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Association between Endometriosis and Prolactin Concentration in Infertile Women

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Abstract

Objective: The present study aimed to determine comparison of prolactin concentration in infertile women with and without endometriosis and to determine association of prolactin with various stages of endometriosis.

Material & Method: 60 infertile women who underwent diagnostichystero laparoscopy for the evaluation of infertility, were included in a cross-sectional study. The presence of endometriosis was evaluated. Women with endometriosis were kept in group-A and women without endometriosis were kept in group-B .Serum prolactin (PRL) level was measured in both groups. The comparison of basal serum PRL levels between the two groups was performed, using independent t-test. Serum prolactin level was also measured according to different stages of endometriosis to find the association between prolactin level and disease severity.

Results: PRL levels were significantly higher in endometriosis group compared to control group(20.23 ± 4.99 ng/ml v/s 11.65 ± 4.34 ng/ml). Statistically significant associations were found between staging of endometriosis and prolactin levels (p=0.001).

Conclusion: High prolactin concentration may be associated with endometriosis and its severity.

Keywords: Prolactin, Endometeriosis, Infertile

Introduction

Endometriosis is the common benign disease affecting approximately 10-15% of reproductive age women . It is defined as the presence of endometrium like tissue outside the normal uterine cavity[(1)]. Symptoms of endometriosis include dysmenorrhea, dyspareunia, dyschezia, pelvic or lower abdominal pain, abnormal bleeding and chronic fatigue[(2)]. The relationship between endometriosis and infertility is strong, as the monthly fecundity rate for a normal couple decreases from 15-20% to 2-5% when the women has endometriosis[(3)]. It has been described in literature that it takes around 4 to 11 years from onset of symptoms for definitive diagnosis of endometriosis[(4)]. Research on the diagnosis of endometriosis currently interfaces with four area including clinical manifestations, imaging, biomarkers and surgical techniques. Considering the prevalence and impact of endometriosis on infertile

women, a complete diagnostic workup for infertility should include a diagnosis of endometriosis. Till date there is no specific blood test for the diagnosis of endometriosis. A general endometriosis screening test may be neither appropriate because of risk of over diagnosis nor feasible. Pathophysiology and pathogenesis of endometriosis are not clear and endometriosis associated infertility is also difficult problem[5]. It has been tried by many researchers to establish the relationship between endometriosis and hyperprolactinemia. Endometriotic implants may secrete prolactin and possibly cause ovarian dysfunction. Prolactin levels among infertile women with endometriosis are reported to be higher than those without endometriosis. Moreover, higher concentrations of prolactin seems to be more prevalent in stage 3-4[6]. The mechanism by which endometriosis and prolactin levels determine infertility are poorly understood, although hyperprolactinemia and the presence of prolactin receptors in ectopic endometrium tissue may contribute[7].

Material & Method

The hospital based comparative cross-sectional study was carried out in Department of Obstetrics & Gynaecology of SMS Medical College, Jaipur from May 2019 to August 2020. Total 60 infertile women were included in this study, 30 infertile women with endometriosis (group-A) and 30 infertile women without endometriosis (group-B).

Inclusion Criteria

- Women with infertility duration ≥1 year.
- Women giving consent for participation in study.

Exclusion Criteria

- Women with a previous surgical diagnosis of endometriosis.
- Patient with active pelvic inflammatory disease diagnosed on basis of history and pelvic examination.
- Women who have husband with azoospermia or severe oligozoospermia (<10 million mobile spermatozoa per ml).
- Women who were using drugs like antiemetic , dopamine antagonists , tranquilizers that could affect prolactin level.
- Women who had taken hormonal medication (including combined oral contraception) within previous 3 months.
- Women with previous endocrine disorders like polycystic ovarian syndrome, thyroid disorders , pituitary adenoma .
- Women with previous tubal ligation.
- Women with known contraindication to anaesthesia and surgical intervention like hysterolaparoscopy.

Methodology

After applying inclusion and exclusion criteria informed written consent was taken and women with infertility duration more than one year and willing to participate were recruited from Department of Obst and Gynae, SMS Medical College, Jaipur. Approval from institutional Research, Review Board and Ethical Committee was taken. Standardized data collection on a predesigned study proforma including a full infertility workup, after the initial visit was done. Serum prolactin was measured in study group. All infertile women underwent diagnostic hysterolaparoscopy and divided into two groups, women with endometriosis (group-A) and women without endometriosis (group-B). Laparoscopic staging was based on American Society of Reproductive Medicine (ASRM) scoring for endometriosis in which findings were divided into four

categories according to severity : stage 1 (minimal disease), stage 2 (mild disease), stage 3 (moderate disease), stage 4 (severe disease).

Statistical Analysis

Linear variables were summarized as mean and standard deviation whereas nominal/categorical variables were expressed as proportions (%).

Unpaired t-test and other parametric tests were used for analysis of linear variables while nominal/categorical variables were analysed by using Chi-square test and Fisher-exact test.

p-value <0.05 was taken as significant. Medcalc 16.4 version software was used for all statistical calculations.

Results

THE study included infertile women who underwent diagnostic hysterolaparoscopy .60 infertile women were selected for our study, 30 were in group-A and 30 were in group-B. In our study, 8 (26.67%) patients were diagnosed with stage-I, 5 (16.67%) were with stage-II, 6 (20.00%) were with stage-III and 11 (36.66%) patients were diagnosed with stage-IV of endometriosis.

Table 1: Description of study population

Group	Group-A	Group-B	P-value
Mean Age (in yrs)	26.07 ± 3.20	25.50 ± 3.90	0.541
Mean Duration of Infertility (in yrs)	4.30 ± 1.42	3.77 ± 2.86	0.364

Mean age in Group–A was 26.07 ± 3.20 yrs and in Group-B was 25.50 ± 3.90 yrs. The difference was not statistically significant. Mean duration of infertility among the study groups. Mean duration of infertility in Group-A was 4.3 ± 1.42 yrs and Group-B was 3.77 ± 2.86 yrs. The difference was not statistically significant.

Table 2: Distribution of Subjects According to Type of Infertility

Type of Infertility	Group-A		Group-B	
	No.	%	No.	%
Primary	22	73.33	19	63.33
Secondary	8	26.67	11	36.67
Total	30	100.00	30	100.00

$\chi^2 = 4.28$ $p = 0.117$

Both the groups were comparable with regards to the type of infertility. Out of 60 patients in our study 41 (68.33%) patients had primary infertility and 19 (31.67%) patients had secondary infertility.

In Group-A occurrence of primary infertility was 73.33% (22 out of 30) and that of secondary infertility was 26.67% (8 out of 30). In Group-B occurrence of primary infertility was 63.33% (19 out of 30) and that of secondary infertility was 36.67% (11out of 30).

Table 3: Comparison of Serum Prolactin Concentration among Study Groups

Variable	Group - A		Group - B		t-test	p-value
	Mean	SD	Mean	SD		
Serum Prolactin (ng/ml)	20.23	4.99	11.65	4.34	50.41	0.001

S. prolactin level was significantly higher in Group-A (20.23 ± 4.99 ng/ml) as compared to Group-B (11.65 ± 4.34 ng/ml).

Table 4: Serum Prolactin Concentration in Endometriosis Group According to Disease Stage

Variable	Stage-I (n = 8)		Stage-II (n = 5)		Stage-III (n = 6)		Stage-IV (n = 11)		P-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Serum Prolactin (ng / ml)	13.94	2.48	18.68	2.51	22.29	2.40	24.39	2.83	0.001

The above table shows serum prolactin concentration in endometriosis group according to disease stage. Serum prolactin concentration was significantly higher in women with severe disease.

Serum prolactin levels in patients with stage-I was 13.94 ± 2.48 ng/ml, in stage-II was 18.68 ± 2.51 ng/ml, in stage-III 22.29 ± 2.40 ng/ml and in stage-IV 24.39 ± 2.83 ng/ml.

Discussion

In our study infertile women with endometriosis (Group-A) were compared to infertile women without endometriosis Group-B). Group-A was older than group-B (26.07 ± 3.20 yrs vs. 25.50 ± 3.90 yrs). Ashrafi M et al (2016) also found the mean age to be higher in endometriosis group as compared to group without endometriosis (32.4 ± 4.9 yrs v/s 31.4 ± 5.2 yrs)[8]. Similar results were also obtained by Moini A et al (2013) In their study the mean age was 31.37 ± 4.79 yrs in endometriosis group and 30.18 ± 4.37 in non-endometriosis group[9].

S.prolactin level was significantly higher (p-value 0.001) in Group-A (20.23 ± 4.99 ng/ml) as compared to Group-B (11.65 ± 4.34 ng/ml). Mirabi P et al (2019) studied prolactin concentration in various stages of endometriosis in infertile women and they found significantly higher S.prolactin level in endometriosis group (28.96 ± 3.88 ng/ml) as compared to non-endometriosis group of infertile women (17.88 ± 2.81 ng/ml)[10]. This finding is also supported by study of Barbosa JS et al (2014) in which S.prolactin level was significantly higher in women with endometriosis (661 ± 54.31 pmol/L) than infertile women without endometriosis (636.04 ± 53.29 pmol/L)[11]. Esmaeilzadeh S et al (2015) conducted a study in which they found that infertile patients with endometriosis had higher prolactin levels (23.02 ± 1.25 ng/ml) than without endometriosis (17.21 ± 1.22 ng/ml)[12]. Lima AP et al (2006) also found S.prolactin level higher in infertile women with endometriosis than without endometriosis[13].

Serum prolactin concentration was significantly higher in women with severe disease (p-value 0.001). Serum prolactin levels in patients with stage-I was 13.94 ± 2.48 ng/ml, in stage-II was 18.68 ± 2.51 ng/ml, in stage-III 22.29 ± 2.40 ng/ml and in stage-IV 24.39 ± 2.83 ng/ml.Results of our study were comparable to study done by Mirabi P et al (2019)[10] in which they concluded that infertile patients with stage III/IV endometriosis had significantly higher level of serum prolactin (31.62 ± 38.09 ng/ml) than patients with stage-I/III endometriosis (23.42 ± 34.05 ng/ml). Esmaeilzadeh S et al (2015)[12] also found higher S.prolactin concentration in severe endometriosis. They found significant relationship between serum prolactin level and stage of endometriosis. The serum prolactin level in their study in stage-I was 16.98 ± 1.29 ng/ml, 18.07 ± 1.50 ng/ml for stage-II, and 25.59 ± 1.96 ng/ml for stage III & IV. A significant relationship is found between endometriosis and hyperprolactinemia in many studies so researchers recommended that suppression of prolactin levels in patients with endometriosis can help in improving fecundity rate. We have investigated only those patients who underwent diagnostic laparoscopy, so the findings of our study cannot be generalized to the

population and further studies are required to assess role of prolactin in infertile women with endometriosis.

Conclusion

Infertile women with endometriosis have higher serum prolactin levels than infertile women without endometriosis. Serum prolactin concentration was found more in women with more advanced endometriosis. Prolactin can be a probable biomarker to detect women with endometriosis and to differentiate between women with early stage and late stage disease.

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