ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

TO COMPARE PROLACTIN LEVELS IN PATIENTS WITH MENSTRUAL DISTURBANCES WITH NORMAL HEALTHY FERTILE FEMALES

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ABSTRACT

Background: The female reproductive tract is controlled by complex interaction between steroid hormones, gonadotrophins and hypothalamic-pituitary-ovarian axis. A disruption in any of these processes can result in menstrual disturbances. The present study was conducted with an aim to test the hypothesis that subtle endocrinal abnormalities detected by intensive hormone evaluation are associated with menstrual disturbances. **Aim & Objective:** To compare Prolactin levels in patients with menstrual disturbances with normal healthy fertile females. **Methods:** The present study was conducted in the Department of Biochemistry. A total of 100 patients reporting to the OPD of Obstetrics and Gynaecology, were studied. Out of 100 patients, 50 patients were with a history of menstrual disturbances, 50 patients of reproductive age group with normal menstrual cycle and with proven fertility were taken as control. Routine investigations were carried out in all the patients. The Prolactin ELISA kit was used for quantitative measurement of prolactin in human serum or plasma. Serial samples were taken for estimation of prolactin. 2 samples were taken on Day 3 of cycle on two consecutive cycles. The serum plasma prolactin reference values used were: Follicular phase upto 22 ng/ml. **Result & Conclusion:** Considering together, our findings support the hypothesis that women with menstrual disturbances have subtle disturbances in the hypothalamic-pituitary-ovarian axis compared with their fertile counterparts and high prolactin levels play a significant role in the etiology of menstrual disturbances.

KEYWORDS: Menstrual disturbances, Prolactin levels, Hypothalamic-pituitary-ovarian axis, Infertility.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

INTRODUCTION

Infertility is defined as inability to conceive after at least one year of unprotected coitus. [1, 2, 3] Infertility is a personal misery and regarded as a disgrace in some communities. Infertility can result in psychological derangements, bitterness in conjugal relations, marital disharmony and feeling of inadequacy, guilt and depression. Seventy five percent perfectly normal couples will conceive within a period of one year [4]. A study [5] reported that 85% of normal couples conceive within one year and 93% within 2 years. It has been suggested that more invasive investigations should be postponed until two years have elapsed and only after two years the couple should be labelled as infertile. To find out the cause for irregular, infrequent menstrual cycles with chronic anovulation, hormonal studies need to be carried out. [6]

PROLACTIN

Prolactin is a single chain alcohol soluble polypeptide of 198 amino acids and is similar to growth hormone and placental lactogen. The glycosylated molecule accounts for about 70% of the total prolactin. The single N linked oligosaccharide mostly occurs at the 31st position in asparagine residues. It is an acidic protein with an isoelectric pH of 5.7. Prolactin molecule contains 3 disulphide bridges and reduction of these disulphide bridges will inactivate the molecule. [7] The synthesis of prolactin is done by the lactotrophs in the anterior pituitary gland and gene for its synthesis is located on chromosome 6. The estrogen and TRH are positive modulators whereas dopamine is a negative modulator of prolactin secretion. Progesterone acts as an inhibitor of prolactin synthesis. A high level of TSH stimulates prolactin secretion and causes ovulatory dysfunction. [8]

Hyperprolactinemia is a common problem in reproductive dysfunction affecting about one third of infertile women. It has been suggested that hypogonadism seen in hyperprolactinemic women is due to circulating levels of prolactin interfering with the action of the gonadotrophins at the ovarian level and impaired gonadal steroid secretion, which in turn alters positive feedback affects at the hypothalamic and pituitary levels. This leads to lack of gonadotrophin cyclicity and infertility. Prolactin can inhibit the follicular estradiol production and this result in infertility. [9]

REVIEW OF LITERATURE

Prolactin Hormone:

Prolactin is a monomeric polypeptide which is secreted by lactotropes, which are acidophilic cells in the anterior pituitary. It is secreted in episodic bursts, particularly during sleep. The secretion of prolactin is increased by stress, stimulation of nipple, exposure to oestrogens and thyrotrophin releasing hormone (TRH). Its secretion is regulated by a short negative feedback control system, hypothalamic prolactin inhibiting factor (PIF) which is probably dopamine. Its main action is on lactation. It has a suppressive effect on the pituitary-ovarian axis, so the patients who suffer from hyperprolactinemia may develop amenorrhea or oligomenorrhea due to anovulatory cycles with or without galactorrhea. Normal prolactin level is 25ng/ml. Upto 100ng/ml occurs in hypoprolactinemia and over 100ng/ml is seen in pituitary hormones. [7]

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action of the gonadotrophin at the ovarian level and impaired gonadal steroid secretion, which in turn alters positive feedback effects at the hypothalamic and pituitary levels. This leads to lack of gonadotrophin cyclicity and infertility. Another cause of infertility seen is the low estradiol production. Prolactin can inhibit the follicular estradiol production and this result in infertility. [9]

Another association between hyperprolactinemia and reproductive functions was postulated by Blackwell et al in 1990[10] that prolactin blocks the action of gonadotrophins on the ovary, inhibits production of progesterone by the granulosa cells and lead to anovulatory infertility along with various menstrual abnormalities.

Kalsum and Jalali [9] studied role of hyperprolactinemia in infertility. Study included 100 women in which 82 were hyperprolactinemic, 18 were normoprolactinemic (control). Fertile hyperprolactinemic women were 30.49% and infertile were 69.51%. Patients were interviewed to record the marital status, hormone levels and type and duration of infertility. The results show that mean serum prolactin level in normoprolactinemic patients was 313.00 ± 40.27 µIu/ml, while in hyperprolactinemia patients it was 669.18 ± 38.11 µIu/ml. Infertile hyperprolactinemic women had significantly ($p < 0.001$) raised prolactin levels. They concluded that alterations in pituitary hypothalamic axis due to any cause leads to abnormal prolactin secretion and this abnormal secretion is further associated with infertility.

Hypoestrogenemia (decreased circulating estrogen concentrations) may occur with prolactin excess. This may result in amenorrhea (a complete lack of menstrual flow or menstrual interval irregularity). If the hyperprolactinemic patient is hypoestrogenemic then medical management that brings that prolactin levels into normal range will frequently reverse the estrogen problem.

Samal et al [11] did prospective study in infertile females. The study group comprised of two hundred cases of infertility which were subjected to serum prolactin estimation and detailed work up. They found that 11% cases were with high values of prolactin levels as compared to none in control group and thus higher values in study group was found to be statistically significant. The results were that study group had serum prolactin values between 26-75 ng/ml.

Avasthi et al [12] studied the incidence of hypoprolactinemia in female infertility after excluding tubal factors and male factors and to find out its correlation with hypothyroidism. They studied 111 women attending the OPD of Gynaecology department, out of which 60% had primary infertility and 40% had secondary infertility. Most of the women were in the age group of 24-28 years in both the groups and results showed that the incidence of hyperprolactinemia, i.e. serum prolactin levels >25 ng/ml, was 46%. The mean serum prolactin levels in hyperprolactinemic women was 76.53±55.97ng/ml (range 48.3 to 200ng/ml). The incidence of hypothyroidism in hyperprolactinemic women was 25.5%. The mean serum prolactin level in hypothyroid women was 124.4 ± 64.32ng/ml. The mean serum TSH level in women with hyperprolactinemia was 9.57 ± 16.74 (range 1.05 – 86.21) mIU/ml and in hypothyroid women with hyperprolactinemia was 27.88 ± 32.57 (range 5.6-86.3) mIU/ml. This difference was statistically highly significant.

The ratio of proportions between hyperprolactinemia and hypothyroidism was 5% i.e. in every four hyperprolactinemic patients one had hypothyroidism. Thus there was a positive

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

correlation. They concluded that there was a high incidence of hyperprolactinemia in infertile women.

In women, high blood levels of prolactin often cause hypoestrogenemia with anovulatory infertility and decrease in menstruation. In some women, menstruation may disappear altogether (amenorrhea) while in others menstruation may become irregular or menstrual flow may change. [13]

AIM AND OBJECTIVE

To compare Prolactin levels in patients with menstrual disturbances with normal healthy fertile females

MATERIAL AND METHODS

The present study was conducted in the Department of Biochemistry in our hospital. A total of 100 patients reporting to the OPD of Obstetrics and Gynaecology, were studied.
Out of 100 patients, 50 patients were with a history of menstrual disturbances, 50 patients of reproductive age group with normal menstrual cycle and with proven fertility were taken as control.

A detailed history of the patients was taken in view to include all other factors of infertility (tubal factors, male factors, etc.) and a detailed history of menstrual disturbances was taken. Complete general physical examination with reference to breast development, distribution of hair and secondary sexual characters etc. was done. Informed consent was taken from every patient before including her in the study.
Routine investigations were carried out in all the patients:

Hemoglobin:	Acid haematin method using Sahli's hemoglobinometer.
TLC:	Thomas-Ziess haemocytometer with improved Neubar counting chamber.
DLC:	Studying peripheral blood film stained with Leishmann stain.
Blood sugar:	Asatoor and King Method. [14]
Blood urea:	Diacetyl Monocrome Method (DAM) method. [15]
Serum Creatinine:	Jaffe Reaction (Method of Brod and Sirota, 1948)

Urine Complete Examination

Prolactin:

The Prolactin ELISA kit was used for quantitative measurement of prolactin in human serum or plasma. [16]

Principle:

The prolactin ELISA is based on a solid phase direct sandwich ELISA method. The samples and the diluted anti-PRL-HRP conjugate are added to the wells coated with Mab to Prolactin. Prolactin in the patient's serum binds to anti- Prolactin Mab on the well and the anti-PRL-HRP then binds to Prolactin. Unbound protein and HRP conjugate are washed off by wash buffer. Upon the addition of the substrate the intensity of the colour is proportional

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

to the concentration of Prolactin in the samples. A standard curve is prepared relating colour intensity to the concentration of the Prolactin.

Content of the Kit and Reagent preparation:

1. Microwell plate: 1 microtiter plate 6 x 8 well strips coated with anti-PRL-HRP conjugate.
2. Enzyme conjugate: Anti PRL-HRP conjugate.
3. Substrate solution: TMB substrate.
4. Stop solution: contain sulphuric acid.
5. Prolactin standards: 5 standards.
6. Concentrations: 0, 5, 20, 80, 200 mIU/ml.

Sample Collection

Serial samples were taken for estimation of prolactin. 2 samples were taken on Day 3 of cycle on two consecutive cycles.

Procedure

1. 25 µl each of standard control and samples were dispensed into the microtiter wells coated with anti-PRL-HRP conjugate.
2. 100 µl of enzyme conjugate was added to each well.
3. Incubation was done for 30 minutes at 37°C.
4. Reaction solution from all the wells was aspirated.
5. Washed with 300 µl of distilled H_2O and washing was repeated by draining the water completely.
6. 100 µl of TMB substrate was added to each well.
7. It was incubated for 10 minutes at room temperature protected from light.
8. 100 µl stop solution was added to each well.
9. Absorbance of each well was read against air with ELISA reader at 450 nm within 30 minutes.

Reference values

The serum plasma prolactin reference values are:

Follicular phase upto 22 ng/ml

OBSERVATIONS

TABLE 1

Groups	No. of Patients
Control	50
Menstrual disturbances	50

The study was conducted on 100 patients attending the Outpatient Department of Obstetrics and Gynaecology. Control Group 1 comprised of 50 normally menstruating females between the age of 15-35 years Group II comprised of 50 patients of menstrual disturbances.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

TABLE 2

AGE WISE DISTRIBUTION OF STUDY AND CONTROL GROUP

Age (in years)	Menstrual Disturbances Group		Control Group	
	No. of cases	%age	No. of cases	%age
15-20	12	24%	7	14%
21-25	12	24%	19	38%
26-30	14	28%	14	28%
31-35	6	12%	10	20%
36-40	6	12%	0	0%
Total	50	100%	50	100%
Range				
Mean	25.86		25.98	
± SD	6.60		4.71	
't'	0.011			
'p'	0.09			
Significance	NS			

Table 2 shows that mean age of study group was 25.86 ± 6.60 years and of control group was 25.98 ± 4.71 years. Statistical analysis showed that there was no significant difference in age ($p > 0.05$). Hence both the groups were comparable.

TABLE 3

ROUTINE INVESTIGATIONS IN STUDY AND CONTROL GROUP

	Control			Menstrual Disturbances			't'	'p'	Sig.
	Range	Mean	± SD	Range	Mean	± SD			
Hb (gm%)	8-11.2	9.59	0.98	8.2-11.0	9.65	0.71	0.35	0.05	NS
TLC/ cumm	6500-10800	8613.40	1527.72	7600-10500	8983.0	1110.40	1.39	0.05	NS
N (%)	62-80	70.26	3.86	64-75	69.5	3.16	1.08	0.05	NS
L (%)	15-36	25.32	4.52	20-32	26.14	3.19	1.05	0.05	NS
M (%)	0-6	2.46	1.83	0-4	1.86	1.07	1.90	0.05	NS
B (%)	0-6	1.62	1.46	0-4	1.58	0.97	1.94	0.05	NS

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

In all 100 patients and 50 control, routine investigations were carried out as per Performa. Table showed that both the groups were comparable. All routine investigations were within normal range.

TABLE 4
ROUTINE INVESTIGATIONS IN STUDY AND CONTROL GROUP

	Control			Menstrual Disturbances			't'	'p'	Sig.
	Range	Mean	± SD	Range	Mean	± SD			
FBS (mg%)	70-96	85.14	6.29	68-96	84.40	7.19	0.55	0.05	NS
Urea (mg%)	20-36	28.58	4.74	20-36	29.56	4.39	1.07	0.05	NS
Creatinine (mg%)	1.0-1.6	1.22	0.20	1.0-1.8	1.22	0.20	0.00	0.05	NS

In all 100 patients and 50 control, routine investigations were carried out as per Performa. Table showed that both the groups were comparable. All routine investigations were within normal range.

TABLE 5
COMPARISON OF PROLACTIN IN MENSTRUAL DISTURBANCES AND CONTROL GROUP

Group	No. of Cases	Range (ng/ml)	Mean ± SD		't'	'p'	Sig.
Control	50	5.33-20.38	13.05	4.57	3.80	0.01	S
M. Disturbances	50	5.6-106.31	25.44	22.56			

Table 5 shows that mean values of prolactin in study group was 25.44 ± 22.56 ng/ml while that of control group was 13.05-4.57 ng/ml. Statistical analysis shows that differences in the mean values in study group was significant when compared with the control group ($p < 0.05$).

DISCUSSION

Irregular infrequent periods are quite embarrassing for women. Their periods are unpredictable, sometimes heavy and painful. Infrequent periods are also associated with infertility due to chronic anovulation.

The purpose of this study was to test the hypothesis which states that, endocrinal abnormalities detected by intensive hormone evaluation are associated with menstrual disturbances.

In the present study, study group included total of 100 patients out of which 50 patients were with the history of menstrual disturbances when normal menstrual cycle is defined as that with a length of 22 to 40 days and moderate bleeding for 3 to 7 days. 50

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

patients with same age group, normal menstrual cycles and with proven fertility were taken as control.

Age

In the present study, the mean age in menstrual disturbances group ranged between 15-40 years with a mean of 25.86 ± 6.60 years when compared with the mean age in the control group which was 15-35 years with mean of 25.98 ± 4.71 years. Both the groups were comparable in terms of age. The age group taken in present study was also comparable to the various studies done which are included in the review.

Routine Investigations:

Routine investigations like hemoglobin, TLC, DLC, blood urea, fasting blood sugar and serum creatinine were carried out in both the study groups as well as the control groups. All the routine investigations were within the normal range. All the groups were comparable in terms of the routine investigations.

Body Mass Index (BMI)

Body Mass Index (BMI) was calculated in all the 100 cases. Maximum patients fell in the normal range 19-24.9 kg/m^2. Mean value of BMI in the menstrual disturbances group was 23.42 ± 2.25 kg/m^2 while in control group mean was 22.90 ± 1.83 kg/m^2. Statistical analysis showed that BMI values were non-significant in study groups as compared to control groups.

PROLACTIN

In humans, prolactin secretion is mainly related to induction of puberty, menarche, breast development, pregnancy and lactation. But now its role in gonadal dysfunction is very well established. Hyperprolactinemia is an extremely common disorder, especially among women of reproductive age group. [17]

Elevated levels of prolactin interfere with the action of gonadotrophins at the ovarian level or they lead to low estradiol production which ultimately lead to infertility. [18]

Any alteration in pituitary-hypothalamic axis due to any cause contributes to abnormal prolactin secretion which further affects gonadotrophin levels and lead to infertility and menstrual disturbances.

Hyperprolactinemia is the most common clinical hypothalamic hypophysis disorder. Amenorrhea and anovulation are the most usual clinical findings but milder alterations of gonadal functions as oligomenorrhea or luteal phase defects are also seen. Galactorrhea is commonly associated with elevated levels of prolactin. The use of many drugs can be associated with hyperprolactinemia but the most common causes are idiopathic hyperprolactinemia and hypophysis secreting adenoma. [19]

Comparison of Prolactin levels in menstrual disturbances by various authors

Author	Menstrual Disturbance Group	Control Group
Murray et al (2000)	14.2 ± 6.7 ng/ml, S	10.5 ± 3.5 ng/ml, S
Mancini (2008)	18.85 ± 9.35 ng/ml, S	10.84 ± 3.33 ng/ml, S
Anwar and Nadir (2008)	> 20 ng/ml, S	< 20 ng/ml, S
Present study (2009)	25.44 ± 22.55ng/ml, S	13.05 ± 4.57ng/ml, S

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

Murray et al [7] investigated role of prolactin levels in menstrual irregularities. They concluded that it has suppressive effect on pituitary ovarian axis so the patient who suffers from hyperprolectinemia may develop amenorrhea or oligomenorrhea due to anovulatory cycles with or without galactorrhea.

Mancini [13] showed that in women, high blood levels of prolactin often cause hypoestrogenemia with anovulatory infertility and decrease in menstruation. In some women, menstruation may disappear altogether (amenorrhea) while in others menstruation may become irregular or menstrual flow may change.

Anwar and Nadir [6] worked to find role of pituitary gonadotrophic hormones i.e. FSH, LH, TSH and PRL levels in women with oligomenorrhea and amenorrhea. Their conclusion was that hormonal assays are mandatory in the evaluation of women with oligomenorrhea, amenorrhea and chronic anovulatory infertility for finding out the cause and explaining the prognosis of the disease to the patient.

The present study was performed to investigate the role of prolactin hormone in menstrual disturbances. Prolactin levels were measured in females suffering from menstrual disturbances to see the incidence of hyperprolactinemia in them. In the study group the range was between 5.60 – 106.31 ng/ml with the mean of 25.44 ± 22.56 ng/ml while in control group it was ranged between 5.33 – 20.38 ng/ml with mean of 13.05 ± 4.57 ng/ml. On comparison the difference was statistically significant. So our study emphasize on the fact that hyperprolactinemia is associated with menstrual disturbances.

SUMMARY

The female reproductive tract is controlled by complex interaction between steroid hormones, gonadotrophins and hypothalamic-pituitary-ovarian axis. A disruption in any of these processes can result in menstrual disturbances.

The present study was conducted with an aim to test the hypothesis that subtle endocrinal abnormalities detected by intensive hormone evaluation are associated with menstrual disturbances.

The study was carried out in our hospital. Total 100 patients were taken. Out of 100, 50 patients were with a history of menstrual disturbances. Control included 50 patients, within reproductive age group with normal menstrual cycle and with proven fertility.

1. The mean age of study group i.e. menstrual disturbances group was 25.86 ± 6.60 years respectively. Mean age of control group was 25.98 ± 4.71 years. Both the groups were comparable with control on the basis of age.
2. Routine investigations like Hb, TLC, DLC, blood urea, serum creatinine and fasting blood sugar were carried out in all the three groups. All the investigations were within normal range and comparable in three groups.
3. Serum prolactin levels were measured. Mean level of prolactin in menstrual disturbances group was 25.44 ± 22.56 ng/ml. In control group mean level was 13.05 ± 4.57 ng/ml. On comparison it was found that prolactin levels were significantly elevated in study group.

It is concluded from the present study that elevated prolactin levels are associated with menstrual disturbances.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

Conclusion:

Considering together, our findings support the hypothesis that women with menstrual disturbances have subtle disturbances in the hypothalmic-pituitary-ovarian axis compared with their fertile counterparts and a high prolactin levels play a significant role in the etiology of menstrual disturbances.

BIBLIOGRAPHY

1. Hammond MG. Evaluation of the infertile couple. Obstetric and Gynaecology clinics of North America 1987; 14(4): 821.
2. Jaffe SH and Jewelewics R. The basic infertility investigation. Fertel Steril 1991; 56: 599-613.
3. Evers JL: Female subfertility. Lancet 2002; 360:151-159.
4. Southam AL. What to do with the normal infertile couple. Fertile Steril 1960; 11: 543.
5. Guttmacher F. Factors affecting normal expectany of conception. J American Medical Association 1956; 161: 856.
6. Anwar S and Nadir S. Pituitary gonadotrophic hormones in women with oligo/amenorrhoea. J Ayub Med Coll Abottabad 2008; 20(3): 38-42.
7. Murray RK, Granner DK, Mayer PA and Rodwill VW. Pituitary and hypothalmic hormones Quoted in Harpes's Biochemistry 2000, 25th Edition, p 550-559.
8. Padubidri VG and Daftary SN: Physiology. In: Shaw's textbook of Gynaecology, 13th ed. New Delhi:Elsevier 2004:38-47.
9. Kalsum A and Jalali S. Role of hyperprolactenemia in infertility. Pakistan J Med Res 2002; 41(3): 18.
10. Blackwell ER, Hammond RK, Knochenhaver SE. Prolactin disorders in infertility, Machele M Seibel. "Infertility – A comprehensive text" 11. Edition 1990: 155-170, USA, Appleton and Large publications.
11. Samal S, Agarwal P and Gupta U. Evaluation of symtomatology in hyperprolactenemic infertile women. J Obstet Gynecol Ind 2002; 52(2): 76-80.
12. Avasthi K, Kaur J, Gupta S and Narang PA. Hyperprolactenemia and its correlation with hypothyroidism in infertile women. J Obstet. Gynecol India 2006; 56(1): 68-71.
13. Mancini T. Hyperprolactenimia and Prolactinmonas. Endocrinology and Metabolism Clinic of North America 2008. 37: 67.
14. Asatoor AM and King EJ: Biochemistry journal 1954; 65: xliv.
15. Marsh WH, Fingerhect B and Miller H. Clinical chemistry. 1965; 11: 624.
16. Shome B and Parlow AF. J Clin Endocr Metab 1974; 39: 199-202.
17. Corenblum B. Disorders of prolactin secretion. Eds. LJ Copeland JF, Jarrell JA, McGreger. Textbook of Gynaecology. Philadelphia Pennseylarea WB Saunders Company 1993: 447-467.
18. Uilenbrock J, Th J and Lenden RU. Effect of prolactin on follicular estradiol production in the rat. J Endocrinol 1984; 102: 245-250.
19. Rosato F and Garofalo P. Hyperprolactinemia: from diagnosis to treatment. Menerver Pediatr 2002; 54(6): 547-52.