ASSOCIATION OF SERUM FOLLICLE STIMULATING HORMONE AND SERUM LUTEINIZING HORMONE WITH SECONDARY INFERTILITY IN OBESE FEMALES IN PAKISTAN

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ABSTRACT

Objective: To finding the association of serum follicle stimulating hormone (FSH) and luteinizing hormone (LH) with secondary infertility in obese females in Pakistan.

Study Design: Cross sectional study.

Place and Duration of Study: District head quarter Hospital Sahiwal, from Mar 2018 to May 2018.

Methodology: The study was conducted at district head quarter hospital Sahiwal after approval from Institutional Review Board of Sahiwal Medical College Sahiwal. The Data was assessed by IBM-SPSS version 24. Frequency distributions of study participants were calculated. Significance of the associations was assessed by independent sample t-test. Bivariate analysis was also done to check the effect of different factors on secondary infertility separately. The p-value less than 0.05 was taken as statistically significant.

Results: Mostly (43.3%) belonged to middle class socioeconomic group. Nearly 54% were from urban residential areas. Majority belonged to (65%) age group between 31-40 years. When we calculated the association of serum follicle stimulating hormone and serum luteinizing hormone with the secondary infertility in these study participants then it was conclusive to find out that mean levels of both follicle stimulating hormone and luteinizing hormone were quite low (12.11 ± 1.14 and 21.97 ± 3.74 respectively) in patients with secondary infertility as compared to those which were not suffering from it. Association of serum follicle stimulating hormone was also found to be statistically significant with secondary infertility (p=0.042).

Conclusion: Hence it is concluded that the low levels of serum follicle stimulating hormone are strongly associated with secondary infertility in obese women.

Keywords: Obese, Secondary infertility, Serum follicle stimulating hormone, Serum luteinizing hormone.

INTRODUCTION

Infertility refers to conception failure by a couple and is perceived as a multifactorial syndrome in all cultures and societies. Approximately 23% couples of reproductive age group are affected in Pakistan, of whom 5% contribute to primary infertility and 18% to secondary causes1. During this process of folliculogenesis, the oocyte undergoes a significant array of genetic, epigenetic and cytoplasmic alterations in order to achieve fertilization proficiency. This whole course of events depends on a continuous cross-talk between oocytes and granulosa cells that safeguard the coordination of all the events sequenced in the ovary under the influence of paracrine and endocrine factors, hormones and peptides2. Maintenance of ovarian reserve is dependent on extrinsic (xenobiotic and anticancer drugs) and intrinsic (endometriosis, diabetes, polycystic ovarian syndrome [PCOS] and ovarian aging) factors3.

Although Pakistan is among the currently most populous countries of the world, and has a population growth rate of around 2%4, it also has high rate of infertility (21.9%); 3.5% primary and 18.4% secondary the prevalence of infertility in Pakistan is 21.9%5.

Increasing prevalence of obesity in recent decades has been preceded by dramatic dietary changes in industrialized societies6. Over the past 100 years, there has been a considerable shift in the human diet, particularly with respect to the
amount and type of consumed fat. High FSH levels strongly predict poor fertility in younger women compared to older women. A study reported that elevated basal day 3 FSH level is strongly correlated with diminished ovarian reserve in women aged more than 35 years and is associated with poor pregnancy rate (6% versus 42%) after induction of ovulation. This objective of this study was to find the association of FSH and LH with secondary infertility in obese women presenting at different outpatient departments of DHQ hospital Sahiwal.

**METHODOLOGY**

The cross sectional study was conducted at District head quarter hospital Sahiwal, from March 2018 to May 2018 after approval from Institutional Review Board of Sahiwal Medical College Sahiwal. A validated questionnaire was filled by the patients after taking informed consent from them. Convenient sampling technique was used. Blood samples of the patients were also taken to calculate serum FSH and serum LH.

Sample size was calculated according to following formula:

\[
\text{Sample Size} = \frac{Z_{1-\alpha/2}^2 \, p(1-p)}{d^2}
\]

\(Z_{1-\alpha/2}\) is standard normal variant (at 5% type 1 error \((p<0.05)\) it is 1.96. As in majority of studies \(p\)-values are considered significant below 0.05 hence 1.96 is used in formula.

\(p\) = Expected proportion in population based on previous studies or pilot studies = 0.20(7)

\(d\) = Absolute error or precision = 0.08

Sample size = 60.

Convenient sampling technique was used. Blood samples of the study participants were taken and serum was separated by centrifugation. Commercially available enzyme-linked immunosorbent assay (ELISA) kits were used for biochemical estimation of serum follicle stimulating hormone (FSH) (Cat# DKO010; Diametra), luteinizing hormone (LH) (Cat # DKO009; Diametra).

The Data was assessed by IBM-SPSS version 24. Frequency distributions of study participants were calculated. Significance of the associations was assessed by independent sample t-test. Bivariate analysis was also done to check the effect of different factors on secondary infertility separately. The \(p\)-value <0.05 was taken as statistically significant.

**RESULTS**

Mean age of our study participants was 32.21 ± 3.22 years. A total of 54 (90%) out of 60 obese females were suffering from secondary infertility. Obesity status of the females was calculated by checking their basal metabolic index. Females with BMI more than 25 were obese. Mostly (43.3%) belonged to middle class socioeconomic group. Nearly 54% were from urban residential areas. Majority belonged to (65%) age group between 31 to 40 years (table-I).

When we calculated the association of serum FSH and serum LH with the secondary infertility in these study participants then it was conclusive to find out that mean levels of both FSH and LH were quite low (12.11 ± 1.14 and 21.97 ± 3.74 respectively) in patients with secondary infertility as compared to those which were not suffering from it. Association of serum FSH was also found to be statistically significant with secondary infertility \((p=0.042)\). Though serum LH levels were not significantly associated (table-II).
We also confirmed the role of FSH in causing secondary infertility in our study subjects by checking our data through bivariate analysis. It was again confirmed as serum FSH was again significantly associated with secondary infertility \((p=0.001)\) with odd’s ratio of 0.117. Other factors like serum LH levels, age, basal metabolic index and socio-economic status all were non-significant (table-III).

Table-II: Association of Serum Follicle Stimulating Hormone (FSH) and Serum Luteinizing Hormone (LH) with secondary infertility in obese women calculated by independent sample t-test \((n=60)\).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Secondary infertility</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Serum FSH (ng/ml)</td>
<td>Yes (n=54)</td>
<td>12.12 ± 1.14</td>
</tr>
<tr>
<td></td>
<td>No (n=6)</td>
<td>17.42 ± 2.24</td>
</tr>
<tr>
<td>Mean Serum LH (ng/ml)</td>
<td>Yes (n=54)</td>
<td>21.97 ± 3.74</td>
</tr>
<tr>
<td></td>
<td>No (n=6)</td>
<td>68.87 ± 1.66</td>
</tr>
</tbody>
</table>

Table-III: Bivariate Analysis of different variables related to infertility in obese women.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Significance</th>
<th>Odd’s Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum FSH</td>
<td>0.001</td>
<td>0.117</td>
</tr>
<tr>
<td>Serum LH</td>
<td>0.17</td>
<td>0.793</td>
</tr>
<tr>
<td>Age</td>
<td>0.09</td>
<td>0.887</td>
</tr>
<tr>
<td>Basal Metabolic Index</td>
<td>0.11</td>
<td>1.12</td>
</tr>
<tr>
<td>Socio-economic Status</td>
<td>0.07</td>
<td>0.472</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Female patients with different gynecological related issues presented at gynecological outpatient department of DHQ Sahiwal and they were assessed after taking proper history and detailed examination. As found in previous study\(^8\) most of our study participants were from urban population and middle socioeconomic group.

A previous study showed that the obese females tend to suffer more from gynecological disorders than the females with normal BMI\(^9\). Another study showed\(^10\) that levels of estrogen and FSH were found to be lower in females with secondary infertility but we did not calculate the serum estrogen levels due to limited budget. In another study\(^11\) they calculated the serum Estrogen, FSH, LH and serum testosterone levels to have a comparison with infertility status but they checked for causes of primary infertility in contradiction to our study. An overwhelming of majority in our study population was suffering from secondary infertility (90%) again in contradiction to previous study\(^12\) which found 65% of their study participants suffering from secondary infertility. Though our study participants presented to different hospitals with gynecological complaints yet the secondary fertility was also found out in them.

Our study found out strong association between mean serum FSH levels with secondary infertility \((p=0.042)\). The mean levels of FSH were found out to be 12.12 ± 1.14 ng/ml which were very low. All the participants also had menstrual irregularities so the levels of FSH were calculated independent of the day of menstrual cycle. A previous study also found strong association of FSH with obesity but not with secondary infertility status\(^13,14\). Patients without secondary infertility showed normal levels of serum FSH and higher than the females with secondary infertility. Though the literature review\(^15-17\) proves that the low levels of serum FSH are good indicator for ovulation of the females and hence related to more chances of females with pregnancy yet our study showed that lower levels of FSH with menstrual irregularities are associated with secondary infertilities. But still other causes of menstrual irregularities should be sorted out.

Though our study failed to find significant association between serum LH levels and secondary infertility status yet the levels of LH were also lower (21.97 ± 3.74) in patients with secondary infertility as compared to those without secondary infertility (68.87 ± 1.66) ng/ml.

We also did bivariate analysis of different factors which can cause the secondary infertilities in such females but it was astonishing to see that only serum FSH was found to be significantly associated \((p=0.001)\). A low odd’s ratio of 0.117 also showed that these serum levels of FSH mainly caused the secondary infertility in our study population. Age, socio-economic status,
serum LH levels and Basal metabolic index were non-significant. A previous study showed the mono variant analysis but they did not take the serum FSH and serum LH levels into the account.

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CONCLUSION

Hence it is concluded that the low levels of serum FSH are strongly associated with secondary infertility in obese women. Our sample size was limited due to constrained budget but the study can be replicated in more participants with larger sample sizes in which more causes of secondary infertility should be sorted out.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES