group of studies have highlighted the wide range of MS prevalence globally (e.g., Ford, 2002) and regionally including the latest statistics of the disease in Iran by Azizi (2004) and Ghayour-Mobarhan (2007). A second group of studies have emphasized the independent CAD prediction role for MS (e.g., Hunt, 2004; Lakka, 2002; Sadeghi, 2006; Chen, 2008). A third group of studies on MS show the biomolecular basis of MS components and their atherogenicity (Villena, 2004; Ginsberg, 2006; Szapary, 2004). The effect of dietary factors, as well as physical factors on the risk of MS have been emphasized by these studies (see Clark SD, 2000; Maki, 2004; Haffner, 2007). A fourth stream of studies (e.g., Laaksonen, 2002; Lee, 2005) has included life style factors (e.g., physical

activity, smoking habit, etc.) as influential on the risk of being involved in MS. Finally, the fifth category of studies (e.g., Ford, 2005; Ghayour, 2007; Azizi, 2004; Sadeghi, 2006) has suggested the need to explore the problem in different populations as a multivariable model.

The results of these studies have shown that patients with MS have a higher risk of developing CVD mortality & morbidity (Isoma et al. 2001, Chen et al., 2008). The main reason for this association is that a combination of risk factors concomitant with MS interacts synergistically with several other factors thereby causing or accelerating the progression of atherosclerosis (Isoma et al., 2002). It has been found that individuals with one or two of the MS components are at a two-fold greater risk of CAD and CAD mortality (Gorter, 2004; MacNeill et al., 2004). Similar studies have shown that the coronary artery disease is the leading cause of death in general population in Iran (Azizi et al., 2004) Although a strong link between MS and coronary artery disease (CAD) has not been well documented (Petra et al., 2004); studies investigating MS (Maki et al., 2004; Lee et al., 2005; Niaura et al., 2000; Raikkonen et al., 2002) have shown that MS can be influenced by biological, behavioral, and social factors which have already been identified as factors affecting the development of CAD. Likewise, The results of a few studies conducted on prevalence of MS and its risk factors in general population in Iran (Zabetian et al., 2007; Azizi et al., 2003) have suggested that MS factors can trigger CAD development although there is little knowledge determination of risk factors of MS in high risk patents in Iran.

Azizi et al., (2003) and Zabetian et al. (2007) note that over the past years general population in Iran have experienced rapid life style changes with drastic reductions in physical activity and increase in consumption of processed food, resulting in an epidemic of obesity and diabetes. The results of these studies indicate that lifestyle changes and dietary habits that carry the risk of MS, can also lead to aggravation of CAD patients' condition; however, research on life style screening for MS risk factors in CAD patients in the setting of this study-Iran has been scarce. Review of the literature on metabolic syndrome demonstrates that MS is a prevalent syndrome both throughout the world and in Iran (Azizi et al., 2004). As discussed earlier in this chapter, the noteworthiness of the epidemiologic studies on MS in Iran is that the prevalence of this syndrome is considerably higher in this region than the world rate. As a result of the combined effect of risk factors of MS, we know that the prevalence of MS is increasing parallel to the trend in overweight and obesity (Azizi et al., 2004). Generally, the prevalence of MS increases with age and its prevalence are considerably different among races and ethnic groups, which supports the probable impact of genetic predisposition. Based on the reviewed literature, it becomes evident that the genetic factors as well as the social, environmental, psychological, and behavioral variable are linked to this clinical syndrome to some extent although the direct association of these factors with CAD is still in need of further research. Previous studies (Azizi et al., 2004; Zabetian et al., 2007) have recommended a strong need for more studies to explain the interrelation between MS components and their association with CAD.

Numerous studies have focused on MS in CAD patients. Most of these studies consider MS as an independent predictor of CAD. Lakka (2002) states that individuals with metabolic syndrome are at increased risk for CAD. Similarly, Kragelund et al., (2007) showed that patients with positive exercise electrocardiogram or myocardial radionuclide imaging can suggest ischemia. They also concluded that the metabolic syndrome in women with stable coronary heart disease provides considerable prognostic information on all-cause mortality; however they did not find the same results in men. It is noticeable that this association was independent of diabetes. The invasive measurements of severity of coronary artery disease and left ventricular function, made this study unique in comparison with previous studies of metabolic syndrome and prognosis. In Iran, Zabetian and colleagues (2007) extended the previous knowledge about the value of MS as a risk factor in the general population to patients with stable coronary disease by emphasizing the prognostic significance of MS in women.

Chen and colleagues (2008) investigating the relationship between MS and CAD in elderly concluded that the CAD–MS patients showed a higher prevalence of multivessel disease, unstable lesions and needed more revascularization procedures than the simple CAD patients. Their study also determined that the prevalence of CAD and the number of blocked coronary vessels were directly correlated with MS their findings suggested that MS as a predictor of the prevalence and extent of future CAD in the elderly. Iribarren (2006) examining the association between the metabolic syndrome (MS) and early-onset coronary artery disease (CAD) concluded that the presence of ATP-III MS without diabetes and with diabetes was a strong independent determinant of early-onset CAD, but neither definition of MS remained significantly associated with early-onset CAD in multivariate models adjusting for individual components. Thus, Iribarren (2006) concluded that the MS is a risk factor of early-

onset clinical CAD, but the prognostic information associated with the syndrome was not greater than the sum of its parts. Numerous studies by other investigators have reached similar conclusions. For example, blood pressure, HDL cholesterol, and diabetes, but not presence of MS, were significant multivariate predictors of prevalent CAD in an analysis of the Third National Health and Nutrition Examination Survey (Alexander et al., 2003). In the Caerphilly and Speedwell population studies, the excess of ischemic heart disease risk associated with MS was no greater than that can be explained by individual effects of the defining variables in a multiple logistic model (Yarnell et al., 1998).

2. Material and Methods

The National Cholesterol Education Program (NCEP)-Adult Treatment Panel (ATP) has introduced one of the most widely accepted diagnostic criteria for the diagnosis of MS. This criteria works on some measurements including waist circumference, serum triglyceride (TG), HDL-C, Blood pressure (BP), and fasting blood sugar (FBS). Recently, as illustrated below the American Heart Association/National Heart Lung & Blood Institute (AHA/NHLBI) has made some minor modifications on the NECP criteria which is currently used in research focusing on MS and its association with Coronary Artery Diseases (CAD) (Grundy, 2005).

1. Waist circumference > 88 cm in women and >102 in men
2. Fasting triglycerides ≥ 150 mg/dL or medication for treatment
3. HDL cholesterol < 50 mg/dL in men and <40 in women or medication for treatment
4. Hypertension (systolic blood pressure ≥ 130 mm Hg, diastolic blood pressure ≥ 85 mm Hg or medication for treatment
5. Fasting glucose ≥100 mg/dL or medication for treatment

The elective coronary angiography was performed using Judkin's approach which has been used by several studies (e.g., Chen, et al., 2007; Jong-youn et al., 2010; Ertek et al., 2010). CAD was defined as > 50% luminal diameter stenosis of at least one major epicardial coronary artery.

All statistical analyses were performed using SPSS version 17 and STATA11. Descriptive statistics such as frequencies, percentages, means, ranges and standard deviations were used to describe the data. The Coronary artery disease was considered as the dependent variable, while all other variables were analyzed as independent variables. After checking for normality, for normally distributed continuous variables Paired Samples t-test was used to determine the differences between the case and control groups. For non-normally distributed continuous variables, the Wilcoxton matched pairs signed rank test was used. McNemar's test (sometimes called McNemar's test of symmetry or McNemar symmetry chi-square) was used to determine the association between categorical variables with the CAD. $p < 0.05$ was used as level of significance. Conditional logistic regression was then applied to quantify the relative odds of CAD associated with MS and its components and other life style risk factors of CAD (The Mantel-Haenszel test could be assessed in the normal stratified analysis method but with the many strata, stratification produces sparse data the CLR algorithm is designed to handle sparse data). Conditional logistic regression (CLR) was used to decide whether MS is a risk factor of CAD independently and quantify the association between CAD and its risk factors via multivariate modeling .seven sequential models were fitted: first a model with no adjustment for covariates (gender and age are adjusted for by design); second a model adjusting for covariates external to MS including smoking and body mass index. In model 3, to ascertain the prognostic importance of the MS above and beyond its components, we then added each of the 5 individual components categorically defined (i.e., all components included in the same model) with CAD. In model 4, we added smoking and BMI to model 3. In model 5,6 and 7, we used (step wised automatically technique), so all the variables added in model if they have related to CAD with p-value <0.2, one time without and other time with BMI.

3. Results

Patients suffering from metabolic syndrome (cases) were identified and compared with the controls. As shown in table 1, abdominal obesity is prevalent in 59.9% (178) of the cases and 46.5%) (138of controls have. High blood pressure was seen among 90.6% (269) of the cases and 79.1 % (234) of controls. High fasting blood glucose or using medication for that were in Sixty five percent (193) of the cases and 45.4% (134) of the controls had high fasting blood glucose or were using medications for that. High triglycerides were observed in the medical profile of 240(80.8%) of the cases and 193(65.6%) of the controls. Low HDL-cholesterol were seen in 236(80.0%) of the cases and 179(60.5%) of the controls. None of the cases showed zero components while only 6(2.0%) of the controls were found with this characteristic. A total of 258(87.5%) of the cases and 190(64.6%) of the controls were found to have metabolic syndrome disease. Seven (2.4%) of cases and 32(10.9%) of the controls had one component of MS. Thirty (10.2%) of the cases and 66(22.4%) of the controls had two MS components. Seventy-one (24.1%) of the cases and 79 (26.9%) of the controls had three components of MS. There were four MS

components in 107(36.3%) of the cases and 83(28.2%) of the controls. There were five MS components in 80(27.1%) of the cases and 28(9.5%) of the controls.

Table 1. Distributionof cases and controls according to Biochemical Data (N=594)

Biochemical analysis	Case		Control	
	n	%	n	%
Total Cholesterol:				
Desirable (<200 mg/dL)	218	73.4	242	81.5
Borderline High (200-239)	50	16.8	43	14.5
High (≥240)	29	9.8	12	4.0
Triglyceride Serum level:				
Normal (<150 mg/dL)	75	25.3	126	42.4
Borderline High (150-199 mg/dL)	105	35.4	95	32.0
High (200-499)	115	38.7	76	25.6
Very high ≥ 500	2	7	0	0
HDL cholesterol:				
Low(<40MG/dL in men,<50 women)	210	70.7	159	53.5
Between low and high	74	24.9	115	38.7
High(>60 mg/dL)	13	4.4	23	7.7
FBS:				
High(≥100)	185	58.7	130	41.3

3.1 MS Components and CAD Risk

Odds ratios of MS components related to CAD are shown in Table 2.

3.1.1 Waist circumference

There were significant positive association between increased waist circumference (OR=2.48, 95% CI =1.56-4.03, P=0.00) and risk of CAD.

3.1.2 Triglycerides and Drug Use

Increased TG (or using medication for that) increased the risk of CAD significantly (OR=2.41, 95% CI =1.57-3.80, P=0.00).

3.1.3 Blood pressure and Drug Use

Increased BP level or using medication for that (OR=2.47, 95% CI=1.50-4.21, P=0.00) increased the risk of CAD significantly.

3.1.4 HDL cholesterol and Drug Use

Decreased HDL-cholesterol or using medication for that increase the risk of CAD significantly (OR=2.70, 95% CI =1.80-4.13, P=0.00).

3.1.5 Fasting blood sugar and Drug Use

Increased FBS level or using medication for that (OR=2.23, 95% CI =1.56-3.22, P=0.00) increased the risk of CAD significantly.

3.2 Number of MS Components

It was also found out that patients with 3, 4, or 5 components of MS increased the risk of CAD significantly with odd ratios of (OR=2.68, 95% CI =1.56-4.61, P=0.00), OR=4.47, 95% CI =2.58-7.74, P=0.00), and (OR=13.08, 95% CI =6.37-26.83, P=0.00), respectively. Finally, MS with ATPIII criteria increased the risk of CAD 4.19 times significantly (OR=4.19, 95%CI=2.603-6.47, P=0.0001).

3.3 MS as an Independent Risk Factor for CAD

Another research question asked if MS was an independent risk factor for CAD among the patients. Test of Independency of Metabolic Syndrome as CAD risk factor was conducted through multivariate modeling, the results of which are presented in the following sections. Conditional logistic regression was conducted to quantify the risk of CAD associated with metabolic syndrome after adjusting for other potential risk factors that were assessed in this study.

Seven sequential models were developed: In the first model, with no adjustment for covariates (age and gender adjusted for by design), before adjusting for external risk factors, the presence of the MS by ATP-III (2005) conferred an almost 4-fold increase in the risk of CAD (odds ratio=4.19, p=0.00).

In model 2, adjustments were made for the two main covariates external to MS which included smoking and body mass index. After adjusting for these external risk factors, the presence of MS by ATP-III conferred an almost 3.5-fold increase in the odds of CAD (odds ratio=3.52, p=0.00).

In model 3, to ascertain the prognostic importance of the MS above and beyond its components, each of the 5 individual components were added with CAD. Multivariate analysis showed that MS conveyed no additional predictive information beyond its components (odds Ratio=0.81, p=0.6).

Table 2. Association between Daily Calorie and Nutriens Intake and Coronary Artery Disease (N=594)

Cal and nutrients	percentile	Odds Ratio	95%CI	P	Prob>Chi2
Energy(kcal)	<25	1.00			
	25-50	0.74	0.46-1.21	0.23	
	50-75	0.69	0.43-1.13	0.14	0.460
	>75	0.74	0.46-4.18	0.20	
Protein (g)	<25	1.00			
	25-50	0.92	0.58-1.46	0.74	
	50-75	0.73	0.45-1.16	0.18	0.190
	> 75	1.19	0.77-1.83	0.42	
Carbohydrate(g)	<25	1.00			
	25-50	**0.41**	0.25-0.69	**0.000****	
	50-75	**0.68**	0.42-1.11	**0.01***	0.006
	> 75	**0.55**	0.33-0.89	**0.01***	
Fat(g)	<25	1.00			
	25-50	0.79	0.50-1.24	0.31	
	50-75	0.69	0.43-1.11	0.12	0.330
	> 75	0.67	0.42-1.06	0.09	
Cholesterol(mg)	<25	1.00			
	25-50	1.07	0.68-1.69	0.75	
	50-75	1.16	0.73-1.85	0.52	0.781
	> 75	0.92	0.59-1.42	0.71	
SFA(g)	<25	1.00			
	25-50	0.90	0.56-1.44	0.67	
	50-75	1.06	0.66-1.69	0.79	0.909
	> 75	0.92	0.58-1.46	0.74	
MUFA(g)	<25	1.00			
	25-50	1.07	0.68-1.70	0.75	
	50-75	0.84	0.53-1.32	0.46	0.674
	> 75	0.89	0.56-1.42	0.63	
PUFA(g)	<25	1.00			
	25-50	1.24	0.78-1.98	0.35	
	50-75	0.72	0.45-1.13	0.16	0.025
	> 75	0.65	0.41-1.04	0.07	
Fiber(g)	<25	1.00			
	25-50	0.96	0.60-1.52	0.86	
	50-75	0.66	0.41-1.05	0.08	0.288
	> 75	0.82	0.53-1.26	0.38	
Na(mg)	<25	1.00			
	25-50	0.75	0.48-1.18	0.22	
	50-75	0.92	0.56-1.51	0.75	0.230
	> 75	**1.21**	0.75-1.94	**0.02***	
K(mg)	<25	1.00			
	25-50	0.95	0.60-1.49	0.83	
	50-75	0.81	0.51-1.27	0.36	0.820
	> 75	0.93	0.59-1.47	0.77	
Iron(mg)	<25	1.00			
	25-50	0.65	0.41-1.04	0.07	
	50-75	0.64	0.39-1.04	0.07	0.220
	> 75	0.83	0.52-1.33	0.43	
Zn(mg)	<25	1.00			
	25-50	1.23	0.79-1.92	0.94	
	50-75	0.76	0.47-1.22	0.63	0.050
	> 75	1.42	0.91-2.22	0.68	

Vit E(µg)	<25	1.00			
	25-50	0.98	0.62-1.54	0.94	
	50-75	1.11	0.71-1.73	0.63	0.860
	> 75	0.91	0.59-1.41	0.68	
Vit A(µg)	<25	1.00			
	25-50	0.89	0.56-1.43	0.65	
	50-75	1.08	0.69-1.69	0.72	0.838
	> 75	0.9	0.57-1.41	0.65	
Vit C(mg)	<25	1.00			
	25-50	1.12	0.71-1.78	0.60	
	50-75	1.12	0.70-1.78	0.61	0.907
	> 75	0.99	0.62-1.56	0.97	
Oleic Acid(g)	<25	1.00			
	25-50	0.83	0.51-1.35	0.46	
	50-75	0.75	0.45-1.23	0.26	0.630
	> 75	0.76	0.48-1.21	0.25	
Linoleic Acid(g)	<25	1.00			
	25-50	1.17	0.74-1.85	0.98	
	50-75	0.70	0.44-1.11	0.13	0.069
	> 75	0.68	0.43-1.08	0.10	
Linolenic Acid(g)	<25	1.00			
	25-50	1.35	0.84-2.17	0.26	
	50-75	1.09	0.69-1.72	0.70	0.497
	> 75	0.97	0.61-1.54	0.90	

*Correlation is significant at the 0.05 level (2-tailed). **Correlation is significant at the 0.01 level (2-tailed).

In model 4, smoking and BMI were added to model three. MS odds ratio still remained with no additional predictive information (odds ratio=0.68, p=0.3).

In model 5 and 6, step wise automatically was used, and all the variables with significant (p-value <0.2) associations with CAD were added to the model once with and once without considering BMI. In both models (with and without BMI), the presence of MS by ATP-III conferred an almost 3.5 till 3.7-fold increase in the odds of CAD (with BMI odds ratio=3.52, p=0.00, and without BMI odds ratio=3.76, p=0.00).

In model 7, to ascertain the prognostic importance of the MS above and beyond its components, each of the 5 individual components were added to the last model with stepwise variables. Multivariate analysis showed that MS conveyed no additional predictive information beyond its components (Odds Ratio=0.53, p=0.3).

In addition to the previous models, hierarchical Conditional (fixed-effects) logistic regression models were also add to these models. In these two hierarchical models (see Hierarchy 1 & 2, next pages), all the variables with significant (p-value <0.2) associations with CAD were added to previous models. Additionally, in the second model, to ascertain the prognostic importance of the MS above and beyond its components, each of the five individual components were added to the first model. The analysis showed that in first model the presence of MS by ATP-III conferred an almost 3.67 -fold increase in the odds of CAD, p=0.00. Multivariate analysis showed that MS conveyed no additional predictive information beyond its components (odds Ratio=0.33, p=0.1) in second model.

4. Discussions

4.1 MS in CAD Patients

Based on the ATP III (revised by the AHA/NHLBI, 2005) guidelines, abdominal obesity was prevalent in 59.9% (178) of the cases and 46.5% (138) of the controls. High triglycerides were observed in the medical profile of 240(80.8%) of the cases and 193(65.6%) of the controls. Low HDL-cholesterol were seen in 236(80.0%) of the cases and 179(60.5%) of the controls. High blood pressure was evident among 90.6% (269) of the cases and 79.1 % (234) of the controls. High fasting blood glucose or using medication for that was observed in 65% (193)of the cases and 45.4%(134) of the controls had high fasting blood glucose or were using medications for that (as shown in Table 3).

Table 3. Metabolic Syndrome Data (ATPIII, AHA/NHLBI* 2005, N=594)

Metabolic Syndrome	Case(n=297)		Control(n=297)	
	n	%	n	%
Abdominal obesity**	178	59.9	138	46.5
Blood pressure ≥130/85 mmHg or using drugs	269	90.6	234	79.1
Fasting blood glucose ≥100 mg/dl or using drugs	193	65.0	134	45.4
Triglycerides ≥150 mg/dl or using drugs	240	80.8	193	65.6
Low HDL-cholesterol <50 mg/dl in women,<40 mg/dl in men or using drugs	236	80.0	179	60.5
Zero component	0.0	0.0	6	2.0
One component	7	2.4	32	10.9
Two components	30	10.2	66	22.4
Three components	71	24. 1	79	26.9
Four components	107	36.3	83	28.2
Five components	80	27.1	28	9.5
Defined metabolic syndrome	258	87.5	190	64.6

*NCEP/ATP The National Cholesterol Education Program-Adult Treatment Panel modified by AHA/NHLBI American Heart Association/National Heart Lung & Blood Institute .

** Abdominal obesity: waist circumference >88 cm for women,>102cm for men

The reasons for the occurrence of these abnormalities and the possible causes for their creation have been discussed in the preceding sections. Among the cases no one was found with zero components while only 6(2.0%) of the controls were found to be characterized as zero-component. Overall, a total of 258(87.5%) of the cases and 190(64.6%) of the controls were found to have metabolic syndrome disease. participants with one component comprised 7 (2.4%) of the cases and 32(10.9%) of the controls. Thirty (10.2%) of the cases and 66 (22.4%) of the controls had two MS components. Seventy-one (24.1%) of the cases and 79 (26.9%) of the controls had three components of MS. Four-component participants comprised 107(36.3%) of the cases and 83(28.2%) of the controls. Finally, 80(27.1%) of the cases and 28(9.5%) of the controls were identified as having five MS components.

The analysis showed that the highest number among both cases and controls were involved with all five components of MS and fewer patients were identified suffering from a single component. Thus, it might be wise to conclude that MS components are less often developed independently of each other. In other words, MS victims are more likely to be interacted with more than one of its components. These results might also be indicative of a close interaction between different components of MS and their possible synergistic effects on the target patients. Such an understanding of the behavior of MS components among susceptible CAD patients can provide insights into the study of MS and CAD as clinical entities in general and shed light on timely diagnosis and treatment of coronary artery diseases, in particular.

4.2 Individual MS Components and CAD Risk

One of the most widely accepted diagnostic criteria for the diagnosis of MS has been introduced by the National Cholesterol Education Program (NCEP) also called Adult Treatment Panel (ATP), which works on some measurements including waist circumference, serum triglyceride (TG), HDL-C, Blood Pressure (BP), and Fasting Blood Sugar (FBS). Recently some minor modifications have later been made to the NECP criteria by the American Heart Association/National Heart Lung & Blood Institute (AHA/NHLBI), on which is currently used in research focusing on MS and its association with Coronary Artery Diseases (CAD) (Grundy, 2005). The ATP III criteria for the metabolic syndrome have been widely used in both clinical practice and epidemiological studies. An advantage of these diagnostic criteria is that it avoids emphasis on a single cause. The AHA and NHLBI affirm the overall utility and validity of the ATP III criteria and suggest that they continue to be used with minor modifications and clarifications. These modifications and clarifications include allowing for adjustment of waist circumference to lower thresholds when individuals or ethnic groups are prone to insulin resistance; allowing triglycerides, HDL-C levels, and blood pressure to be counted as abnormal when a person is taking drug treatment for these factors; clarifying that the definition of elevated blood pressure is a level that exceeds the threshold for either systolic or diastolic pressure; and reducing the threshold for counting elevated fasting glucose from 110 mg/dL to 100 mg/dL, in accordance with the American Diabetes Association's (ADA's) revised definition of impaired fasting glucose (IFG).

The results of applying these criteria in measurement of MS components this study revealed that the prevalence of these components among the cases were: BP (90.6%), TG (80.8%), HDL-C (80.0%), FBS (65%) and WC (59.9 %) while the frequency of observed MS components in controls were: BP (79.1%), TG (65.6%), HDL-C (60.5%), WC (46.5%), and FBS (45.4%). These results indicate that BP is the most prevalent MS component among the patients followed by TG and HDL-C; however, BP is more prominent among the cases than the controls. This can be due to the fact that there are several factors that may be the cause for high BP among the participants. The participants' low socioeconomic status, lack of knowledge about healthy diet, low levels of literacy and education, and large numbers kids in the family can give rise to unhealthy diet and obesity among the participants. Since hypertension is a major risk factor for CAD, its control in the community should be integrated into a comprehensive preventive program for CAD control. Therefore, screening for high blood pressure, in addition to patients' adherence to the medical management of controlling blood pressure can also is effective in reducing the incidence of the development of CAD.

More specifically, the results of examining the association of PB to CAD showed that increased BP level or using medication for that (OR=2.47, 95% CI =1.50-4.21, P=0.00) increased the risk of CAD significantly. Based on ATPIII criteria, 65.75% (195) of cases and 54.2 % (161) of controls had high Systolic BP, while 42% (125) of the cases and 16% (48) the controls had high Diastolic BP. Increased systolic (OR=1.78, 95%; CI=1.26-2.51; P=0.00) and diastolic blood pressure (OR=3.5, 95% CI=2.22-5.50, P=0.00) increased the risk of CAD significantly.

The data also showed that having history of using drugs for blood pressure significantly increases the risk of CAD. Although patients who used to take medication for lowering PB had normal BP at the time of blood collection, indeed they used to have elevated BP based on their medical profile. The odds ratio (OR=1.93) and 95% CI (1.34-2.77) for the use of blood pressure drugs in association with their risk of CAD development were both statistically significant (P=0.001).

Additionally, the effects of having high triglycerides (TG) or using medication for that on the risk of CAD observed through the medical profile of the patients indicated that increased TG or using medication for that increased the risk of CAD significantly (OR=2.41, 95% CI =1.57-3.80, P=0.00). It is worth noting that 35% of cases and 22% of controls used lipid lowering medications that decreased TG. The highest risk of CAD was recorded for high and very high categories (OR=2.85, 95% CI =1.82-4.47, P=0.0001) of TG suggesting that the higher the level of TG in patients, the greater the risk of CAD. Similarly, history of using blood lipid drugs that increase HDL as well as previous history of using blood lipid drugs that decrease TG put the patients at significantly greater risk of CAD both (OR=1.80, 95% CI=1.25-2.58, P=0.001). The findings are also supported by the studies by Washio et al. (2001) and Fava et al. (2008) who indicated that elevated fasting triglycerides level is a risk factor for CAD and CVD, and it works independently from other risk factors. Therefore, from a public health perspective it is not enough to focus only on serum triglyceride levels to decrease the burden of CAD in any population. It appears that reduction and /or modification in serum lipids and lipoproteins all together in addition to other risk factors could beneficial.

Low HDL-cholesterol or using medication for that were seen in 236(80.0%) of the cases and 179 (60.5%) of the controls. Lower HDL cholesterol concentrations were 70.7% and 4.4% and higher HDL cholesterol levels were 53.5% and 7.7% in cases and controls, respectively. It was found that decreased HDL-cholesterol or using medication for that increases the risk of CAD significantly (OR=2.70, 95% CI =1.80-4.13, P=0.00). More specifically, the results showed that decreased HDL-C approximately doubled the risk of CAD.

High fasting blood glucose or using medication for that were observed in 65%(193) of the cases and 45.4%(134) of the controls. The results indicated that increased FBS level (more than 100 mg/dL) or using medication for that (OR=2.23, 95% CI =1.56-3.22, P=0.00) increased the risk of CAD significantly. High FBS levels were 185(58.7%) and 130(41.3%) in the cases and controls, respectively (See Table 4). The odds ratio and 95% CI for the use of blood sugar drugs in association with their risk of CAD development were OR=5, 95% CI =2.69-9.29, P=0.001 respectively. Increased FBS is caused due to several factors including obesity. In this study the relatively high prevalence of high FBS may be due the impact of increased sedentary lifestyle and high prevalence of obesity. Based on the fact that the cause of CAD is multifactorial, diabetes mellitus is just one of the contributors. Therefore, there is a need to promote health awareness among the population with an emphasis on controlling and carrying out periodic check up of blood sugar.

Table 4. Biochemical Data (N=594)

Biochemicals	Case			Control			z or t	P
	Mean	95% CI	SD	Mean	95% CI	SD		
Total cholesterol mg/dl	178.48	173.54-183.41	42.67	163.92	159.05-168.80	42.67	t= -4.20	**0.000****
Triglyceride mg/dl	195.09	186.31-203.88	76.93	169.16	160.63-177.68	74.66	Z= -4.94	**0.000****
HDL mg/dl	39.71	38.25-40.89	10.40	44.10	42.92-45.29	10.35	Z= -5.09	**0.000****
FBS mg/dl	124.32	118.67-129.45	46.80	106.28	100.98-111.59	46.46	t= -4.76	**0.000****

*Difference is significant at the 0.05 level (2-tailed).**Difference is significant at the 0.01 level (2-tailed)

In sum, a brief look at the mean values of the five MS components (i.e., BMI, fasting glucose, HDL cholesterol, TG, and BP discussed above) shows diversified values of each component among the patients. This diversity seems a common trend on similar research results. For instance, in Mottillo et al.'s (2010) study in Canada, the 5 components of the metabolic syndrome in different studies related to MS and CAD were reported as: 1) BMI ranged from 22 to 33 kg/m2; 2) fasting glucose ranged from 82 to 196 mg/dl; 3) HDL cholesterol ranged from 37 to 64 mg/dl; 4) triglycerides ranged from 88 to 199 mg/dl; and 5) systolic blood pressure ranged from 117 to 174 mm Hg. In the same vein, Chen et al (2008) in a comparison of the prevalence of MS symptoms in CAD and non-CAD groups (by using NCEP ATP III, 2002 criteria) showed that in CAD group the value of BMI, prevalence of hypertension and hyperglycemia were higher than those of non- CAD group ($p < 0.05$, $p < 0.05$ and $p < 0.01$, respectively) whereas TG and HDL-C did not differ significantly between the two groups. Similar results were achieved by Irribaren et al. (2006) in a case control study comparing CAD and non-CAD patients regarding their MS components. The study, which used the AHA/NHLBI criteria, showed that hypertension followed by low HDL cholesterol and large waist circumference were the most common components among case subjects; low HDL cholesterol and hypertension were also the most common components among control subjects.

The study used two criteria to assess the values of each component. It was found that while 31% of case subjects and 8% of control subjects had high FBS by ATP-III criteria, 49% and 15%, respectively, did by AHA/NHLBI criteria. The case/control prevalence ratio was highest for ATP-III fasting glucose (3.9) and lowest for high triglycerides (Irribaren et al. (2006). The study further discusses that that the components of MS that were more strongly associated with early-onset CAD were hypertension, low HDL cholesterol, and increased FBS. Notably, FBS defined by the lower AHA/NHLBI threshold was more strongly associated with the outcome than FBS defined by the ATP-III criteria (100 and 110 mg/dl respectively). It was concluded that waist circumference and triglycerides were not independently related to early-onset CAD (Irribaren et al, 2006).

Consistent with these studies, in Chen et al.'s (2008) study, of all the aged CAD-patients with MS, obesity, hypertension, hyperglycemia, disorder of TG and hyperfibrinogenemia were more common than the CAD- patients without MS. Obesity, especially abdominal obesity, was found to be the initiating factor of IR (Insulin Resistance), and the hyperglycemic patients corresponding to IR, could had atherosclerosis much more easily. This could be due to the accumulation of fat in the pancreas which causes the dysfunction of b cells and IR accelerates the apoptosis of b cells. The authors concluded that both these procedures evoke the inflammation and thereafter atherosclerosis through the change of the endothelium. Chen et al. (2008) further maintained that because of the smaller stature of Chinese population comparing with the Western people, BMI rather than waist nor was hip circumference chosen as the threshold level for obesity. Moreover, they found that although MS patients only had low to medium grade hypertension, it developed heart disease as in a target organ, while it was known as the main factor to cause CAD. The disorder of serum lipids increases the risk of atherosclerotic cardiovascular disease in MS patients. The hyperglycemic patients showed an increased level of TG and TG-rich remnant-like particles, considered to be the mainly dangerous factors of CAD as contended by Akayanagi et al. (2004). The study also reports that LDL-C is easier to be oxidized and deposited in the vessel wall, and is difficult to be diminished by the classic metabolic ways, which gives rise to easier development of the atherosclerosis. Research also shows that decreased

HDL-C might reduce the clearance of the peripheral cholesterin and diminish the efficacy of anti-atherosclerotic effects.

4.3 MS and CAD Correlation

A total of 258(87.5%) of the cases and 190(64.6%) of the controls were found to have metabolic syndrome. The results indicate that individuals suffering from MS, as measured by ATPIII criteria, had about four-fold increased risk of CAD. (OR=4.19, 95%CI=2.603-6.47, P=0.0001). These results suggest that patients who show symptoms of MS are also at greater risks of coronary artery diseases and therefore need to take necessary actions to uphold their health. Hence, certain health-maintaining actions such as controlling dietary intake, receiving appropriate and timely medication, avoiding smoking, and performing regular physical exercises, which were shown in this study to improve the conditions of CAD patients, are recommended. Previous research (e.g., Chen et al., 2008; Irribaren et al., 2006; Mottillo et al., (2010) has also documented that patients with MS symptoms are exposed to higher risk of CAD. Chen et al. (2008) using NCEP ATP III, 2002 criteria showed that the cumulated occurrence of MS symptoms was significantly higher in the CAD group than in the non-CAD group (48.7% versus 23.4%, $p < 0.01$). The study also demonstrated through a logistic regression analysis, that the risk of having future CAD was in direct correlation with MS (b = 1.475, 0.670 (S.E.), Wald = 4.852, p = 0.028, exp (b) = 4.371). Similarly, Irribaren et al (2006), using the AHA/NHLBI criteria, found a 32% prevalence of MS among case subjects and 11% among control subjects. In the same study, it was seen that the presence of the MS by ATP-III criteria in the absence of diabetes conferred an almost 5-fold increase in the odds of early-onset CAD. Irribaren et al (2006) held that the AHA/NHLBI definition resulted in a slightly better prediction of outcome. Likewise, in a study by Mottillo et al.(2010) in Canada, the prevalence of the metabolic syndrome ranged from 1% in a study of women without type 2 diabetes mellitus (Takahashi et al., 2007) and 78% in a study of patients with type 2 diabetes mellitus (Butler et al., 2006). The study also showed that the point estimates for cardiovascular risk were consistently higher in women compared with men. Overall, consistent with previous research, results of the current study reconfirm the fact the metabolic syndrome is strongly linked to the increased risk of CVD.

4.4 CAD and MS as an Independent Risk Factor

Having discussed the correlation of individual MS component with severity of CAD, the study also intended to find out whether adding all the components of MS together will have different effects on severity of CAD among the patients. In other words, the association of MS as an independent risk factor for CAD was assessed using multivariate modeling programs. To quantify the risk of CAD associated with metabolic syndrome after adjusting for other potential risk factors conditional logistic regression was conducted. It is also assumed that if the metabolic syndrome operates independently of its individual components, its potential interventions may modify the risk of CAD above and beyond intervening on individual risk factors, such as hypertension. In this study all the designed models show that MS is a significant predictor of CAD even in the presence of the other confounders and potentially CAD risk factors (Odds Ratio between 3.5 till 4.15, $p<0.000$), however by adding MS components to ATPIII(2005) criteria MS conveyed no additional predictive information (Odds Ratio=0.33 up to 0.81 , $p>0.1$). Previous research shows that although both the presence of multiple risk factors and MS itself (Gami et al.,2007) confer an increased risk of CAD, it is unclear whether the adverse impact on health by the MS is greater than those related to the sum of its components (Grundy et al. , 2004). It has also been argued that the concept of syndrome implies that the risk associated with having the syndrome ought to be greater than the sum of its parts, and that all the factors should have a common underlying physiology which is responsible for their clustering (Kahn et al., 2005). Alexander et al. (2003) in a large cross-sectional study conducted in the US population aged over 50 (participants of the NHANES III survey), pointed out that MS does not improve prediction of CAD events in the presence of its components considering the ATPIII definition.

On the contrary, in a prospective study on older individuals, the MS by the ATPIII definition but not by the WHO criteria appeared to be an independent predictor of cardiovascular events after adjusting for its components and the traditional cardiovascular risk factors. Additionally, Ford (2003) found that the MS defined by the ATPIII and WHO definitions only had the modest job of predicting cardiovascular disease (estimated summary relative risk of 1.7 to 1.9). Iribarren (2006) examining the association between the metabolic syndrome (MS) and early-onset coronary artery disease (CAD) concluded that the presence of ATP-III MS without diabetes and with diabetes was a strong independent determinant of early-onset CAD, but neither definition of MS remained significantly associated with early-onset CAD in multivariate models adjusting for individual components. Thus, Iribarren (2006) concluded that the MS is a risk factor of early-onset clinical CAD, however, the prognostic information associated with the syndrome was not

greater than the sum of its parts. Hadaegh et al.'s (2009) findings also confirmed MS as an independent predictor of CAD over and above its individual components in this study. Numerous other studies have not been able to establish the role of MS as an independent risk factor for CAD severity. For example, Alexander et al. (2003) pointed out that blood pressure, HDL cholesterol, and diabetes, but not the presence of MS, were significant multivariate predictors of prevalent CAD in an analysis of the Third National Health and Nutrition Examination Survey. Similarly, Yarnell et al. (1998) reported that the excess of ischemic heart disease risk associated with MS was no greater than that can be explained by individual effects of the defining variables in a multiple logistic model. This finding implies that MS conveyed no additional predictive information beyond its components. A logical interpretation of this finding is that clinicians would be better off addressing the individual risk factors rather than "treating the syndrome." It is also arguable that the identification of a condition like MS, even if it does not provide incremental value over its components, may better motivate physicians to treat the condition and its accompanying risk factors. Previous investigators have reached similar conclusions.

Irrespective of the fact that the result of this study indicate a significant association between MS as an independent risk factor for CAD, the overall results of the above cited investigations are equivocal. Hence, without evaluating whether or not specific biological mechanisms may explain the association between the metabolic syndrome and CAD, it would still remain unclear if the metabolic syndrome should be viewed as an etiologic entity above and beyond its individual components.

In an attempt to offer a logical solution regarding the uncertainty of research over MS as an dependant risk factor, Orchard et al. (2005) suggest that more intensive efforts should be directed toward prevention and management of the individual risk factors than to "diagnosing" the syndrome assert based on the strength of associations observed for the individual components and the fact that the association of the MS with CAD was greatly attenuated and no longer significant after adjustment for its components.. From the standpoint of primary prevention, interventions designed to increase exercise and achieve weight loss have been shown to effectively reduce these risk factors. Finally, the present study in line with previous studies (e.g., Hadaegh et al., 2009; Iribarren et al., 2006; Alexander et al., 2003; Yarnell et al., 1998) provides important information and adds useful insights regarding MS and CAD severity mostly . Based on this body of research, it is recommended that to reduce the risk of CAD, physicians target individual CAD risk factors for modification and/or treatment. Therefore, it might seem that using information on the metabolic syndrome will not help prediction of CAD as compared with detailed information on well-established individual CAD risk factors.

Acknowledgements:

Authors are grateful to the Department of Nutrition and dietetics (Universiti Putra Malaysia) and Imam Ali Heart Center (Kermanshah University of Medical Sciences, Iran) for their support to carry out this work.

Corresponding Author:
Shila Berenjy
Faculty of Food Sciences and Technology
Varamin-Pishva Branch, Islamic Azad University
Varamin, Iran
E-mail: shila135071@yahoo.com

References

1. Alexander, C., Landsman, P., Teutsch, S., & Haffner, S. (2003). NCEPdefined metabolic syndrome, diabetes, and prevalence of coronary heart disease among NHANES III participants age 50 years and older. Diabetes, 52, 1210-1214.
2. Azizi F, Salehi P, Etemadi A,Zahedi –Asl S. Prevalence of metabolic syndrome in an urban population: Tehran Lipid and Glucose Study .Diabetes Res Clin Pract2003;61:29-37.
3. Azizi, F., Esmailzadeh, A., & Mirmiran, P. (2004). Obesity and cardiovascular disease risk factors in Tehran adults:a population based study. East Mediterr Health J, 10, 887-897.
4. Butler, J., Rodondi, N., & Zhu, Y. (2006). Metabolic syndrome and the risk of cardiovascular disease in older adults. J Am Coll Cardiol, 47, 1595-1602.
5. Clarke SD Polyunsaturated fatty acid regulation of gene transcription: a mechanism to improve energy balance and insulin resistance Br J Nutr 2000; 83 Suppll: S59 - S66
6. Chen Q, Liu Y, Huang w, et al. Relationship between metabolic syndrome and coronary heart disease in an aged group. Archives of Gerontology and Geriatrics; 46(2008):107-115.
7. Ertek, e. a. (2011). The severity of coronary atherosclerosis in diabetic and non-diabetic metabolic syndrome patients diagnosed according to different criteria and undergoing elective angiography. Acta Diabetol, 48, 21-27.
8. Fava, S., Herrington, D., Reboussin, D., & Sherman, M. (2008). Plasma levels of HDL subpopulations and remnant lipoproteins predict the extent of angiographically88 defined coronary artery disease in postmenopausal women. Atherosclerosis, Thrombosis and Vascular Biology, 28, 575-579.
9. Ford,ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: finding from the third National Health and Nutrition Examination Survey. JAMA 2002; 287:356-9.
10. Gami, A. S., Witt, B. J., Howard, D. E., Erwin, P. J., Gami, L. A., & Somers, V. K., et al. (2007). Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. J Am Coll Cardiol, 49, 403-414.
11. Ghayour-Mobarhan M, Aziminezhad M, Kazemi SM, et al. Comparing different definitions of metabolic syndrome in Iranian population. Abstract.76th Congress of the European

Atherosclerosis Society,June 10-13,2007, Helsinkey, Finland, PO 16-448.
12. Ginsberg HN. Review : efficacy and mechanisms of actions in the treatment of diabetic dyslipidemia. J Clin Endocrinol Metab 2006;91(2):383-392
13. Gorter PM, Olijhoek JK, Graff Y, et al. Prevalence of the metabolic syndrome in patients with coronary heart disease, cerebrovascular disease, peripheral arterial disease or abdominal aortic aneurysm. Atherosclerosis; 173(2004):363-369.
14. Grundy, e. a. (2004). Definition of Metabolic Syndrome Report of the National Heart, Lung, and Blood Institute/American Heart Association Conference on Scientific Issues Related to Definition. Circulation, 109, 433-438
15. Grundy SM, Cleeman J I, Daniels S R, et al. Diagnosis and Management of the Metabolic Syndrome Scientific Statement Executive Summary Circulation 2005;112; e285-e290; originally published online Sep 12, 2005;DOI: 10.1161/CIRCULATION AHA.105.169405
16. Grundy, S. (2005). A constellation of complication: the metabolic syndrome. Clinical cornerstone. Cardio metabolic risk management., 7(2/3), 36-45.
17. Hadaegh, F., Harati, H., Ghanbarian, A., & Azizi, F. (2009). Prevalence of coronary heart disease among Tehran adults: Tehran Lipid and Glucose Study. Eastern Mediterranean Health Journal, 15(1).
18. Haffner, S. (2007). AM J Med. Abdominal adiposity and cardio metabolic risk: Do we have all the answers? 120(9), 6-10.
19. Hunt KJ, Resendez RG, Williams K, Haffner SM, Stern MP. National Cholesterol Education Program versus World Health Organization metabolic syndrome in relation to all cause and cardiovascular mortality in the San Antonio Heart Study. Circulation 2004;110:1251-7.
20. Iribarren, C., Alan, S., & Husson, G., et al. (2006). Metabolic Syndrome and Early-Onset Coronary Artery Disease. J Am college of cardiology 48, 1800-1807.
21. Jong-Youn Kim, Hee-Sun Mun, Byoung Kwon Lee, Seong Bo Yoon,* Eui-Young Choi, Pil-Ki Min, Young-Won Yoon, Bum-Kee Hong, Se-Joong Rim, and Hyuck Moon Kwon,Impact of Metabolic Syndrome and Its Individual Components on the Presence and Severity of Angiographic Coronary Artery Disease, Yonsei Med J 51(5):676-682, 2010.
22. Kahn R, Buse J, Ferrannini E, Stern M. The metabolic syndrome: time for a critical appraisal: joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2005; 28:2289 –304.
23. Kragelund, x., et al., (2007). Metabolic syndrome and mortality in stable coronary heart disease: Relation to gender. International Journal of Cardiology, 121, 62-67.
24. Laaksonen, D. E., Lakka, H. M., Salonen, J. T., Niskanen, L. K., Rauramaa, R., & Lakka, T. A. (2002). Low levels ofleisure-time physical activity and cardiorespiratory fitness predict development of the Metabolic Syndrom. Diabetes Care, 25, 1612-1618.
25. Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle aged men.JAMA2002; 288:2709-16.
26. Lee IM et al: Vitamin E in the primary prevention of cardiovascular disease and cancer: the Women's Health Study; a randomized controlled trial, JAMA 294:56, 2005.
27. MacNeill AM, Rosamond WD, Girman CJ, et al. Prevalence of coronary heart disease and carotid arterial thickening in patients with the metabolic syndrome (the ARIC study). Am J Cardiol 2004;94:1249-54.
28. Maki, K. C. (2004). Dietary factors in the prevention of Diabetes Mellitus and Coronary Artery Disease associated with the Metabolic Syndrome. The American Journal of Cardiology, 93 (llA), 12C-17C.
29. Mottillo S., Filion K B., Genest J., Joseph L., Pilote L., Poirier P., Rinfret S., Schiffrin E. L., and Eisenberg M. J. The Metabolic Syndrome and Cardiovascular Risk, A Systematic Review and Meta-Analysis. J Am Coll Cardiol, 2010; 56:1113-1132. doi:10.1016/j.jacc.2010.05.034
30. Niaura, R., Banks, S. M., Ward, K. D, Stoney, C. M., Spiro, A., Aldwin, C. M. & et al. Hostility and the metabolic syndrome in older males: The Normative Aging Study. Psychosomatic Medicine, 2000; 62:7-16.
31. Orchard TJ, Temprosa M, Goldberg R, et al. The effect of metformin and intensive lifestyle intervention on the metabolic syndrome: the Diabetes Prevention Program randomized trial. Ann Intern Med 2005;142:611–9.
32. Petra, M., et.al. (2004). Prevalence of metabolic syndrome in patients with coronary heart disease, cerebrovascular disease, peripheral arterial disease or abdominal aortic aneurism. Atherosclerosis, 173, 363-369.
33. Raikkonen, K., Mtthews, K.A., & Kuller, L.H. The relationship between psychological risk attributes and the Metabolic syndrome in healthy women: Antecedent or consequences? Metabolism, 2002;51(12):1573-1577
34. Reaven GM. Banting Lecture 1988: Role of insulin resistance in human disease. Diabetes 1988;37: 1595-1607.
35. Sadeghi M,Garak-Yaraghi M,rt al.Relationship between the metabolic syndrome and coronary artery disease in patients with stable angina. ARYA J. 2006;2(1):10-14
36. Stern, M. (1995). Diabetes and cardiovascular disease the commen soil hypothesis. Diabetes 44(4), 369-374.
37. Szapary PO, Reader DJ. The triglyceride-high-density lipoprotein axis: an important target of therapy? AM. Heart J 2004;148(2):211-221.
38. Takahashi K, Bokura H, Kobayashi S, Iijima K, Nagai A, Yamaguchi S. Metabolic syndrome increases the risk of ischemic stroke in women. Intern Med 2007;46:643–8.
39. Villena JA, Viollet B, Andreelli F, Kahn A, Vaulont S et al. Induced adiposity and adipocyte hypertrophy in mice lacking the AMP-activated protein kinase-alpha2 subunit. Diabetes 2004;53(9):2242-2249.
40. Washio, M., Sasazuki, S., Kodama, H., & Yoshimasa, K. (2001). Role of hypertension, dyslipidemia and diabetes mellitus in the development of coronary arthrosclerosis in Japan. Japanese Circulation Journal, 65, 731-737.
41. Yarnell, J., Patterson, C., Bainton, D., & Sweetnam, P. (1998). Is metabolic syndrome a discrete entity in the general population? Evidence from the Caerphilly and Speedwell population studies. Heart, 79, 248-252.
42. Zabetian A, Hadaegh F, Tohidi M, et al. Prevalence of metabolic syndrome by the ATPIII, IDF and WHO definition and their association to coronary heart disease in Iranian elderly population. Iranian Journal of Diabetes and Lipid Disorders, fall 2007; 7(1(22)):91-101.

12/12/2011