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Level of uric acid and its relationship with lipid peroxidation in sera of patients with acute coronary syndrome

Sura Ahmed Al-Emami*  Aliaa Hashim Faraj*

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Abstract
Unstable angina pectoris often leads to acute myocardial infarction. Since uric acid is thought to be risk factor for cardiovascular disease and considered a major antioxidant in human blood. The level of uric acid and lipid peroxidation in the sera of patients with unstable angina and myocardial infarction were measured and compared to the healthy individuals. Twenty-nine patients with unstable angina and twenty-nine patients with myocardial infarction were studied and compared to twenty-five healthy individuals. Uric acid was measured by using Human Kit. Malondialdehyde (MDA) a lipid peroxidation marker, was measured by thiobarbituric acid method. Significant elevation of uric acid and MDA were observed in the sera of patients with unstable angina and myocardial infarction compared to the control group, while a non significant correlation between uric acid and lipid peroxidation were found in the present study in the sera of patients with unstable angina and myocardial infarction.

Key words: uric acid, acute coronary disease, lipid peroxidation

Introduction
Acute coronary syndrome (ACS) encompass a continuum of ischemic heart disease from unstable angina (UA) with reversible myocardial cell injury through myocardial infarction (MI) with large areas of necrosis[1,2]. The definition of acute coronary syndrome depends on specific characteristics of each elements of triad of clinical presentation including a history of coronary artery disease electrocardiographic changes and biochemical cardiac markers [3]. Unstable angina and myocardial infarction have a common aetiology in the formation of thrombus on an inflamed and complicated atheromatous plaque[4]. Over the last 40 years, a number of clinical and laboratory variables have proven predictive of the incidence of cardiovascular disease and thus qualify as cardiovascular disease risk factors [5]. Recent studies have shown that in addition to the classic risk factors, such as age, male gender, hypertension, hyperlipidemia, diabetes mellitus, obesity, high serum uric acid concentration is a cardiovascular factor[6-9]. Uric acid generated from xanthine by xanthine oxidase is the final product of purine metabolism in humans[10]. Sources of purine are either endogenous from de nova synthesis and nucleic acid breakdown, or exogenous from dietry purine intake[11]. The association between uric acid and coronary artery disease was not limited to the hyperuricemic range[12]. Jelic I et. al. were demonstrated that uric acid determination could be useful as one of the markers of clinically significant

*Al-Mustansiriyia University / College of Science / Department of Chemistry
coronary artery disease[12]. Despite elevated of uric acid associated with increased risk for cardiovascular disease, its considered a major antioxidant in human blood that may protect against aging and oxidative stress[13,14]. Oxidative stress is defined as the tissue damage resulting from an imbalance between an excessive generation of oxidant compounds and insufficient antioxidant defence mechanisms [15,16].

It is thought to play an important role in the pathogenesis of acute coronary disease[17,18]. Given that free radicals have very short half-lives (seconds) the clinical assessment of oxidative stress is based on the measurement of different stable oxidized compounds such as lipid peroxidation[19]. The process of lipid peroxidation is one of oxidative conversion of polyunsaturated fatty acid to products known as malondialdehyde or lipid peroxides which is the most studied, biologically relevant, free radical reaction[20].

The present study aims to evaluate levels of uric acid and its relationship with lipid peroxidation in sera of patients with unstable angina and myocardial infarction diseases.

**Subject and Methods**

**Subjects** - This study included 58 patients (29 with unstable angina and 29 with myocardial infarction) attending Albitar hospital in Baghdad city and diagnosed by Dr. Mahdi Al Zaydi. As a control 25 healthy individuals were included in the present study.

**Serum Sampling** - Venous blood (5ml) were taken from healthy donors and patients. Blood samples were centrifuged at (3000 rpm) for 10 min after blood coagulation, serum thus separated and stored at -20°C until being used.

**Methods** -

**Determination of uric acid** - Serum levels of uric acid were determined by enzymatic colorimetric test[23,24] using uric acid kit (Human Company).

**Determination of lipid peroxidation** - Malondialdehyde a lipid peroxidation marker was measured by the thiobarbituric acid method[23], according to the modified method of saturation[24].

**Statistical Analysis** - The results are expressed as mean ± SD. Statistical and correlation analysis were undertaken using student t-test, and pearson's correlation coefficients. Values of P<0.05 were considered significant.

**Results** - Uric acid was measured in the sera of control and patients with UA and MI using Human Kit. The mean values presented in Table (1) reflect a highly significant increase in uric acid levels in sera of patients with UA (P<0.001) and patients with MI (P<0.001) in comparison with that of the control group. Since the serum levels of uric acid is higher in males than in females, gender specific serum uric acid levels was also investigated.
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Table (1) Mean values of uric acid levels in the sera of control and patients with UA and MI

<table>
<thead>
<tr>
<th>Group</th>
<th>Sample Number(n)</th>
<th>Range (mg/dL)</th>
<th>Mean mg/dL</th>
<th>± Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (Age -21-69 years)</td>
<td>25</td>
<td>(1.6-7.8)</td>
<td>4.10</td>
<td>1.38</td>
</tr>
<tr>
<td>Male</td>
<td>17</td>
<td>(2.2-7.8)</td>
<td>4.38</td>
<td>1.43</td>
</tr>
<tr>
<td>Female</td>
<td>8</td>
<td>(1.6-4.6)</td>
<td>3.43</td>
<td>1.06</td>
</tr>
<tr>
<td>Patients with UA (Age:46-78 years)</td>
<td>29</td>
<td>(3.3-12.8)</td>
<td>6.92</td>
<td>3.00</td>
</tr>
<tr>
<td>Male</td>
<td>21</td>
<td>(3.3-12.8)</td>
<td>6.77</td>
<td>2.76</td>
</tr>
<tr>
<td>Female</td>
<td>8</td>
<td>(3.5-11.2)</td>
<td>6.16</td>
<td>2.38</td>
</tr>
<tr>
<td>Patients with MI (age:46-75 years)</td>
<td>29</td>
<td>(3.4-9.8)</td>
<td>6.37</td>
<td>1.6</td>
</tr>
<tr>
<td>Male</td>
<td>22</td>
<td>(3.4-9.8)</td>
<td>6.60</td>
<td>1.67</td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
<td>(4.5-7.6)</td>
<td>5.91</td>
<td>1.10</td>
</tr>
</tbody>
</table>

A highly significant increase in uric acid levels were observed in the sera of male patients with UA (P<0.001) and male patients with MI (P<0.001) in comparison with that of the control group. Meanwhile, in female serum uric acid levels were significantly higher in patients with UA (P<0.001) and patients with MI (P<0.005) in comparison with that of the control group.

Table (2) Mean values of MDA in sera of control and patients with UA and MI

<table>
<thead>
<tr>
<th>Group</th>
<th>Sample number(n)</th>
<th>Range (mmol/L)</th>
<th>Mean (mmol/L)</th>
<th>± Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>25</td>
<td>(3.0-13.8)</td>
<td>7.63</td>
<td>2.65</td>
</tr>
<tr>
<td>Patients with UA</td>
<td>29</td>
<td>(6.5-40.7)</td>
<td>19.49</td>
<td>8.08</td>
</tr>
<tr>
<td>Patients with MI</td>
<td>29</td>
<td>(1.15-22.2)</td>
<td>12.58</td>
<td>5.60</td>
</tr>
</tbody>
</table>

A non significant correlation between uric acid and lipid peroxidation were observed in sera of patients with UA (r = -0.243 , P=0.05) and patients with MI (r = 0.28 , P>0.05) as in figures (1&2).

Fig(1) The correlation between uric acid concentration and MDA in sera of patients with unstable angina
Discussion

Unstable angina pectoris and acute myocardial infarction are hallmark events of acute coronary syndromes\(^{(21)}\). The association between elevated serum uric acid and coronary artery disease has been observed in numerous studies\(^{(12)}\).

Despite this, there is still no agreement on whether uric acid is a cause, a consequence, or just a marker of cardiovascular disease\(^{(8,12,20)}\).

In the present study, increased levels of uric acid were observed in sera of patients with UA and patients with MI in comparison with that of the control group. This result is in agreement with the results obtained by Gur M. et al. who found that serum uric acid levels in patients with coronary artery disease were significantly higher than those of the control group\(^{(27)}\).

Also Tatt E. et al. have showed that high serum uric acid levels were associated with critical coronary artery disease in young patients < 35 years with acute myocardial infarction\(^{(28)}\). Kojima S. et al. have suggested that serum uric acid level is suitable marker for predicting acute myocardial infarction\(^{(29)}\).

Although the mechanisms by which uric acid may play a pathogenetic role in cardiovascular disease is unclear, hyperuricemia is associated with deleterious effect on endothelial dysfunction, oxidative metabolism, platelet adhesiveness, hemorheology, and aggregation\(^{(30,31)}\).

Serum uric acid levels reflect circulating xanthine oxidase activity and oxidative stress production\(^{(20)}\). Ames et al. have proposed that uric acid may act as an important physiological antioxidant defense against such oxidative injuries\(^{(30)}\). The basis for this hypothesis was the observation that uric acid is oxidized to allantoin (and other products) in a process that scavenges singlet molecular oxygen, hydroxyl radicals, lipid hydroperoxide, and oxohaem oxidant, while inhibiting lipid peroxidation\(^{(31)}\). Another important antioxidant property of uric acid is the ability to form stable co-ordination complexes with iron ions\(^{(29,31)}\).

Increasing appreciation of the causative role of oxidative injury in many disease states great importance on the reliable assessment of lipid peroxidation. Malondialdehyde is one of several low molecular weight end products formed via the decomposition of certain primary
and secondary lipid peroxidation products. Most often, malondialdehyde assay used its reactivity at high temperature and low pH, towards thiobarbituric acid. In the present study lipid peroxidation was observed to be significantly higher (P<0.001) in sera of patients with UA and patients with MI in comparison to the healthy controls. These results were in agreement with the results obtained previously which indicated that plasma MDA levels were highly significant in patients with acute coronary syndrome compared to the control. Duboss - Ramde II et al. have reported that plasma MDA levels of patients presenting with unstable angina and acute myocardial infarction were higher than those of patients with stable angina and of normal angina and non-Q wave myocardial infarction groups.

A non significant correlation (P>0.05) between uric acid and MDA in sera of patients with UA and MI were found in the present study. This finding can be supported by the results obtained from previous studies which suggested that uric acid has a variable behavior where its not necessary an antioxidant and, depending on the chemical milieu, may become a prooxidant. In the presence of lipid peroxides uric acid even becomes a strong prooxidant. Muraoka S. and Miura T. reported that uric acid loses its antioxidant activity in the hydrophobic environment. Moreover it can form free radicals either alone or in combination with peroxynitrite.

References:


مستوى حمض الاليكويك وعلاقته بتفاعل الدهون مع البيروكسيد في امراض القلب المزمن

فهد سري احمد

قسم الكيمياء - كلية العلوم - الجامعة المستنصرية

الخلاصة

تؤدي النتائج المثمرة غير المستقرة في اغلب الأحوال إلى الصدمة بالاختسام العضلي القلبي الحاد، وتشير إلاكية اعراض حمض الاليكويك على مرض القلب الوعائي، وللوالد عامل أساسي ضد للكبدة. تم قياس مستوي حمض الاليكويك ومالون داي الدييدي في مصطلح كلا المرضى المصابين بالاضطراب غير المستقر والاختسام العضلي القلبي حيث تضمنت الدراسة الحالية جميع 29 حالة من مرضى المصابين بالاضطراب غير المستقر و 29 حالة من مرضى المصابين بالاختسام العضلي القلبي، وتم مقارنتها ب 25 حالة من الأشخاص الصحاء.

تم قياس حمض الاليكويك باستخدام عدة Human وقياس مالون داي الدييدي كذات الأكماة الفوقية للدهون باستخدام حمض تيبريك بارتيك. حيث لوحظ وجود زيادة ملحوظة في مستوي كلا من حمض الاليكويك ومالون داي الدييدي في مصطلح كلا المرضى المصابين بالاضطراب غير المستقر والاختسام بالاختسام العضلي القلبي مقارنة مع مستوياتها في مصطلح الدم الإصحاء في حين لوحظ عدم وجود علاقة ملحوظة بين حمض الاليكويك ومالون داي الدييدي في مصطلح كلا المرضى المصابين بالاضطراب غير المستقر والاختسام العضلي القلبي.