INTRODUCTION

Metabolic syndrome (MS) is considered to be a significant risk factor for type 2 diabetes mellitus and cardiovascular disease. An overall 23.7% prevalence of metabolic syndrome is recently reported in the U.S. adults of above 20 years age. Marjani et al. showed that metabolic syndrome and lipid peroxidation alter in different ethnic and age groups and in different diseases.

Oxidative stress occurs when there is instability between anti-oxidants system and reactive oxygen species. This instability leads to oxidative damage and has been shown to play a key role in the causation of different pathologies. Studies have indicated that glucose uptake by muscle and fat cell is altered by oxidative stress and pancreas secrets insulin in a decreased amount.

Oxidative stress may be increased by constituents of metabolic syndrome (type 2 diabetes, hypertension, insulin resistance, dyslipidemia, visceral obesity) and vascular disease. These diseases may associate with metabolic syndrome. Elevated oxidative and inflammatory stress has been shown to be significantly contributing in the beginning and development of atherosclerotic vascular disease in different studies. It has reported that low density lipoprotein oxidation as a marker of oxidative stress increased in patients with coronary heart disease and subclinical atherosclerosis. It has been shown that the metabolic syndrome has an association with elevated oxidative stress and inflammatory burden. The risk of coronary heart disease was seen more in obese subjects with metabolic syndrome. IL-6 is a pro-inflammatory cytokine and is secreted in atherosclerotic lesions by smooth muscle cells and macrophages. Adipocytes and white blood cells secret plasma IL-6.
It has been shown that IL-6 was a significant factor in the etiopathogenesis of cardiovascular disease, obesity and inflammatory process\textsuperscript{44}.

Some other findings have shown that increased interleukin (IL)-6 is a marker of systemic inflammation and diagnostic marker of future cardio-vascular events\textsuperscript{45-46}. Clinical studies showed that the level of interleukin-6 (IL-6) is used as inflammatory marker for diagnosis of early stages of coronary artery disease\textsuperscript{47}. Low-grade inflammation was recently reported as one of the components of metabolic syndrome\textsuperscript{47,48}. There are limited studies on the relationship between inflammatory marker such as IL-6 and lipid peroxidation and metabolic syndrome. The aim of present study was to assess IL-6 and lipid peroxidation in subjects with and without the metabolic syndrome and their association with metabolic syndrome components.

**METHODOLOGY**

Age and gender matched 40 subjects with metabolic syndrome and 40 control groups took part in this study. Blood samples were collected after overnight fasting from all subjects who were referred to the Jelleyin health center in Golestan University of Medical Sciences, 2014. Commercial kit (With the use of photometer techniques, Model CLINIC II-Photometer) were used for determination of serum fasting glucose, triglycerides, LDL-cholesterol and HDL-cholesterol levels in the Metabolic Disorders Research Center, Gorgan Faculty of Medicine. Weight measurement of all subjects was done, using digital scales, while subjects were without shoes and minimally clothed.

Using a tape meter, height was measured in standing position. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Subjects with BMI=25.0-29.9 Kg/m\textsuperscript{2} and BMI ≥30 Kg/m\textsuperscript{2} were indicated as overweight and obese subjects, respectively\textsuperscript{49}. Waist circumferences were determined at the point halfway between the lower border of ribs and the iliac crest in a horizontal plane\textsuperscript{50}. Systolic and diastolic blood pressure was measured in sitting position in the right hand. Subjects with 3 or more of the below mentioned criteria were considered as having metabolic syndrome subjects according to Adult Treatment Panel III definition\textsuperscript{51}:

A. Waist circumference >102 cm in men and >88 cm in women.

B. Serum triglycerides level ≥ 150 mg/dl.

C. Low HDL-cholesterol: < 40 mg/dl in men and < 50 mg/dl in women.

D. Systolic blood pressure (SBP) ≥ 130 mmHg and/or diastolic blood pressure (DBP) ≥ 85 mmHg or on treatment for hypertension.

E. Serum glucose level ≥110 mg/dl or on treatment for diabetes.

Serum IL-6 (Picogram/mL) and malondialdehyde (Nano mol/L) were determined by Immunoassay (LOT: IL6041453, REF: EIL06001, Germany) and Kei Satoh (using spectrophotometer technique, JENWAY6305) \textsuperscript{52}methods, respectively ((the level of lipid peroxidation expressed as Malondialdehyde (MDA)). Collected data was analyzed using SPSS–16 version software. Data was expressed as percentage and means and standard deviations were carried out. Chi squared, independent sample t and Pearson’s correlation tests were used to evaluate data. Statistical differences were considered significant if p<0.05.

**RESULTS**

The clinical and biochemical data of the subjects with metabolic syndrome and control group are shown in Table1. The mean malondialdehyde level was significantly higher in overweight and obese subjects with metabolic syndrome than control groups (P<0.05). Table 2 shows characteristic of the men and women with metabolic syndrome and control groups. The mean level of IL-6 in men and the mean level of malondialdehyde in women with metabolic syndrome were significantly higher than control groups (p < 0.05). Correlation between metabolic syndrome components and IL-6 and malondialdehyde are shown in Table 3. There were significant positive correlation between malondialdehyde and fasting blood

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Parameter</th>
<th>Subject with metabolic syndrome</th>
<th>Control groups</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td>48.50±7.80</td>
<td>46.20±9.70</td>
<td>0.227</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td></td>
<td>29.95±3.82</td>
<td>26.35±4.14</td>
<td>0.0001</td>
</tr>
<tr>
<td>IL-6 (pgm/L)</td>
<td>Overweight</td>
<td>3.74±0.24</td>
<td>3.50±0.01</td>
<td>0.342</td>
</tr>
<tr>
<td>Malondialdehyde (nmol/L)</td>
<td></td>
<td>3.40±0.20</td>
<td>1.90±0.19</td>
<td>0.02</td>
</tr>
<tr>
<td>IL-6 (pgm/L)</td>
<td>Obese</td>
<td>6.85±2.07</td>
<td>4.40±0.93</td>
<td>0.063</td>
</tr>
<tr>
<td>Malondialdehyde (nmol/L)</td>
<td></td>
<td>3.58±050</td>
<td>1.89±0.15</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Table 1: Characteristics of subjects with metabolic syndrome and control groups.
THE ASSOCIATION BETWEEN METABOLIC SYNDROME AND SERUM LEVELS OF MALONDIALDEHYDE & IL-6

Table 2: Characteristics of subjects with metabolic syndrome and control groups in men and women

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Subject with metabolic syndrome</th>
<th>Control groups</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects (%)</td>
<td>18(100%)</td>
<td>18(100%)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>49.11±8.74</td>
<td>45.72±11.40</td>
<td>0.324</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>30.88±3.53</td>
<td>25.98±2.34</td>
<td>0.0001</td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>7.14±0.24</td>
<td>3.50±0.01</td>
<td>0.0001</td>
</tr>
<tr>
<td>Malondialdehyde (nmol/L)</td>
<td>3.36±0.23</td>
<td>2.01±0.11</td>
<td>0.262</td>
</tr>
</tbody>
</table>

| Number of subjects (%)  | 22(55%)                         | 22(55%)        |         |
| Age (years)             | 48±7.11                         | 46.59±6.86     | 0.507   |
| BMI (kg/m2)             | 29.18±3.96                      | 26.65±5.01     | 0.071   |
| IL-6 (pg/mL)            | 3.77±0.21                       | 3.92±0.42      | 0.351   |
| Malondialdehyde (nmol/L)| 3.65±0.45                       | 1.75±0.14      | 0.001   |

Table 3: Correlation between metabolic syndrome components and IL-6 and Malondialdehyde

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Malondialdehyde (nmol/L)</th>
<th>IL-6 (pg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>P-value</td>
</tr>
<tr>
<td>Glucose(mg/dl)</td>
<td>0.474</td>
<td>0.0001</td>
</tr>
<tr>
<td>Triglyceride(mg/dl)</td>
<td>0.224</td>
<td>0.003</td>
</tr>
<tr>
<td>HDL-C(mg/dl)</td>
<td>0.064</td>
<td>0.573</td>
</tr>
<tr>
<td>Waist Circumference(cm)</td>
<td>0.388</td>
<td>0.0001</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>0.232</td>
<td>0.038</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>0.151</td>
<td>0.183</td>
</tr>
</tbody>
</table>

There were no significant correlation between IL-6 and other metabolic syndrome components. There were no significant correlation between IL-6 and malondialdehyde (P= 0.917, not shown in result section).

**DISCUSSION**

In present study, we observed that the levels of IL-6 were significantly higher in subjects with the metabolic syndrome (Table 1). Studies have shown that there is an association between the participation of IL-6 and systemic inflammatory responses that leads to metabolic syndrome. Higher levels of IL-6 in men than in women show that abdominal obesity, which is more prevalent in men, causes more proatherogenic cytokines production. This may show that men are in higher risk for cardiovascular diseases than women. Men having higher IL-6 levels than women, is not in agreement with some other studies. IL-6, as a pro-inflammatory cytokine, was higher in obese subjects than overweight subjects with metabolic syndrome. This may show a relationship between obesity and IL-6 levels. Some studies have indicated that serum IL-6 are not associated with metabolic syndrome. It revealed that IL-6 has an important role in development of insulin resistance while some other studies reported IL-6 prevents insulin resistance. Oxidative stress may play a significant role in the development of metabolic syndrome. In the present study malondialdehyde level was high in subjects with metabolic syndrome which is in agreement with some studies while it is in agreement with some other. The results of this study show that the metabolic syndrome intensifies oxidative stress in subjects. The present study also shows that oxidative stress was significantly higher in overweight and obese subjects with metabolic syndrome in comparison with subjects without metabolic syndrome which is in agreement with the findings of other studies that they have shown independent association of obesity.
and metabolic syndrome with elevated oxidative stress and inflammatory burden. In the present study, we also determined the correlations between oxidative stress and metabolic syndrome components. Our findings showed that the oxidative stress was positively correlated with triglyceride, glucose, systolic blood pressure and waist circumference (Table 3). Therefore, it can be suggested that subjects with metabolic syndrome may have a higher level of oxidative stress. In general, abdominal obesity has been seen in subjects with metabolic syndrome. Obesity causes oxidative stress that may lead to the decrease of antioxidant enzymes activities. This may have influence on inflammation which plays a pathogenic role in the development and progression of metabolic syndrome.

**CONCLUSION**

Our results suggest that higher levels of IL-6 and malondialdehyde may cause insulin resistance and metabolic disorders in all subjects with metabolic syndrome. Malondialdehyde level shows strong association with some metabolic syndrome components.

**REFERENCES**


THE ASSOCIATION BETWEEN METABOLIC SYNDROME AND SERUM LEVELS OF MALONDIALDEHYDE & IL-6


CONTRIBUTORS

HMS conceived the idea, planned the study, and drafted the manuscript. MK helped acquisition of data and did statistical analysis. AM drafted and critically revised the manuscript. All authors contributed significantly to the submitted manuscript.