Research Article

Serum Leptin as a Marker for Severity of Endometriosis

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Received 29 March 2020; Revised 21 August 2020; Accepted 26 August 2020; Published 7 September 2020

Academic Editor: Curt W. Burger

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Background. Endometriosis a disease of theories, and one of the important causes of chronic pelvic pain, dysmenorrhea, dyspareunia, and subfertility. Surgery is the mainstay step for the diagnosis; noninvasive test is the goal in the future. Aim of Study. To test the role of serum leptin in determination of severity of endometriosis. Study Design. A cross-sectional study done in Al-Yarmouk Teaching Hospital from 1st of January 2018 to 1st of January 2019. Methods. 60 BMI-matched patients were involved in the study. A study group of 30 patients were operated either by laparoscopy or laparotomy for many reasons diagnosed as endometriosis by histopathology, and 30 normal women as a control group underwent elective surgery. Blood sample was taken from all patients in the theater room when laparoscopy finding went with endometriosis, and classifying according to surgical staging of endometriosis, the level of serum leptin was measured by ELISA using Human LEP (Leptin) ELISA Kit. The recording of finding of laparoscopy after conforming of diagnosis by histopathology was compared with the result of serum leptin. Result. The result shows no significant difference between the two groups regarding parity and age; however, the level of serum leptin was significantly high in the endometriosis group than in the control group. The P value was less than 0.05. Also, the result shows no significant differences between serum leptin in both groups according to the symptom but there was a significant difference with surgical staging. The mean of the level of serum leptin in stage 1 was 214.8, while it was 340.3 in stage 4. Conclusion. Serum leptin can be used as a marker of severity of endometriosis.

1. Introduction

Endometriosis is an enigmatic disease associated with serious morbidity and change in quality of life among childbearing-age females. Early diagnosis and focus management of the disease were a big challenge for both gynecologists and patients. It is defined as endometrial tissue (stroma and gland) present outside the uterus [1]. Determination of the endometriosis incidence is challenging because some women do not show symptoms; prevalence was estimated to be between 10 and 15 percent of women [2]. Also, with Mullerian abnormality, incidence increased up to 40%. The endometrial tissue may present in any site according to the process of its development and progress such as ovary, peritoneum, bladder, vulva, and scar of operation [3] or in rare sites such as brain tissue [4]. These ectopic tissues remain under the effect of ovarian hormones which cause cyclical change of growth and shedding that lead to wide variation of symptoms due to fibrosis and adhesion formation and infiltration [5].

More than 100 years ago when endometriosis was first described, its nature, progression, and the way by which it was related to infertility and occurrence of pelvic pain remain unclear [6].

The etiology of endometriosis appears to be of multiple theories, including hematological metastasis, immunological changes, abnormal proliferation of the cell and apoptosis, endocrine abnormality, and genetic predisposition (stem cell theory) [7].

There is no specific test for diagnosis of endometriosis. While many markers were evaluated in many research studies for the noninvasive diagnosis of disease, none were revealed to be of great benefit. CA125 concentrations show a high level in patients with endometriosis but they are not specific [8].
Leptin is a 167 amino acid protein with a 21 amino acid
signal peptide and a product of ob gene. Leptin is present in
the plasma in two forms, free or bound to leptin-binding
proteins. This hormone had a role in basal metabolism, re-
production, and food intake. Leptin also had immune-reg-
ulatory, proinflammatory, and neoangiogenesis functions, so
it may play a role in pathogenesis of endometriosis [9].

2. Patient and Methods

A cross-sectional study was performed in Al-Yarmouk
Teaching Hospital (tertiary hospital in Baghdad) from 1st of
January 2018 to 1st of January 2019.

60 BMI-matched patients were involved in the study. A
study group of 30 patients were operated (laparoscopy or
laparotomy for ovarian cyst, chronic pelvic pain, and painful
lump at the site of previous scar) and all were diagnosed as
endometriosis by histopathology. 30 normal women under-
went laparoscopy for other gynecological causes such as
sterilization, diagnostic laparoscopy for infertility, and chronic
pelvic pain and no endometriosis) as the control group. Verbal
consent was obtained from all patients involved in the study.

Inclusion criteria included pregnant patients, la-
dynamically not stable patients, obese patients, and patients
with medical disease. Detailed history includes the chief
complaint signs and symptoms and medical, surgical, drug,
and menstrual history. Blood sample was taken from pa-
tients in the theater room when laparoscopy finding went
with endometriosis and it was confirmed lately by histo-
pathological examination, and the level of serum leptin was
measured by ELISA by using Human Leptin ProQuantum
ImmuNoassay kit and recording of finding of laparoscopy
and the severity was classified according to the revised
American Society for Reproductive Medicine Scoring
system:

(i) Stage I: minimal, isolated implants, and no signif-
icient adhesions.

(ii) Stage II: mild, superficial implants <5 cm in ag-
gerate, scattered on the peritoneum and ovaries,
and no significant adhesions.

(iii) Stage III: moderate multiple implants, both super-
ficial and deeply invasive. Peritubal and periovarian
adhesions present.

(iv) Stage IV: severe, multiple superficial and deep
implants. Presence of large ovarian endometriomas.
Filmy and dense adhesions are usually present [10].

Also, the result of serum leptin was then compared
between the study groups.

3. Statistical Analysis

Data analysis was performed by using Statistical Packages for
Social Sciences-version 25 (SPSS-25).

The relation between differences of variable means was
tested using Student’s- t-test, and ANOVA test was used for
difference among more than two independent means. The
significance of difference of different percentages (qualitative
data) was tested using Pearson’s chi-square test (χ²-test) with
application of Yate’s correction or Fisher’s exact test
whenever applicable. Statistical significance was considered
whenever the P value was equal to or less than 0.05.

4. Results

Table 1 shows the demographic differences between the two
groups, and it shows significant difference regarding parity
and age because most of the patients with endometriosis
present with infertility and low parity and more prevalence
at 30–40 years.

Serum leptin is significantly high in the endometriotic
group than in the control group. The P value is less than 0.05
as shown in Table 2 and Figure 1.

Table 3 shows no significant differences between serum
leptin in both groups according to symptoms, but there was
a significant difference with surgical staging with a P value
of 0.0001.

Figure 2 shows that the mean level of serum leptin was
214.8 in stage 1 and increase indirect relation of increment to
be 340.3 in stage 4.

5. Discussion

Endometriosis is a progressive, chronic condition. It has
been recently reported that serum concentrations of leptin
play a role in reproduction. On the basis of these findings,
studies evaluating the serum leptin level try to show the
relationship between the serum leptin level and endo-
metriosis and if it had a role in the pathogenesis of this
disease, the relationship between the serum leptin and
endometriosis severity is still controversial; several studies
revealed there was no relation while others have shown a
positive correlation with more severe forms of endometriosis.

In Zendron et al.’s [11] study, 25 women were enrolled, 10
as control and 15 patients undergoing surgery for adnexal
mass, and the leptin levels in both serum and peritoneal fluid
(PF) and the protein expression in different peritoneal im-
plants were studied. The study revealed that the level of leptin
was higher in the endometriosis group but had no clear role in
the progression of disease. The result matches our study in
relation to increase in the serum leptin level significantly in
the patient with endometriosis, but our study revealed that
there was a direct significant relation with the severity.

In [12], 13 women with variable stages of endometriosis
and 15 patients as control were enrolled. The serum leptin
level and the result revealed statically significant increase in
the endometriotic group which has a similar match with our
study which indicates the possible role in the pathogenesis of
endometriosis.

Leptin has recently been suggested to be involved in
unexpected functions, specifically the process of angiogen-
essis and immune response which are one of the most
Table 1: Demographic characteristic features of both groups.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Endometriosis (30)</th>
<th>Controls (30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>0 (0.0)</td>
<td>2 (6.7)</td>
<td>0.031*</td>
</tr>
<tr>
<td>20–24</td>
<td>0 (0.0)</td>
<td>7 (23.3)</td>
<td></td>
</tr>
<tr>
<td>25–29</td>
<td>8 (26.7)</td>
<td>6 (20.0)</td>
<td></td>
</tr>
<tr>
<td>30–34</td>
<td>14 (46.7)</td>
<td>10 (33.3)</td>
<td></td>
</tr>
<tr>
<td>≥35</td>
<td>8 (26.7)</td>
<td>5 (16.7)</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD (range)</td>
<td>32.3 ± 4.4 (25–42)</td>
<td>29.0 ± 6.6 (16–42)</td>
<td>0.029#</td>
</tr>
</tbody>
</table>

Parity

<table>
<thead>
<tr>
<th>Parity</th>
<th>Endometriosis (30)</th>
<th>Controls (30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>8 (26.7)</td>
<td>1 (3.3)</td>
<td>0.016*</td>
</tr>
<tr>
<td>1–4</td>
<td>20 (66.7)</td>
<td>22 (73.3)</td>
<td></td>
</tr>
<tr>
<td>≥5</td>
<td>2 (6.7)</td>
<td>7 (23.3)</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD (range)</td>
<td>1.7 ± 1.5 (0–6)</td>
<td>3.0 ± 1.6 (0–6)</td>
<td>0.002#</td>
</tr>
</tbody>
</table>

*Significant difference between proportions using Pearson's chi-square test at 0.05 level. #Significant difference between two independent means using Student's-t-test at 0.05 level.

Table 2: Relation between serum leptin and both groups.

<table>
<thead>
<tr>
<th>Serum leptin level (pg/ml)</th>
<th>Endometriosis (30)</th>
<th>Controls (30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>150</td>
<td>0 (0.0)</td>
<td>8 (26.7)</td>
<td>0.0001*</td>
</tr>
<tr>
<td>200</td>
<td>8 (26.7)</td>
<td>17 (56.7)</td>
<td></td>
</tr>
<tr>
<td>250</td>
<td>11 (36.7)</td>
<td>1 (3.3)</td>
<td></td>
</tr>
<tr>
<td>300</td>
<td>5 (16.7)</td>
<td>4 (13.3)</td>
<td></td>
</tr>
<tr>
<td>350</td>
<td>2 (6.7)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>400</td>
<td>4 (13.3)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD (range)</td>
<td>289.73 ± 65.08 (201.245–431.479)</td>
<td>222.66 ± 40.40 (180.492–340.450)</td>
<td>0.0001*</td>
</tr>
</tbody>
</table>

*Significant difference between proportions using Pearson's chi-square test at 0.05 level. #Significant difference between two independent means using Student's-t-test at 0.05 level.

Figure 1: Serum leptin curve in both groups. (a) Endometriosis. (b) Controls.
important factors involved in the pathogenesis of endometriosis.

Viganò et al.’s [13] study involved 67 women divided into those proved to have endometriosis and remaining as control. The result revealed no significant difference so it is not a marker for diagnosis of endometriosis or does not detect its severity. This result disagrees with our study.

Osman et al. [14] studied the role of leptin and some other antioxidants in infertile women, with endometriosis blood sample collected from 38 patients, about two thirds of them being in the study group and the others in the control group. It was revealed that there was no important difference in serum leptin concentrations between the studied groups. Again, this study disagrees with our study.

Wertel et al. [15] compared the level of serum and peritoneal level of leptin in different stages of endometriosis in two study groups, fertile and nonfertile, and the study revealed that higher level PF leptin concentration was observed in patients with stages III and IV of endometriosis than in those with the minimal stage of the disease, a similar result from our study in serum leptin level.

Leptin may be used with other markers as combination to predict the severity of endometriosis.

Data Availability

The patient data used to support the findings of this study are currently under embargo while the research findings are commercialized. Requests for data 6/12 months after publication of this article will be considered by the corresponding author.

Ethical Approval

This article has been approved by the Medical Committee of Obstetrics and Gynecology Department of Al-Yarmouk Teaching Hospital.

Consent

Verbal consent has been obtained from all participants before starting this work.
Conflicts of Interest
The authors declare that they have no conflicts of interest.

Acknowledgments
The authors would like to express their deepest appreciation to all those who helped to complete this article.

References