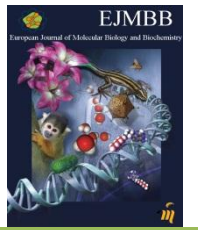
e - ISSN - 2348-2206
Print ISSN - 2348-2192

European Journal of Molecular Biology and Biochemistry

Journal homepage: www.mcmed.us/journal/ejmbb



CORRELATION OF FSH, LH AND PROLACTIN WITH INFERTILITY IN REPRODUCTIVE AGE GROUP WOMEN

Santosh Fupare*[1], Rajesh K. Jambhulkar[2], Archana Tale[2]

[1]Department of Biochemistry, Seth G. S. Medical College and KEM Hospital, Mumbai, Maharashtra, India.
[2]Department of Biochemistry, Shri. V.N. Government Medical College, Yavatmal, Maharashtra, India.

Article Info
Received 02/09/2015
Revised 16/10/2015
Accepted 02/11/2015

Key words:- Infertility, FSH, LH, Prolactin, Chemiluminescence, etc.

ABSTRACT
The infertility problem is more common phenomenon among the women now days and has increased over past 30 years. The present study was carried out to correlate FSH, LH and prolactin with infertility in the reproductive age group of women. The aim of this research work was to correlate FSH, LH and prolactin with infertility in the reproductive age group of women. Total 120 infertile women, and 80 normal fertile women volunteers were selected on OPD basis between age group of 19 to 45 years. Out of 120 infertile women, 80 were of primary infertility and 40 of secondary infertility. They were screened for FSH, LH and prolactin status by Chemiluminescence Immunoassay (CLIA). Prolactin is significantly high in primary infertility as compared to secondary infertility. LH and FSH values were low in infertile as compared to fertile, but among primary and secondary infertility their values not differ. Hyperprolactinemia may result in menstrual disorders. Oligomenorrhoea was most common in infertile women. Hyperprolactinemia patients exhibit ovulatory failure. Hence, assessment of serum prolactin levels is mandatory in the work up of all infertile women, especially those presenting with menstrual irregularities. So the basic approach should be to identify those individuals who have hyperprolactinemia because they are at greatest risk for the development of infertility. So FSH, LH and Prolactin screening of all females of early reproductive age group should be done so as to detect subclinical hormonal problem and to prevent infertility risk.

INTRODUCTION

Hormonal disorders of female reproductive system are comprised of a number of problems resulting from dysfunction of hypo-thalamic-pituitary ovarian axis. These relatively common disorders often lead to infertility [1].

Parenthood is undeniably one of the most universally desired goals in adulthood, and most people have life plans that include children. However, not all couples who desire a pregnancy will achieve one spontaneously and a proportion of couples will need medical help to resolve underlying fertility problems. Infertility has been recognized as a public health issue worldwide [2].

Many people may be infertile during their reproductive years. They may be unaware of this infertility. Many parameters are outlined for the cause of infertility like age, lifestyle and physical problems etc.

The infertility problem is more common phenomenon among the women now days and has increased over past 30 years [3].

The prevalence of infertility is estimated to be between 12 and 14%. It thus represents a common condition, with important medical, economic and psychological implication [4]. Proper evaluation of these disorders involves a multidimensional diagnostic approach.

Corresponding Author

Santosh Fupare
Email: - drsantoshfupare@rediffmail.com

Despite the fact that infertility is common in both men and women, it differs from life threatening diseases including cancer or AIDS, so no one worries about the possibility that he or she may be infertile or makes an effort to prevent infertility. The reason for this may be that, even if the individual is infertile, various organs of the cardiovascular system, alimentary system, etc., which are important for the health and life sustaining of the individual are normal and cause no problems in daily living activities. Therefore, individual patients generally do not recognize abnormalities of the reproductive system until they marry and attempt to conceive a child [5].

Hyperprolactinemia adversely affects the fertility. This disorder has been implicated in menstrual and ovulatory dysfunctions like amenorrhea, oligomenorrhoea, anovulation, inadequate corpus luteal phase and galactorrhea [6]. Estimation of serum prolactin levels is recommended in women with unexplained infertility, any menstrual irregularity with or without hirsutism, galactorrhoea with or without amenorrhea, luteal phase defects anovulation, an ovulatory bleeding, and delayed puberty. Apart from these groups of women, infertile women with regular menses also may have hyperproplactinemia [7].

Pituitary hormones such as TSH, prolactin or growth hormone may act synergistically with FSH and LH to enhance the entry of non-growing follicles into the growth phase [8]. Morphological changes observed in the follicles in hypothyroidism can be a consequence of higher prolactin production that may block both secretion and action of gonadotropins [9]. Adequate thyroid supplementation also restores prolactin levels as well and normalizes ovulatory function [10]. Clinical and experimental studies have suggested a close relationship between the hypothalamic-pituitary-thyroid axis and the hypothalamic-pituitary-ovarian axis

FSH stimulates follicle development in the ovaries and is often used as a gauge of ovarian function. Elevated FSH level indicate poor follicle development and consequently, an ovulatory cycles. Reduced levels of FSH may indicate hyperprolactinaemia [11].

LH triggers the release of the ovum from the ovary – the LH surge at around day 12 leads to ovulation within 48 hours. Elevated LH levels can indicate ovarian dysfunction. Reduced levels of LH may indicate hyperprolactinaemia [11].

The aim of our study is to correlate FSH, LH and Prolactin with female infertility.

AIM AND OBJECTIVES

The aim of this research work was to correlate FSH, LH and Prolactin with infertility in the reproductive age group of women.

Specific objectives are

1. To estimate serum FSH, LH and Prolactin level in infertile women
2. To estimate serum FSH, LH and Prolactin level in normal healthy control
3. Comparison of FSH, LH and Prolactin between infertile women and normal healthy control
4. To find out the correlation FSH, LH and Prolactin with infertility in the reproductive age group of women.

MATERIAL AND METHODS

Study design - Cross sectional Study

Time period – 2010-2012

Institute – department of Biochemistry, Government Medical College, Aurangabad

Age group- 19-45 years

After written and informed consent, total 120 infertile women, and 80 normal fertile women volunteers were selected on OPD basis between age group of 19 to 45 years. Out of 120 infertile women, 80 were of primary infertility and 40 of secondary infertility.

Participants were selected on the basis of detailed history, clinical examination and laboratory investigations. Detailed history of participants including age, menstrual history, obstetric history, history of any medications, addictions, was taken.

Inclusion criteria

1. Infertile women age between 19 to 45 years.
2. Normal fertile women age between 19 to 45 years.

Exclusion criteria

1. Male factor infertility.
2. Patient who received medication that could alter TFT. (amiodarone an phenytoin excluding β- blockers, heparin & dopamine)
3. Amongst the female factors were tubal factor, any congenital anomaly of the urogenital tract, or any obvious organic lesion.
4. Any history of thyroid disease or previous thyroid surgery.

Biochemical investigations

After written informed consent, 12 hour fasting venous blood samples were collected from all participants in there early follicular phase of menstrual cycle i.e. between day 3^{th} to 5^{th} in plane bulbs. Serum was separated after 1 hour by centrifugation at 3000 rpm for 10 minutes, and was tested for following parameters.

- Serum FSH
- Serum LH
- Serum Prolactin

Method

Quantitative estimation of all hormones done by Chemiluminescence Immunoassay (CLIA) using Acculite CLIA microwells.

Assay kits from Monobind INC., Lake Forest, CA 92630, USA.

RESULT

Regular menstrual cycle was observed in 30 participants in (Group IA) primary infertile women (37.5%) and14 participants in (Group IB) secondary infertile women (35%). 66 participants in (Group II) control (82.5%). Overall 110 participants out of 200i.e(55%).

Oligomenorrhoea was observed in 36 participants in (Group IA) primary infertile women (45%) and 20 participants in (Group IB) secondary infertile women (50%). 14 participants in (Group II) control (17.5%). Overall 70 participants out of 200i.e (35%).

Amenorrhoea was observed in 14 participants in (Group IA) primary infertile women (17.5%) and 6 participants in (Group IB) secondary infertile women (15%). Amenorrhoea not observed in (Group II) control.

Overall 20 participants out of 200 i.e. (10%) Menstrual irregularity found in 74.4% of infertile women &17.5% of control. Oligomenorrhoea is most common in infertile women 46.6%.

Mean level of Prolactin is increased in infertile women as compared to control, the difference is highly significant (P< 0.001). Mean level of Prolactin is increased in primary infertile women as compared to secondary infertile women, the difference is statistically significant (P=0.02).

Mean levels of LH & FSH is decreased in infertile group as compared to control the difference is highly significant (P< 0.001). Mean level of LH is increased in secondary infertile women as compared to primary infertile women, the difference is statistically significant (P< 0.002).

Fig 1. Graphical comparison of menstrual pattern

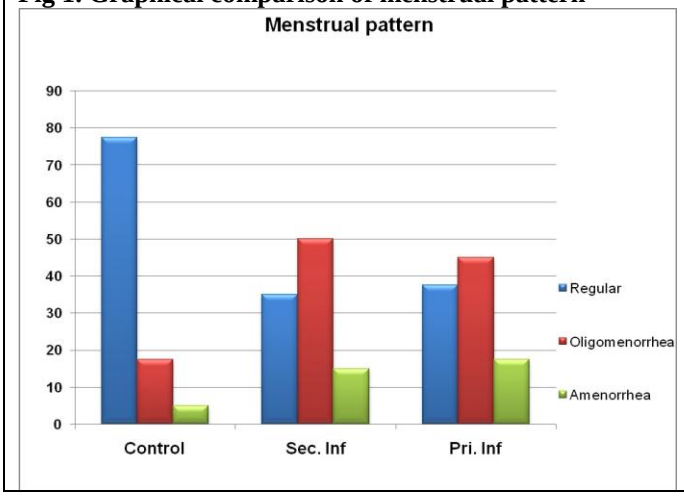


Fig 2. Serum Prolactin, LH And FSH

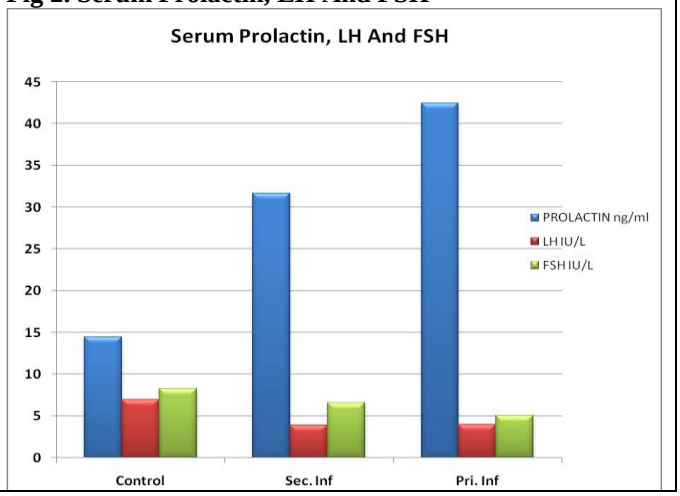


Table 1. Showing number of study subjects and their groups

Group	Subjects	Number (n)
I	Infertile women (cases)	120
II	Normal fertile women (control)	80

Table 2. Showing number of subgroups in group I

Group	Subjects	Number (n)
IA	Primary infertile women	80
IB	Secondary infertile women	40

Table 3. The mean age distribution of subjects

Variable	Group IA n= 80	Group IBn= 40	Group II (Control) n= 80
Age	23.525 ± 2.48	27.575 ± 1.94	27 ± 2.12

Table 4. Menstrual pattern in study groups

Parameter	Group IA n=80	Group IB n=40	Group II n=80	Total
Regular	30	14	66	110
Oligomenorrhoea	36	20	14	70
Amenorrhoea	14	6	0	20
Total	80	40	80	200

Table 5. Prolactin, LH & FSH in Cases and Controls

Parameter	Group IA n=80	Group IB n=40	Group II Control n=80	P value
PRL (2 - 25ng/ml)	42.47 ± 23.27	31.66 ± 24.68	14.46 ± 6.18	< **0.001***
LH (8 - 20IU/L)	5.03 ± 2.53	6.53 ± 2.66	8.27 ± 2.03	< **0.001***
FSH (8 - 20IU/L)	3.98 ± 2.47	3.9 ± 2.57	6.98 ± 1.85	< **0.001***

Table 7. Hyperprolactinemia in study groups

Parameter	Control	Primary Infertility	Sec. Infertility
Hyperprolactinemia	6	44	10

Serum prolactin levels > 25ng/ml.(Ref. range: 2 – 25) were observed in 6/80 participants in control (7.5%), 44/80 participants in primary infertile (55%) and 10/40 participants in sec. infertile (25%)

DISCUSSION

The current study was designed to correlate FSH, LH and prolactin with infertility in reproductive age group women.. The individuals were divided in 2 groups according to fertility i.e. Group I Infertile women (cases), Group II Normal healthy fertile women (controls); Cases are further sub classified as Group IA (Primary infertile women) and Group IB (secondary infertile women).

The increase in prolactin secretion can be physiological e.g. during pregnancy and lactation or pathological due to hypothalamic and pituitary diseases, or it can be iatrogenic. Hyperprolactinemia induces suppression of the hypothalamic-pituitary-gonadal axis and resistance of the ovary to gonadotropin action, which results in amenorrhea and lack of ovulation.

Menstrual pattern

In our study menstrual abnormalities were detected in about 74.2% of the infertile cases as compared to control (22.5%) and the percentage of menstrual abnormality presented by the infertile group was Oligomenorrhoea (46%). In this study 73% of hypothyroid cases had menstrual disturbances, out of which 63% had Oligomenorrhoea.

Joshi et al [12] found menstrual irregularities in 68% of hypothyroid women compared to 17% in healthy controls. Likewise, study revealed that 62.5 % of hypothyroid cases had menstrual disturbances. Kumkum *et al*, had reported the menstrual abnormality to be 57.6% in their study. Oligomenorrhoea was observed in (50%) [6]. In the study done by Krasses *et al*, the prevalence of menstrual irregularities (mainly Oligomenorrhoea) reached 23% among 171 hypothyroid patients, while being only 8% in 214 controls ($p<0.05$) [7].

Serum Prolactin

In this study higher occurrence of hyperprolactinemia (45%) was seen in the infertile group as compared to control (7.5%). Prevalence of hyperprolactinemia was 55% and 25% in primary and secondary infertile women respectively. Kumkum *et al* in their study involving 111 patients, 67 had primary infertility and 44 secondary infertility. Most of the women were in the age group of 24-28 years in both the groups.

The prevalence of hyperprolactinemia was 46% in their study, which is in agreement with the findings of our study [13].

In study hyperprolactinemia (41%) was seen in the infertile group as compared to the controls (15%).

Where as in the [14] prevalence of hyperprolactinemia was 43% and 21% in primary and secondary infertility respectively. The prevalence of hyperprolactinemia to be 41% in their study of 100 infertile women [15].

In our study and all above studies, there is high prevalence of hyperprolactinemia in infertile women, in that primary infertility has higher prevalence than secondary infertility.

Causes of infertility in hyperprolactinemia

Hyperprolactinemia inhibits follicle growth and maturation and steroidogenesis at several levels:

- At hypothalamus level, suppressing together with a consequent increased secretion of dopamine and gonadotrophin releasing hormone.
- At the ovarian level directly interfering with LH induced steroidogenesis and production of androgen in theca cells of internal follicle.
- In the follicle granulosa cells suppressing synthesis of estrogen by inhibiting FSH induced aromatase enzyme activities. Hypoestrogenaemia causes a reduced mitosis and differentiation of follicle granulose cells as well as reduction of steroidogenesis potential in corpus luteum due to inadequate prepared follicle.

According to Thorner and Besser it has been suggested that hypogonadism seen in hyperprolactinemic women is due to the high circulating levels of prolactin interfering with the action of the gonadotrophins at the ovarian level and impairing normal gonadal steroid secretion, which in turn alters positive feedback effects at the hypothalamic and pituitary levels. This leads to lack of gonadotrophincyclicity and to infertility [16].

LH and FSH

In our study serum LH & FSH was decreased in infertile women as compared to control, the differences

among three groups being highly significant (P< 0.001). LH & FSH both are negatively correlated with prolactin.

K. Mohan and Mazher Sultana in their study of 70 women, found lower level of serum FSH in infertile women were when compared to control groups, difference being statistically significant (P<0.001). Serum LH concentration was lower in the infertile group than in the control group(P<0.001) [17].

Azima Kalsum, SaminaJalali in their study shows a significant decrease in serum LH in follicular, ovulatory and luteal phase in hyperprolactinemic women having primary and secondary infertility. Significantly (P<0.05) low serum FSH levels were observed in ovulatory phase in women reported with primary infertility. Similarly significant (P<0.05) decrease in serum FSH in luteal phase in hyperprolactinemic women reported with secondary infertility was observed [18].

Yamaguchi *et al*, found decreased LH secretion in nocturnal hyperprolactinemic women [19].

Mc Neilly A.S showed similar association between increased level of prolactin and a reduction in both LH and FSH during infertility in women with pathological hyperprolactinemia [20].

From the present study we observed proportional increase in TSH and serum Prolactin in relation with decreasing T3, T4, LH and FSH in infertile women. There was significant positive correlation of Prolactin with TSH. LH & FSH were decreased with increasing Prolactin.

Hyperprolactinemia resulting from longstanding primary hypothyroidism has been implicated in ovulatory dysfunctions ranging from inadequate corpus luteal progesterone secretion when mildly elevated, to oligomenorrhoea or amenorrhea when circulating prolactin levels are high. Amenorrhea occurs in hypothyroidism due to hyperprolactinemia resulting from a defect in the positive feedback of estrogen on LH, and because of LH and FSH suppression. Our study revealed a significant association between abnormal menstrual patterns, with hyperprolactinemia & hypothyroidism in the infertile group (p<0.001).

For these reasons, prolactin is commonly-ordered clinical tests in evaluating infertile women.

SUMMARY AND CONCLUSION

The present study was carried out in 200 women classified according to fertility in normal fertile women (control), primary infertile women and secondary infertile women. The concept behind our work was to correlate thyroid hormones with infertility.

Prolactin is significantly high in primary infertility as compared to secondary infertility. LH and FSH values were low in infertile as compared to fertile, but among primary and secondary infertility their values not differ.

Hyperprolactinemia may result in menstrual disorders. Oligomenorrhoea was most common in infertile women. Hyperprolactinemia patients exhibit ovulatory failure. Hence, assessment of serum prolactin levels is mandatory in the work up of all infertile women, especially those presenting with menstrual irregularities. Although hyperprolactinemia causes infertility, the most fundamental fact is that, not all infertile women are hyperprolactinemic. So the basic approach should be to identify those individuals who have hyperprolactinemia because they are at greatest risk for the development of infertility. So FSH, LH and Prolactin screening of all females of early reproductive age group should be done so as to detect subclinical hormonal problem and to prevent infertility risk.

ACKNOWLEDGMENT

None.

CONFLICT OF INTEREST

No interest

REFERENCES

1. Goswami B, Patel S, Chaterjee M, Koner BC, Saxena A. (2009). Correlation of prolactin and thyroid hormone concentration with menstrual patterns in infertile women. *J ReprodInfertil*, 10(3), 207-12.
2. Jacky B, Laura B, John A, Collins and Karl GN. (2007). International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. *Human Reproduction*, 22(6), 1506–1512,
3. Stephen EH, Chandra A. (2000). Use of infertility services in the United States: 1995. *Fam PlannPerspect*, 32, 132.
4. Nasima A, Sufi AH. (2009). Sub-clinical hypothyroidism and hyperprolactinemia in infertile women: Bangladesh perspective after universal salt iodination. *The Internet Journal of Endocrinology*, 5(1), 8.
5. Harumi K. (2009). Epidemiology of Infertility and Recurrent Pregnancy Loss in Society with Fewer Children. *JMAJ*, 52(1), 23–28.
6. McNeilly AS, Anna G, Julie J. (1982). Evidence for direct inhibition of ovarian function byProlactin. *J Reprod Fert*, 65, 559-569.
7. Amballi AA, Dada OA, Adeleye AO and Jide S. (2007). Evaluation of the determination of reference ranges for reproductive hormones (prolactin, FSH, LH, andtestosterone) using enzyme immuno assay method. *Scientific Research and Essay*, 2(4), 135-138.
8. Micińsk P, Wielgus E, Wojcieszyn M, Pawlicki K. (2006). Abnormal ovarian reserve test reflects thyroid dysfunction. *Pol J Gyn Invest*, 9(1), 30-4.
9. Armada Dias L, Carvalho JJ, Breitenbach MM, Franci CR, Moura EG. (2001). Is the infertility in hypothy-roidism mainly due to ovarian or pituitary functional changes? *Braz J Med Biol Res*, 34(9), 1209-15.

10. Stoffer SS, McKeel DW, Randall RV, Laws ER. (1981). Pituitary prolactin cell hyperplasia with autono-mous prolactin secretion and primary hypothy-roidism. *FertilSteril*, 36(5), 682-5.
11. Givens JR, Kohler PO, John Wiley & Sons. (1986). Ovarian Disorders. Clinical Endocrinology, New York, 303 – 312.
12. Bals-Pratsch CH, *et al*. (1997). Episodic variations of prolactin, thyroid-stimulating,hormone, luteinizing hormone, melatonin and cortisol ininfertile women with subclinical hypothyroidism. *Human Reproduction*, 12(5), 896–904.
13. Kumkum A, Kaur J, Gupta S, Narang PA. (2005). Hyperprolactinemia and its correlation with hypothyroidism in infertile woman. *Obstetrics and Gynecology of India*, 56, 68-71.
14. Akhter N, Hassan SA. (2009). Sub-clinical hypothyroidism and hyperprolactinemia in infertile women: Bangladesh perspective after universal salt iodination The Internet *Journal of Endocrinology*, 5(1), 67.
15. Prathibha D, Govardhani M, Krishna PT. (1994). Prolactin levels in infertility and bromocriptine therapy in hyperprolactinaemia. *J Indian Med Assoc*, 92, 397-99.
16. Thorner MO and Besser GM. (1978). Recent advances in Endocrinology and Metabolism.1st ed. Churchill Livingstone, Edinburg, 6-8.
17. Mohan K and Mazher Sultana. (2008). Follicle Stimulating Hormone, Luteinizing Hormone and Prolactin Levels in Infertile Women in North Chennai, Tamilnadu. *J. B io s c i. Re s*, 1(4), 279-284.
18. AzimaKalsum, SaminaJalali. (2002). Role of hyperprolactinemia in fertility. *PJM*, 41, 3-15.
19. Yamaguchi M, Aono T, Koike K, Nishikawa Y, Ikegami H, Miyake A and Tanizawa O. (1991). Effect of nocturnal hyperprolactinemia on ovarian luteal function and galactorrhea. *Eur. J. Obstet.Gynecol*, 39, 187-191.
20. McNeilly AS. (1987). Prolactin and the control of gonadotrophin secretion. *J. Endocrinol*, 115, 1-5.