Research Article

Study of serum Prolactin and 17-β estradiol levels in patients with primary infertility

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Abstract

Defects of Hypothalamo-pituitary-ovarian axis are major causative factors in the etiology of primary infertility in women. Hormonal imbalances leading to disruption of H-P-O axis cause ovarian dysfunction which is the main etiological factor for primary infertility in women. The present study was conducted in the department of Biochemistry of GMC, Nagpur over a period of One and half years to assess the changes in the levels of serum Prolactin and 17-β Estradiol in women with primary infertility, to study the prevalence of hyperprolactinemia in primary infertility and to see if there is any changes in serum 17-β Estradiol levels in relation to hyperprolactinemic and normal prolactin primary infertile women.
Keywords: Infertility, Hypothalamo-pituitary-ovarian axis, Prolactin, 17-β Estradiol.

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INTRODUCTION

The estimates of prevalence and/or incidence of infertility are based on either demographic data or on health-service statistics. These sources produce diverse and inaccurate assessments. As reported by health services the incidence of infertility was calculated to be approximately 16.7%.[1] The percentage of childless marriages, voluntary or involuntary, varies considerably according to society and time period. Infertility is defined as inability of a couple to achieve conception after 1 year of unprotected coitus.[2]

Approximate prevalence of cases of primary infertility in infertile females[3]

1. Ovulatory dysfunction - 30 to 45%
2. Tubal factors - 30 to 45
3. Unexplained factors - 10 to 15%
4. Miscellaneous - 10 to 15%

Ovulation is a complex process and depends on an adequate amount of appropriate hormones at appropriate time of menstrual cycle. Anything that disrupts the hormonal regulation of female cycle may result in ovulatory dysfunction leading to an anovulation. Prolactin is a mammotropic hormone secreted by anterior pituitary and increasing amount of prolactin is accompanied by cyclic disturbances ranging from irregular menstrual bleeding or inappropriate luteal function to anovulatory periods and cessation of menses. The mechanism by which hyperprolactinemia exerts an anovulatory effect is complex. It affects initial interference with ovarian function, followed by suppressive effect at the level of cyclic center. Hyperprolactinemia leads to a failure of the positive feedback response of gonadotropin secretions induced by estrogen. Estrogens are secreted by the ovarian follicles, synthesized from cholesterol and is produced by aromatization of androgens. It is secreted as 17-β estradiol, inactivated by liver and excreted as conjugates of estrone, estradiol and estriol in urine. Since success of therapeutic measure in cases of female infertility is dependent upon the optimum serum level of gonadotropin and prolactin, it would seem appropriate to measure the circulating levels of these factors in such infertile female patients which would help in determining the prevalence of hormonal disorders in them.

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MATERIALS AND METHODS

The present study was carried out in the department of biochemistry, Government medical college, Nagpur from January 2004 to March 2005.

Selection of study subjects: 50 Primary infertility cases were selected from OBGY OPD of GMC, Nagpur. 50 normal fertile age matched controls were taken.

Inclusion criteria

1. Known patients of primary infertility in the age group 19 to 35 years
2. Age matched healthy fertile women taken as controls

Exclusion criteria

1. Patients with H/o tubal blockage or gross cervicouterine anomaly
2. Patients with H/o Tuberculosis or any other chronic illness
3. Patients with oligospermic or azospermic husband

Sample collection

Fasting blood was collected in sterile plain and Fluoride bulb under aseptic precaution with the consent of patient. Sample was allowed to stand for clotting for 25 to 30mins. Then centrifuge the sample for 10 min to separate the serum. Sample was collected in midluteal phase especially between 5 and 10 days prior to the following menstrual period.

Method of estimation

PARAMETER	METHOD OF ESTIMATION
Serum Prolactin	UBI MAGIEL™ PRL quantitative ELISA kit
Serum 17-β Estradiol	Equipar diagnostic ELISA kit

RESULTS

Table 1: Distribution of study subjects according to age

Age in years	Number of study subjects			
	Controls	Percentage (%)	Patients	Percentage (%)
≤ 20	2	4	7	14
21 to 25	31	62	23	46
26 to 30	14	28	12	24
31 to ≤ 35	3	6	8	16

Table 2: The distribution of study subjects according to duration of infertility

Duration of infertility (years)	Number of patients	Percentage (%)
1 to 3	23	46
4 to 6	18	36
7 to 10	5	10
>10	4	8

Table 3: Table showing the prolactin (PRL) levels in study subjects and controls (Values are expressed as ng/ml; Mean ± SD)

	Controls (n=50)	Infertile women 50				
		Normal PRL (n=23)	%	Increased PRL (n=27)	%	Decreased PRL (n=0)
	Mean ± SD	Mean ± SD		Mean ± SD		Mean ± SD
Prolactin level	16.36 ± 3.95	15.10 ± 4.34 (p=0.2338)	46	63.18 ± 23.49 (p 0.000)	54	Nil

The above table shows that amongst the infertile women nearly half i.e. 46% had normal PRL level; whereas more than half i.e. 54% had increased circulating PRL level.

Table 4: Studies showing mean values of 17- β estradiol (E2) in study subjects (Values of E2 are expressed as pg/ml, Mean ± SD)

Study Subjects	E2 (Mean ± SD)
Control (n=50)	72.96 ± 20.97
Patient (n=50)	63.73 ± 24.52
P value	0.0458

The above table shows the levels of serum 17- β estradiol in patients and controls. p value< 0.05- Statistically significant

Table 5: Table showing values 17- β estradiol (E2) in relation to prolactin in infertile women

Study subjects	17- β estradiol (E2)
Controls	72.96 ± 20.97
Hyperprolactinemia (n=27)	60.03 ± 25.37
P value	0.0066
Normal PRL (n=23)	67.43 ± 28.35
Hyperprolactinemia (n=27)	60.03 ± 25.37
P value	0.1721

The above table shows the occurrence of 17- β estradiol E2 in the light of prolactin levels in the infertile patients.

DISCUSSION

Infertility may severely affect the couples' psychological harmony, sexual life and social function. Examination and treatment of infertility may pose additional psychological difficulties interfere with the sexual life of couple and impose a financial burden on the family.[4] Hence it is essential to carry out appropriate investigations in appropriate patients within appropriate time. As ovulatory dysfunction leading to anovulation amounts for 30-45% of all causes of female infertility and these disorders are generally among the easily diagnosed and best treatable cause of infertility, they need to be investigated thoroughly.[3] For diagnosing this disorder it is desirable to establish the functional state of hypothalamic pituitary ovarian (H-P-O) axis. It is best done by direct measurement of serum prolactin and E2 level. Following results were obtained during the course of investigations in the present study. The mean levels of prolactin in control, infertile women with normal prolactin level and patients with increased levels are 16.36 ± 3.95, 15.10 ± 4.34 and 63.18 ± 23.49 respectively. Increased PRL level was seen in about 54% patients and normal PRL level in 46% patients. There was significant increase in PRL level in patients with increased PRL level as compared to control ($p<0.000$) while no significant change was observed in patients having normal prolactin level as compared to control. While study done by Audu Idrisa *et al*[5] found 31.7% patients had abnormal prolactin level. Kuku SF *et al*[6] observed hyperprolactinemia was the commonest hormonal abnormality in about 26.2% patients. Nokano R *et al*[7], Roumen FJ *et al*[8], Geeta Sinha *et al*[9] also studied prolactin levels in infertile females and they found increased PRL level in infertile women. The mean levels of 17-β estradiol (E2) in controls and patients were 72.96 ± 20.97 and 63.73 ± 24.52 respectively. A highly significant decrease was observed in mean values of patients as compared to control ($p=0.0458$). When the levels of 17-β estradiol were correlated with prolactin levels, a significantly reduced serum 17-β estradiol levels were obtained in Hyperprolactinemic patients compared to controls ($p= 0.0066$). But there was no significant decrease in serum 17 β estradiol levels in normal prolactin patients compared to controls ($p= 0.1721$). Increased PRL level is accompanied by cyclic disturbances ranging from irregular menstrual bleeding or inappropriate luteal function to anovulatory periods. It affects initial interference with ovarian function. It affects, the GnRH pulse generator leading to impaired LH and FSH pulsality and decreased 17-β estradiol (E2) secretion from the ovaries leading to ovulatory dystfunction.[10]

CONCLUSION

In the present study, it was observed that there was significant overall increase in mean serum prolactin values of patients as compared to the controls and a significant reduction in the level of 17-β estradiol (E2) in patients compared to controls. It was also found that serum 17-β estradiol (E2) level in hyperprolactinemic patients was decreased significantly when compared to normoprolactinemic infertility patients and normal healthy controls. Finally, there was also significantly increased PRL level in infertile women as compared to control. This indicates a definite role of prolactin in fertility of women. The hyperprolactinemia leads to a failure of positive feedback response of gonadotropin secretions induced by estrogen as the level of 17-β estradiol was decreased. We can conclude from this study that treatable endocrine abnormalities identifiable by direct hormonal assay may occur in a high proportion of female partners of infertile relationship. Considering this medical and social implications of infertility in the society and limited reproductive health resources in the developing country like India, direct hormonal evaluation should be an important part of work up of infertile females.

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