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S.Prolactin-Novel Marker For Predicting Endometriosis

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Abstract

Endometriosis is a benign gynaecologic pathology. It is predominantly found in women of reproductive age but is reported in adolescents and in post menopausal women receiving hormone replacement therapy. Endometriosis is mostly under-diagnosed which is due to the requirement for surgical diagnosis. New biomarkers are being studied which can be used for diagnosis of endometriosis; thus patients can be identified at an earlier stage and that too by non surgical methods.

Keywords: Endometriosis, benign pathology

Introduction

Endometriosis is defined by the presence of endometrial like tissue {glands and/or stroma}, outside the uterine cavity. Pelvic viscera and peritoneum are the most frequent sites of implantation. Pericardium, pleura, lung and brain may also be involved. Endometriosis affects 10–15% of all women of reproductive age. However, its prevalence in women experiencing pain, infertility, or both is as high as 35-50%[1]. Yet, endometriosis is under- diagnosed and associated with a 6.7 year mean latency from onset of symptoms to definitive diagnosis, which is due to the requirement for surgical diagnosis[2].

Endometriosis has many signs and symptoms and has higher chances of progression and recurrence. Various signs of endometriosis include dysmenorrhea, dyspareunia, chronic pelvic pain, abnormal uterine bleeding and infertility. Lesions identified during laparoscopy are categorized as superficial peritoneal lesions, endometriomas or deep infiltrating nodules, with high degree of individual variability in lesion colour, size, and morphology. Histopathological analysis requires the presence of at least two features for a diagnosis of endometriosis, the features being endometrial epithelium, endometrial glands, endometrial stroma, and hemosiderin filled macrophages[3].

Endometriosis is an oestrogen dependent disese. There are various theories explaining its etiopathogenesis. Retrograde menstruation (Sampson's theory), metaplastic transformation (Meyer's theory), direct transplantation from endometrium or surgery, lymphatic or hematogenous spread distant to pelvis (Halban's theory) are some of the possible theories of histogenesis of endometriosis. Retrograde menstruation, in which uterine epithelial and stromal cells are disseminated and implanted into the peritoneal cavity via the fallopian tubes, is the most accepted mechanism for the pathogenesis of endometriosis[5]. Endometriotic implants may also secrete prolactin (PRL) and possibly cause ovarian dysfunction. Women with endometriosis have reduced cellular immunity and more specifically a decreased natural killer activity in peripheral blood and in peritoneal fluid[3]. It is also well known that parameters associated with stress can significantly alter several immunological parameters, consisting of the number of cells as well as their function. PRL is

discharged in response to stress or stimuli, although its true role in response to stress is not known. As both endometriosis and hyperprolactinemia are associated with infertility it became an attractive theory to implicate raised PRL levels as the cause for infertility in women with endometriosis [4,5].

An elevated level of PRL produces anovulation because it prevents LH pulsatility and interferes with hypothalamic function through the blockage of estrogen receptors. Actions on the ovary maybe due to a decreased affinity of LH receptors in the corpus luteum and an associated decrease in the production and secretion of progesterone, resulting in not only anovulation but also suppression of follicular maturation and an inadequate corpus luteum, often termed as "short luteal phase." These have all been found to exist in infertile women with endometriosis of varying degrees[5].

Material And Methods

This is a hospital based comparative cross-sectional study done in Department of Obstetrics and Gynaecology, SMS Medical College and Hospital, Jaipur for a period of one year. It includes women (of age group 18-45 years) attending the general outpatient gynaecology clinic with chief complains of infertility and/or chronic pelvic pain who were admitted for diagnostic laparoscopy. The study population was divided into two groups: -

Case – Women with endometriosis

Control – Women without endometriosis

Laparoscopically confirmed endometriosis subjects were considered as cases and their extent of the disease was further staged according to the American Society of Reproductive Medicine (ASRM) classification; whereas the one without endometriosis on diagnostic laparoscopy were considered as controls. Results were collected and statistical analysis was done.

Observation And Results:

Table 1: Distribution of the Participants in Terms of Endometriosis (n = 220)

Endometriosis	Frequency	Percentage
Present	74	33.6%
Absent	146	66.4%
Total	**220**	**100.0%**

Table 2: Demographic Profile

AGE	Endometriosis Present	Endometriosis Absent	P-value
19-30	66(89.1%)	136(88.3%)	0.099
31-40	8(10.8%)	18(11.6%)	
RESIDENCE			
Rural	26(35.1%)	82(56.2%)	

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Urban	48(64.9%)	64(43.8%)	0.037
RELIGION			
Hindu	46(62.2%)	118(80.8%)	0.034
Muslim	28 (37.8%)	28 (19.2%)	

Table 3 : Endometriosis and distribution of Women and Control Group according to Age of Menarche

Age of Menarche	Endometriosis			
	Present	Absent	Total	P Value
≤13 Years	52 (70.3%)	146 (100.0%)	198 (90.0%)	<0.001
>13 Years	22 (29.7%)	0 (0.0%)	22 (10.0%)	
Total	**74**	**146**	**220**	

Association between Endometriosis and Age of Menarche

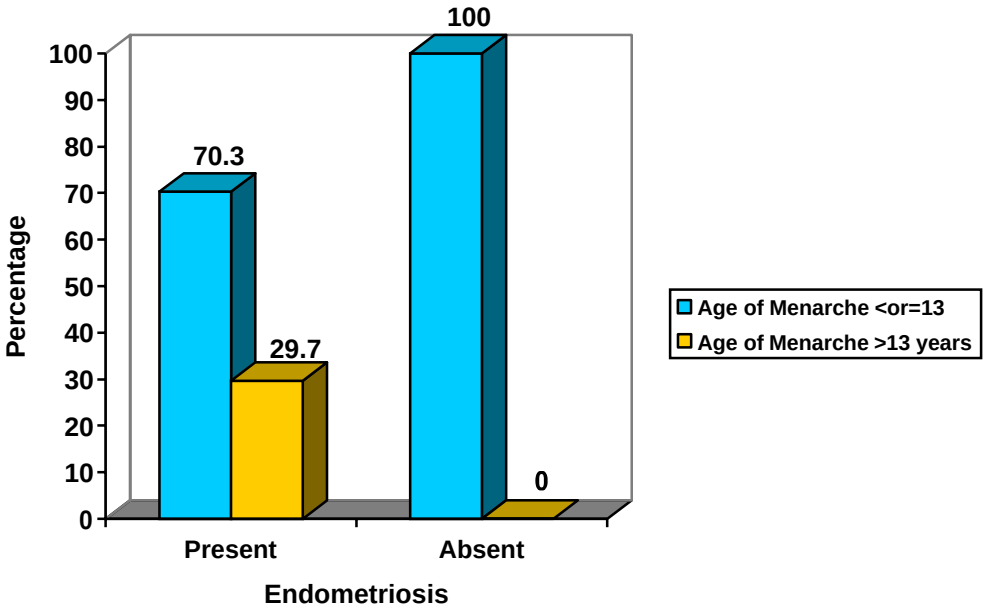

Table 4 : Distribution of the Participants in Terms of Stage of Endometriosis

Stage of Endometriosis	Frequency	Percentage

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Stage 1	8	10.8%
Stage 2	14	18.9%
Stage 3	38	51.4%
Stage 4	14	18.9%
Total	**74**	**100.0%**

Distribution of Stage of Endometriosis

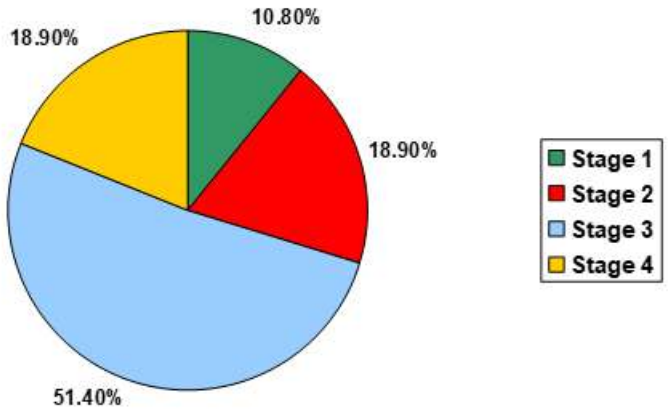

Table 5 : Distribution of Endometriosis cases and Control Group According to Serum Prolactin

S. Prolactin	Endometriosis			
	Present	**Absent**	**Total**	**P Value**
5-20 ng/mL	22 (29.7%)	114 (78.1%)	136 (61.8%)	<0.001
20-35 ng/mL	40 (54.1%)	28 (19.2%)	68 (30.9%)	
35-50 ng/mL	6 (8.1%)	2 (1.4%)	8(3.6%)	
50-65 ng/mL	2 (2.7%)	2 (1.4%)	4 (1.8%)	
65-80 ng/mL	4(5.4%)	0 (0.0%)	4 (1.8%)	
Total	**74**	**146**	**220**	

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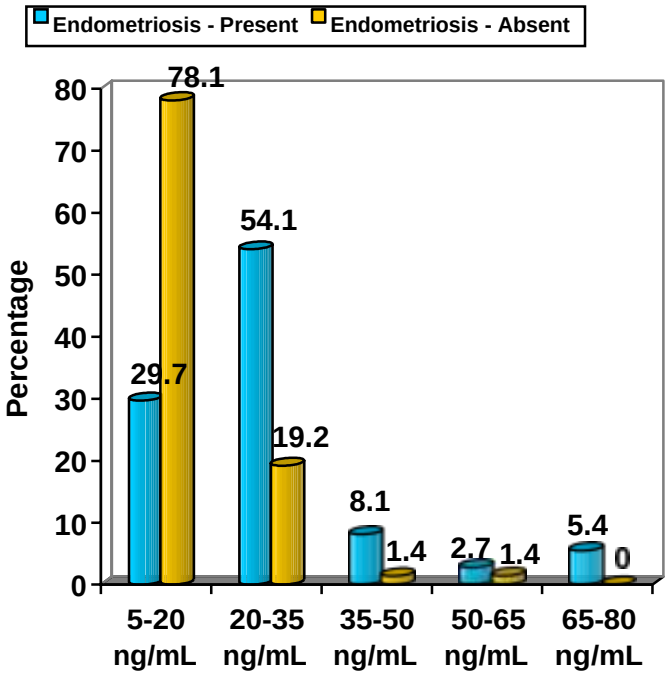
Association between Endometriosis and S.Prolactin



Discussion

In the present study, patients with endometriosis were compared to patients without endometriosis; the case group was significantly younger vs the controls (p=0.09) since most of the patients who came to OPD were in the early phase of reproductive life. According to Speroff the mean age at the time of diagnosis of endometriosis ranges between 25 and 35 years[6]. In study done by Pauwel et al; no significant difference was shown in the case and control mean age.

In this study 43.8% of the participants with Endometriosis were residing in urban area which was statistically significant. 62.2% of women with endometriosis were of Hindu religion and 37.8% were Muslim which was statistically significant (p=0.03). 70.3% women in the endometriosis group had menarche before 13 years of age which was statistically significant (p value = <0.001). A study by Kelechi E Nnoaham et al (2012)[7] represents a probability of 55% that a woman with endometriosis had earlier menarche than one without endometriosis if both were randomly chosen from a population.

Mean value of serum prolactin in endometriosis was 26.66 ± 14.58 vs 16.78 ± 6.95 in control group. Association of hyperprolactinemia with endometriosis was statistically significant (p<0.001). Similar results were obtained in a study by Esmaeilzadesh et al (2015)[8], where the mean PRL level in the endometriosis group was (23.02 ± 1.25 ng/mL) while in the controls was (17.21 ± 1.22 ng/mL). The PRL levels were significantly higher in infertile women with endometriosis than those without endometriosis (p=0.004).

In the current study of 220 women with infertility or chronic pelvic pain 33.6% had endometriosis with 10.8% in stage 1, 18.9% in stage 2, 51.4% in stage 3 and 18.9% in stage 4.Gregoriou *et al* found a direct correlation between endometriosis stages, with serum PRL concentration progressively increasing from stage I (minimal) to stage IV (severe), a pattern was also observed in the present study, in which infertile women with moderate stage to severe endometriosis

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presented significantly higher PRL concentrations compared to control group[9]. In a similar study serum PRL levels were significantly higher in infertile women with stage III- IV endometriosis (28.9 ± 2.1 ng/mL) than in healthy controls (13.2±2.1 ng/mL), but they did not detect a significant difference in PRL concentrations in peritoneal fluid or follicular fluid, between case and control groups[10]. The ability of ectopic. endometrium to secrete PRL is controversial. While the normal endometrium retains the ability to discharge prolactin in the late luteal phase. Studies on PRL levels in the peritoneal fluid show no evidence that the implants secrete prolactin. Machida *et al* reported no significant relationship between basal PRL levels and the stage of endometriosis after analyzing the samples from 70 patients with and without endometriosis[11]. Based on the data presented in some studies, infertile women with endometriosis exhibit latent hyperprolactinemia, which is more evident in infertile women who fail to, become pregnant after several therapeutic schemes. However, more studies aimed at identifying the role of PRL in infertile women with endometriosis are required.

Acien *et al* and He *et al* also found significantly higher basal PRL levels in patients with infertility and endometriosis[12]. On the contrary, other investigators however, did not find a significant difference between the groups in terms of basal PRL levels[13,14]. Both the above mentioned studies chose low sample size maybe, that's why, the results were not significant.

Conclusion

Endometriosis is a common gynaecological problem in women of reproductive age around the globe. The preponderance of evidence of the present study suggests that hyperprolactinemia does exist in infertile patients with endometriosis. However; further studies of basal PRL concentrations in various stages of endometriosis are needed to confirm this relationship.

Limitations Of Study

This study was performed in a single centre which is a tertiary referral centre .It is not representative of the whole population. More multi centric trials need to be done.

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