The association of isoprostane levels with cardiovascular disease risk factors in Iraqi women with polycystic ovary syndrome

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Abstract
The current study emphasis assay the association of 8-Isoprostane levels with cardiovascular disease risk factors in polycystic ovary syndrome patients, which is conceded as a current endocrine metabolic disorder that uncovers many serious rates outcomes to female good health, inclusively terrible ratio of infertility. This study including a total of 90 women divided into two groups (50 PCOS patients and 40 healthy controls). Homeostasis model assessment (HOMA-IR), lipid parameters, atherogenic index of plasma (AIP) as well as anthropometric measurements were measured. The level of 8-Isoprostane in serum was measured by a commercially available ELISA kit. The level of 8-Isoprostane was no significantly higher in women with polycystic ovary syndrome (61.97±51.86 pg/mL) compared with the healthy control group (52.44±28.49 pg/mL) (p>0.05). There were significantly higher in the mean of insulin, homeostatic model assessment for insulin resistance, triglycerides and atherogenic index of plasma in polycystic ovary syndrome patients than the control group (p<0.05). There was no correlation between 8-Isoprostane with any parameter in patients with polycystic ovary syndrome as showed the Pearson correlation analyses. In conclusion, increased levels of serum 8-Isoprostane are not associated with elevated CV risk in women with polycystic ovary syndrome.

Keywords: 8-isoprostane, polycysticovarysyndrome, cardiovascular disease risk factors.

How to cite this article: Khudair HY, Taha EM (2020): The association of isoprostane levels with cardiovascular disease risk factor in Iraqi women with polycystic ovary syndrome, Ann Trop Med & Public Health; 23(S13B): SP231381. DOI: http://doi.org/10.36295/ASRO.2020.231381

Introduction
Polycystic ovary syndrome (PCOS) is considered one of the most important endocrinal diseases affecting women of reproductive age, clinically evinced by an ovulation and hyperandrogenism and different other metabolic disorders that may have important effects for long term health [1]. Oxidative stress is a phenomenon present in properly functioning living organisms. When exacerbated, it can lead to harmful effects such as damage to DNA and cellular structures which may impact the development of many various diseases such as cancer [2].

As recognized that PCOS is correlating with oxidative stress (OS) that leads to a lower in the total levels of antioxidants in the serum and thus the production of free radicals. Fatty acid oxidation, adipose tissue, hyperglycemia and enzymatic sources (Nox) from mononuclear cells, are the most probable important sources of free radicals in polycystic ovary syndrome [3]. One of the best biomarkers of endogenous lipid peroxide is Isoprostane because they are present in every place in the body and usually in biological liquids are chemically stable when stored properly [4]. The most important results of non-enzymatic lipid peroxidation that accompanied by free radicals are8-
Isoprostane and measuring its concentration is one of the most important tools to determine the severity of oxidative stress.[5]

Isoprostane is a group of compounds create via encouraging of free radicals for non-enzymatic peroxidation of arachidonic acid that is similar to prostaglandins [6]. Since Isoprostane's discovery by Roberts and Morrow in 1990[7], proposed many studies the good biomarker reliable for endogenous lipid peroxidation is the level of Isoprostane, consequently in vivo is important tool reverse the damage and oxidative status [6]. The high concentrations of 8-Isoprostane promote atherosclerosis and cardiovascular disease. Maybe Patients with polycystic ovary syndrome have higher levels of this marker. One possible indication of the risk of atherosclerosis and insulin resistance is the increased level of isoprostane, subsequently, measure it may be from diagnostic and therapeutic tools that are used to monitor patients with PCOS.

Materials and methods
This study included 90 volunteered women. The volunteers divided into two groups 50 patients with PCOS and 40 healthy women as control recruited in this study, the patients have been collected from the outdoor patients of Kamal Alsamaray hospital. The study protocol was approved by the ethical committee of the University of Baghdad, college of science for women. The study was conducted in accordance with the guidelines of the ministry of Iraqi health. Depending on the presence of two of the three main characters of PCOS which include hyperandrogenemia (HA), oligo-/amenorrhea or anovulation (AO) and polycystic ovaries morphology (PCOM) the syndrome was diagnosed. The control group consisted of healthy volunteers who had a regular menstrual cycle, normal ovarian morphology with no biochemical features of hyperandrogenism. All contributors involved in the study were assessed in the initial follicular phase, between 2-5 days of a spontaneous or induced menstrual cycle. Medical checkup was made and anthropometric information was documented. Blood samples were collected after 12h fasting. The biochemical study involved; fasting glucose and insulin, triglyceride (TG), total cholesterol, high-density cholesterol (HDL-C), low-density cholesterol (LDL-C) as well as FSH, LH, and testosterone. Prior to recording clinical trials, all participants provided informed written consent.

Laboratory assays
The chemistry system (Pentra C200, Horiba) was used to determine serum levels of total cholesterol, LDL-C, TG and glucose whereas LDL-C level was identified using Friedewalds formula. Insulin was determined by an electrochemiluminescence immunoassay (Cobas e 411, Roche). An automated quantitative enzyme-linked fluorescent immunoassay (ELFA) was used for the determination of FSH, LH, and testosterone in serum (VIDAS, bioMerieux). Human 8-Isoprostane ELISA Kit (MyBioSource, MBS109360, USA) had been used to determine serum 8-Isoprostane concentration, the intra-assay and intra-assay coefficients of variability (CV) for 8-Isoprostane was less than 15%. The detection range was 6.25 pg/ml - 200 pg/ml, and the sensitivity was 1.0 pg/ml. HOMA-IR was calculated according to the specific formula which including fasting glucose and basal insulin levels [8, 9]. The atherogenic index of plasma (AIP) was calculated according to a specific formula as well.

Results
The anthropometric data
A total of 90 subjects (50 patients with PCOS and 40 control subjects) were included in the present study. The anthropometric data for the women with PCOS and controls are mentioned in Table 1.

**Table 1: The anthropometric data of the control and PCOS patients**

<table>
<thead>
<tr>
<th>Demographic data</th>
<th>Control (n=40)</th>
<th>Patients (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>24 (15-43)</td>
<td>25 (18-39)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>161 (154-165)</td>
<td>160 (148-172)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>64.5 (49-95)</td>
<td>72.5 (53-110)</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>83 (72-106)</td>
<td>89.5 (74-117)</td>
</tr>
<tr>
<td>BMI (kg/m^2)</td>
<td>25.29 (18.67-34.89)</td>
<td>28.08 (21.23-46.66)</td>
</tr>
</tbody>
</table>

**Biochemical characteristics of the studied groups**

The biochemical values of the PCOS and control patients are shown in Table 2. PCOS patients significantly had higher levels of AIP, insulin, HOMA-IR and glucose in comparison with control (p < 0.05). Regarding lipid profile, TG was significantly higher in PCOS patients when compared to control (p < 0.05). While HDL-c was significantly lower in PCOS patients when compared to control (p < 0.001). There was no significant difference between the two groups for FSH (p > 0.05). PCOS patients had significantly higher serum testosterone and LH levels than the control subjects (p < 0.05).

**Table 2: Hormonal and biochemical characteristics of the studied groups**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mg/dl)</td>
<td>85.6±9.0</td>
<td>94.4±12.8*</td>
</tr>
<tr>
<td>CHO (mg/dl)</td>
<td>123.4±26.3</td>
<td>154.1±33.1*</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>81.2±22.4</td>
<td>98.4±50.7*</td>
</tr>
<tr>
<td>HDL-c (mg/dl)</td>
<td>50.2±6.3</td>
<td>39.2±10.3*</td>
</tr>
<tr>
<td>LDL-c (mg/dl)</td>
<td>56.9±27.6</td>
<td>94.6±29.6*</td>
</tr>
<tr>
<td>VLDL-c (mg/dl)</td>
<td>16.2±4.5</td>
<td>19.6±10.1*</td>
</tr>
<tr>
<td>Insulin (μIU/mL)</td>
<td>11.7±3.5</td>
<td>18.5±10.1*</td>
</tr>
<tr>
<td>LH (mIU/mL)</td>
<td>3.2±1.0</td>
<td>6.2±3.4*</td>
</tr>
<tr>
<td>FSH (mIU/mL)</td>
<td>4.3±1.4</td>
<td>4.6±1.6</td>
</tr>
<tr>
<td>Testosterone (ng/mL)</td>
<td>0.4±0.1</td>
<td>0.5±0.2*</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>2.4±0.76</td>
<td>4.4±2.9*</td>
</tr>
<tr>
<td>AIP</td>
<td>0.19±0.15</td>
<td>0.35±0.26*</td>
</tr>
</tbody>
</table>

* Significant at 0.05 level

**Comparison of 8-Isoprostane for the entire cohort**

8-Isoprostane values of the PCOS patients and healthy controls are shown in Table 3. 8-Isoprostane was statistically no significantly higher in PCOS patients than in controls (p > 0.05).

**Table 3: 8-Isoprostane values of the control and PCOS patients**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Patients</th>
</tr>
</thead>
</table>

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Mean ± SD

| 8-Isoprostane (pg/ml) | 52.44±28.49 | 61.97±51.86 |

* Significant at 0.05 level.

Correlation between 8-Isoprostane and other parameters
There were no statistically significant correlations between 8-isoprostane with other parameters for the patient group. There was negative weak correlate between 8-isoprostane with LDL, glucose, insulin, FSH, HOMA-IR and AIP, non-correlation with LH, positive weak correlate with other parameters as shown in Figure 1. There were intermediate positive correlations between 8-isoprostane with each of FSH and testosterone in the control group (p<0.05), no statistically significant correlations with other parameters as shown in Figure 2.

Figure 1: Correlation between 8-Isoprostane and other parameters in PCOS patients.
Figure 2: Correlation between 8-Isoprostane and other parameters in control.

Study the best cut-off point of 8-Isoprostane
According to Receiver Operating Characteristic (ROC) curve there is no cut-off point clear as shown in Figure 3.
Oxidative stress (OS), according to recent studies, plays an essential role in the pathogenesis of polycystic ovary syndrome and used lipid peroxidation in tissues and cells as an indicator of OS. As 8-Isoprostane is biomarkers of lipid peroxide, its identification is a significant step forward in free radical studies as it reflects oxidative status and damage in vivo and does not affect fat intake. The OS parameters are increased in the PCOS patients as many studies indicate. This can be seen when comparing patients with PCOS and the control group where the concentrations of many OS parameters and products are high and decrease of several circulation antioxidant parameters [10, 11].

The present study shows statistically no significantly higher serum levels of 8-Isoprostane in women with PCOS compared with controls. The present study showed no evidence that the 8-Isoprostane used to evaluate oxidative stress in association with risk factors of CVD, which is not consistent with the commonly held notion that oxidative stress significantly contributes to CVD where there were no statistically significant between 8-Isoprostane with another parameter and the results of this study were that 8-Isoprostane levels showed negative weak correlate with most parameters in patients and this was not consistent with the previous study which showed presence association between 8-Isoprostane with higher CV risk in women with polycystic ovary syndrome [7].

The present study consistent with shown by one of the studies which are found that the increased levels of 8-Isoprostane are associated with an increase in oxidized HDL apolipoproteins[12] that are rapidly removed by the liver [13]. Therefore these specific forms of oxidized apolipoproteins may be useful markers of in vivo HDL oxidation and, hence, possibly atherosclerosis [14, 15].

In conclusion, our study showed that in women with polycystic ovary syndrome there was no association between 8-Isoprostane with the presence of IR and dyslipidemia that participate in the
increased risk of cardiovascular disease. Therefore, it is suggested that routine 8-Isoprostane measurement in women with PCOS may not be a tool to help determine the risk of cardiovascular disease and cannot be adopted and incorporated into clinical practice.

References