ABSTRACT
Endometriosis is a disease with unknown pathogenesis that can lead to infertility; it is benign, an estrogen-dependent gynecological disease characterized by the implantation, growth, and development of endometrial tissue is outside of uterine tissue may lead cause to endometrial cancer because it considered a common, chronic inflammatory disease, and etiology of the disease remains unclear. The main challenge of endometriosis in diagnosis and management is because it considers as a benign gynecological disorder. Many factors play a crucial role in the inflammatory process of endometriosis chronically, such as age, weight, interleukins, hormones, and other factors, which have been implicated in the disease’s pathogenesis. The present study was designed to measure the serum cancer antigen 125 (CA-125) and interleukin-17 (IL-17) levels in endometriosis patients to explain the role of these markers in the pathogenesis of disease and their correlation with age, body mass index BMI and correlation of these markers with each other. A total of 30 endometriosis patients and 30 healthy women, matching in average age and body mass index (BMI), were enrolled in this study. Patients with endometriosis and healthy women were attending Kamal Al-Samarrai Fertility and Infertility Hospital. Blood samples were aspirated from both groups to measure the serum CA-125 IL-17 levels by using enzyme-linked immunosorbent assay (ELISA) technique. The obtained results of serum cancer antigen-125 (CA-125) levels showed a highly significant elevation (p < 0.0001) in patients when compared with a control group. Also, the results recorded a highly significant elevation (p < 0.0001) in serum levels of interleukin-17(IL-17) between patients and the control group. On the other hand, the results declared that there was a highly significant inverse correlation between age and markers cancer antigen-125(CA-125) and interleukin-17(IL-17). The findings of the present study showed no significant correlation between serum cancer antigen (CA-125) levels and interleukin-17(IL-17) with BMI and, regarding highly direct correlation among the studied markers (CA-125, IL-17), these results explain the role of CA-125 and IL-17in the pathogenesis of endometrioses.

Keywords: Cancer Antigen-125 (CA-125), Endometriosis, Enzyme-linked Immunosorbent Assay (ELISA) technique, Interleukin-17(IL-17).

INTRODUCTION
Endometriosis is a common chronic gynecological estrogen-dependent disorder. The prevalence of endometriosis is between 2–10% in young women and up to 50% in infertile women, and it increases the risk for developing in case of fibromyalgia, autoimmune inflammatory diseases, chronic fatigue syndrome, and atopic diseases more than the general population. High association between endometriosis and stress may be associated with the deregulation of the stress system, riskiness of the disease is that it is one of the causes of female infertility.  

Endometrioses characterized by the presence of uterine endometrial tissue external the uterine cavity may present as superficial may be deep in pelvic peritoneal implants, adhesions, and ovarian cysts (endometriomas). Endometriosis cause pelvic pain and infertility. Endometriosis is classified into four stages (minimal, mild, moderate, and severe disease) according to the staging system of the American Society for Reproductive Investigation (ASRM). Ultrasound is used to diagnose deep endometriotic nodules, laparoscopic visualization of lesions, and ovarian endometriotic cysts. Several factors play a crucial role in the chronic inflammatory mechanism of disorder, such as age, weight interleukins, hormones and cancer marker, and others, which have been implicated in the disease’s pathogenesis.

This study deals with a correlation of cancer antigen-125(CA-125) and IL-17 with endometriosis and the role of
age and body weight in developing a disease in symptomatic women with primary or secondary fertility.

Cancer antigen (CA-125) has been reported to be elevated in endometriosis patients and is the most commonly described, extensively studied endometriosis biomarker to date, it’s a high molecular-weight glycoprotein normally expressed on tissues derived from the coelomic and Mullerian epithelia, including the uterus endometrium making it strong pathogenesis factor in the disease.

Interlukine-17 is produced by TCRα/β+CD4−CD8− thymocytes and activated CD4+ and CD4+CD5RO+ memory T cells, play a crucial role in inflammations, polycystic ovarian syndrome (PCOS) and may be involved in the pathogenesis of endometriosis by inducing the production of pro-inflammatory cytokines IL-1β, IL-6, IL-8 and TNF-α.

The current study hypothesized that IL-17 might be involved in the pathogenesis of endometriosis by inducing the production of pro-inflammatory cytokines with the role of other markers evaluated in this study.

SUBJECTS, MATERIALS, AND METHODS

Sixty Iraqi women participated in this study, Thirty women were already diagnosed with endometriosis, and the other thirty were healthy apparent. Proceeding to enrollment of participants, history information like age, BMI, concomitant diseases, other treatment were taken after achieving diagnoses by a consultant gynecologist based on abdominal ultrasound.

Measurement of Body Mass Index (BMI)

The BMI was determined by dividing the individual weight (in kilogram) by the squared value of height (in meter) as follow:

\[ \text{BMI} = \frac{Wt}{ht^2} \]

Blood Samples Collection and Measurement of Biochemical and Hormonal Markers

Blood samples were collected from subjects, was placed in gel tubes (contain a clotting activator), and centrifuged within 10 minutes at speed (3000 r.p.m) for 3 min. Then sera of all blood samples were separated and stored at - 20°C until the assay time. The collected sera were used for detection of Cancer antigen-125 (CA-125), Interleukin-17(IL-17) by enzyme-linked immunosorbent assay (ELISA) technique, using readymade kits (Mybioscource, USA for cancer antigen (CA-125), Interleukin-17).

Statistical Analysis

Data were collected and analyzed as the following:

- Statistical Analysis System (SAS) 2012 program was used to show the mean and standard error of the mean (M± SE).
- A dependent t-test was used to compare between mean values.
- The probability considered significantly different when p < 0.05, a highly significant difference when p < 0.01, and non-significant (NS) when p > 0.05.
- Correlation coefficient (r-value) was used to test the linear relationship between markers.

The r-value or correlation coefficient was expressed as a negative value when there is an inverse correlation, positive value when there is a direct correlation, and zero when there is no correlation.

RESULTS

Demographics and Baseline Characteristics

In the current study, Sixty Iraqi women have participated. Thirty of them were diagnosed with endometriosis; they were considered patients group, other thirty healthy apparent women were considered as a control group. The results recorded matching in mean ages and BMI between two groups. The mean ages of the patient’s group were 32.70 ± 0.98 years. The mean age of the control group was 31.46 ± 1.20 years, there BMI mean was 29.52 ± 0.54 kg/m² of the control group while 28.77 ± 0.34 kg/m² of patients, as illustrated in Table 1.

In the current study, the patient group was participated. Nineteen of them were diagnosed with primary infertility, representing 63.33% of the group, while the remaining 36.67%, 11 patients, were diagnosed with secondary infertility, as shown in Table 2.

Serum Level of Cancer Antigen-125(CA-125)

The results demonstrated that the mean level of CA-125 has been elevated significantly in sera of patients group (54.43 ± 2.27 IU/mL) in comparison with a control group (3.92 ± 0.16 IU/mL), (p < 0.0001), as clarified in Table 3 and Figure 1.

Serum Level of Interleukin (IL-17)

The results demonstrated that the mean level of IL-17 has been elevated significantly in sera of patients group (28.77 ± 0.34 IU/mL) in comparison with a control group (197.96 ± 11.77 IU/mL), (p < 0.0001), as clarified in Table 4 and Figure 2.

Correlation Coefficient between Age, BMI, CA-125, IL-17, Inpatient Group.

The results of the current study clarified that age has a non-significant direct correlation (p > 0.05) with BMI highly

**Table 1: Demographics and Baseline Characteristics.**

<table>
<thead>
<tr>
<th>Group</th>
<th>No</th>
<th>Mean ± SE</th>
<th>Age (year)</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>30</td>
<td>31.46 ± 1.20</td>
<td>29.52 ± 0.54</td>
<td></td>
</tr>
<tr>
<td>Patients</td>
<td>30</td>
<td>32.70 ± 0.98</td>
<td>28.77 ± 0.34</td>
<td></td>
</tr>
<tr>
<td>T-test</td>
<td>---</td>
<td>3.118 **</td>
<td>2.0017 NS</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>---</td>
<td>0.0001</td>
<td>0.2400</td>
<td></td>
</tr>
</tbody>
</table>

**= highly significant difference (p < 0.01).

**Table 2: Caption missing**

<table>
<thead>
<tr>
<th>Infertility</th>
<th>No</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>19</td>
<td>63.33</td>
</tr>
<tr>
<td>secondary</td>
<td>11</td>
<td>36.67</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>100%</td>
</tr>
<tr>
<td>P-value</td>
<td>---</td>
<td>0.0002 **</td>
</tr>
</tbody>
</table>

**= highly significant difference (p < 0.01).
Figure 1: Mean Serum level of Cancer Antigen-125 in Patients and Control group. CA-125 = Cancer antigen-125, **=highly significant difference (p<0.01).

Table 3: Mean Serum level of Cancer Antigen-125 in patients and control group.

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean ± SE of CA-125 (IU/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>3.92 ± 0.16</td>
</tr>
<tr>
<td>Patients</td>
<td>54.43 ± 2.27</td>
</tr>
<tr>
<td>T-test</td>
<td>4.567 **</td>
</tr>
<tr>
<td>p-value</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

CA-125 = Cancer antigen, **=highly significant difference (p<0.01).

Table 4: Mean serum level of interleukin-17 in patients and control group.

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean ± SE of IL-17 (IU/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>129.93 ± 5.10</td>
</tr>
<tr>
<td>Patients</td>
<td>197.96 ± 11.77</td>
</tr>
<tr>
<td>T-test</td>
<td>25.686 **</td>
</tr>
<tr>
<td>P-value</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

IL-17 = Interleukin, **=highly significant difference (p<0.01).

discussion

Endometriosis and infertility are associated clinically; the current study was to explain the relation between endometriosis and CA-125, IL-17 and show the role of these biomarkers in the development of disease complications.

An elevated level of CA-125 in serum may also be caused by the inflammatory reactions that alter the endothelial permeability leading to the liberation of the marker into circulation. Depending on the results of this study that shows a highly significant difference between patients and control group in serum level of CA-125, as shown in Table 3 and Figure 1, this result agrees with the study explain the role of CA-125 levels to identify endometriosis-associated ovarian cancer, and agree with the result of Budak E et al. (2019) study showed significant elevation of serum level of CA-125 levels in endometrial carcinomas.

As a result, showed in this study, CA-125 showed a high inverse correlation coefficient with ages of patients; this result agrees with the result of Deutsch K et al. (2019) study shows the correlation between CA-125 and Grade 1 endometrial cancer. And disagree with the study of Karimi-Zarchi M et al. (2016) explain the Correlation of CA-125 serum level of patients with endometriosis.

Interleukin-17 (IL-17) plays a very important role to increase immunity in general, by induction the immune response against the foreign body, helper T cell 17 (Th17) cell also play a pivotal role in the pathogenesis of endometriosis, miscarriage, preterm labor, and preeclampsia, and complete pregnancy process. The current study shows the relation between IL-17 and endometriosis in Table 4 and Figure 2. The results demonstrated that the mean level of IL-17 has been elevated significantly in sera of patients group in comparison with the control group; these results agree with many studies Tarokh M et al. (2019), Miller JE et al (2020) and Kitazawa J et al. (2020).

On the other hand, the results of the current study have shown inverse correlation of serum IL-17 levels with the age of patients at a highly significant level because the decrease of immunity with increasing age and bad life style, otherwise the result show a direct correlation coefficient at highly significant level between CA-125 and IL-17 that ensure the role of CA-125 in stimulation immune system to protect the body and useful prognostic power to predict severity of the disease.
Evaluation of CA-125 and IL-17 in a Sample of Iraqi Women with Endometriosis

CONCLUSIONS
Serum cancer antigen 125 (CA-125) and interleukine-17 (IL-17) levels are elevated in the serum of endometriosis patients and play an important role in the pathogenesis of disease by different mechanisms like stimulation immune system and produced cancer antigens and interleukins.

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REFERENCES