Role of Prolactin and β-hCG in Female Infertility

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Abstract

The World Health Organization (WHO) describes infertility as a disability for couples in childbirth to attain pregnancy within 12 months of daily sexual intercourse. Infertility affects 13–20 per cent of couples worldwide, regardless of race or ethnicity. Human chorionic gonadotropin (hCG), also known as the "pregnancy hormone," plays a significant role in human reproduction. The present study was conducted in the departments of biochemistry and dept. of obstetrics and gynaecology. The study was conducted on two groups of 40 infertile Females and 40 healthy controls. Blood sample was collected for the estimation of prolactin and hCG was assessed by dry chemistry analyzer. Serum prolactin levels in infertile females is 33.96±11.46 and hCG levels was86.38±12.45 which was higher in infertile female as compare to healthy control with a p value of<0.05. Present study concludes that hyperprolactinemia is a major contributing hormonal factor in infertility among infertile women and, as such, prolactin and hCG should be measured in infertile women.

Keywords: *Prolactin, female infertility, hCG.*

Introduction

The reproductive years of women begin when she starts her menstrual cycle during puberty (about 13 years of age, and the capacity to have a child typically ends about age (45) years, although it may be possible for a woman to become pregnant before her cycles end with menopause (about 51 years of age)[1]. Already born girl bears around (400000) immature eggs (oocytes) in her body. These are stored in small, fluid-filled sacs, called follicles, in her ovaries. Upon reaching her reproductive years, she begins to have one egg (or, less generally, more than one) monthly, which can join a male mobile sperm cell during fertilization and become pregnant[2].

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The production and release of the egg is largely dependent on hormone balance (chemicals that signal the body organs to perform a particular task). Some of these hormones are produced in the ovaries, while others are derived from the two brain glands, the hypothalamus and the pituitary[3]. Primary infertility is a term that describes a pair who has never been able to conceive through unprotected sex after a minimum of one year of attempting to do so. Primary infertility causes include a wide array of both physical and emotional factors[4]. Infertility is described as the failure of a couple to achieve conception after one year of unprotected and adequately timed intercourse (regardless of cause) [5]. It may be primary i.e. if a couple never conceived following cohabitation and exposure to sexual activity over a two-year span or secondary infertility i.e. if a couple had previously achieved pregnancy but frequent unprotected sexual intercourse did not result in a second pregnancy[6]. Human infertility is a complicated issue that has various implications depending on the context of society and culture, gender, lifestyle, the sexual history of the people it affects. Infertility is a major problem for

public health, partially due to its importance in etiology as well as its difficulty in preventing, diagnosing, and treating it[6]. Although some find infertility primarily a woman's problem, men also contribute to it and are also affected[7]. Essentially, infertility is graded into two primary infertility and secondary infertility. Predominant infertility in a couple who have never had a child is infertility. Secondary infertility means the inability to conceive following a previous pregnancy. Infertility can be caused by male or female infection, Infertility is often perceived as a predominantly female disorder, although male-factor infertility is equally prevalent, and half of the infertile couples fail to reproduce due to man fertility problems. Prolactin (PRL) is a 198 polypeptide amino acid hormone secreted from the anterior pituitary and synthesized by lactotroph cells. It weighs 23 kDa and many factors affect its secretion including stress, sleep, pregnancy, food ingestion, and stimulation of the chest wall (trauma, or pain). Prolactin plays an important role in controlling reproductive functions. Although it's level increase beyond normal (hyperprolactinemia) can be either physiological, pathological, or idiopathic, its clinical manifestations can vary from extreme to none [8]. Endometrial cells were found to have prolactin receptors. Endometrial prolactin secretion helps to preserve endometrial receptivity and has been shown to provide an ideal environment for implanting blastocyst transferred during periods of in-vitro fertilization (IVF). A sufficiently high level of prolactin may inhibit the proliferation of luteinizing granulosa cells, and may also interfere with the function of the corpus luteum resulting in luteal phase defects as well as irregular implantation and embryo growth. Specific studies have shown the presence of a state of hyperprolactinemia during cycles of IVF/Intra cytoplasmic Sperm Injection (ICSI)[9,10,11]. In the early stages of pregnancy, hCG is luteotropic, preserving progesterone development and endometrial support. In maternal semen, hCG can be detected eight days after ovulation[12] and in blastocysts as early as seven days after fertilization [13]. HCG levels in the maternal blood steadily rise in early pregnancy until peak levels are reached at seven to nine weeks.[14] They progressively decrease until about 20 weeks when plasma levels remain relatively small and steady until the end. Episodic fluctuation in maternal hCG levels occurs in the first trimester, indicating pulsatile secretion, with a nadir at 1900 hours and peak at 0700 hours. The daily variation in concentrations of maternal serum hCG can be up to 20 percent. Early in pregnancy, there is no link between hCG rates and fetal sex or birthweight. Higher rates of hCG are therefore associated with female fetuses in late pregnancy [15,16].

Aim and Objective:

Aim: To study the levels of prolactin and beta hCG in female infertility.

Objective: To correlate the levels of prolactin and beta hCG in infertile womens and healthy controls (age matched) attending AVBRH Wardha and SMHRC Nagpur.

Material and Method

The present Study was carried out in the Dept. of Obstetrics and Gynecology and Department of Biochemistry at Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi (Meghe) Wardha Maharashtra in collaboration with Datta Meghe Medical College, Shalinitai Meghe Hospital & Research Centre, Nagpur.

Total 80 subjects were selected for study. Out of which 40 infertile female and 40 age and gender matched healthy control.

Sample Collection: Blood sample was collected, prolactin and beta hCG level was measured in Dry Chemistry Analyzer.

Inclusion Criteria: Women with primary and secondary infertility.

Exclusion Criteria:

- Urogenital tract anomalies
- History of thyroid disease/thyroid surgery/thyroid medication.
- Women unwilling to participate or sign the informed consent

Statistical Analysis: All estimated results were expressed as mean ±SD. Mean values will be assessed for significance by unpaired student –t test. A statistical analysis will be performed using the Statistical Package for the Social Science program (SPSS, 24.0). Frequencies and percentages will be used for the categorical measures. Probability values $p < 0.05$ will be considered statistically significant.

Observation and Results

Table 1: Age Distribution

Groups	Number	Age	P value
Cases (Infertile Female)	40	31.67±9.05	0.2531
Control (Fertile Female)	40	29.62±6.70	

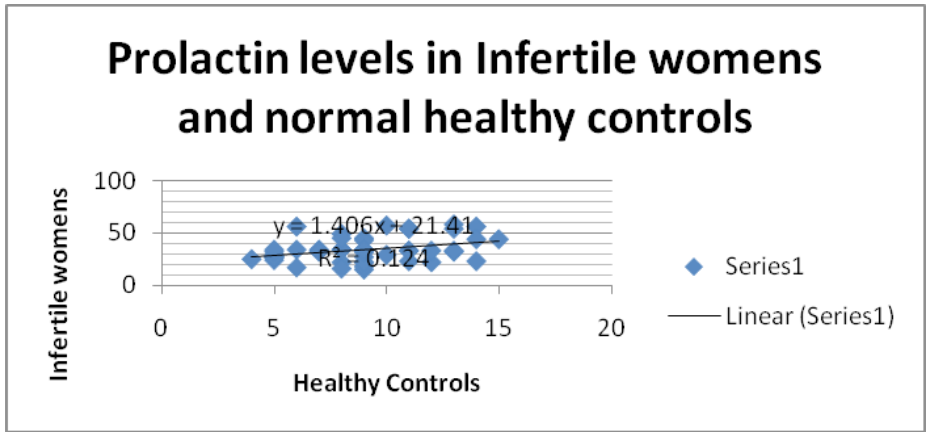
The above table depicts the age distribution in cases and controls, the mean age in cases is 31.67 and in control 29.62, no significant correlation was seen in between cases with a p value of 0.2531.

Table 2: Levels of Prolactin and beta hCG in infertile Female and Healthy control.

	Infertile Female Mean±SD (n=40)	Healthy Control Mean±SD (n=40)	t Value	P Value
Prolactin	33.96±11.46	8.92±2.87	-13.405	<0.0001
Beta hCG	86.38±12.45	6.6±1.988	-40.021	<0.0001

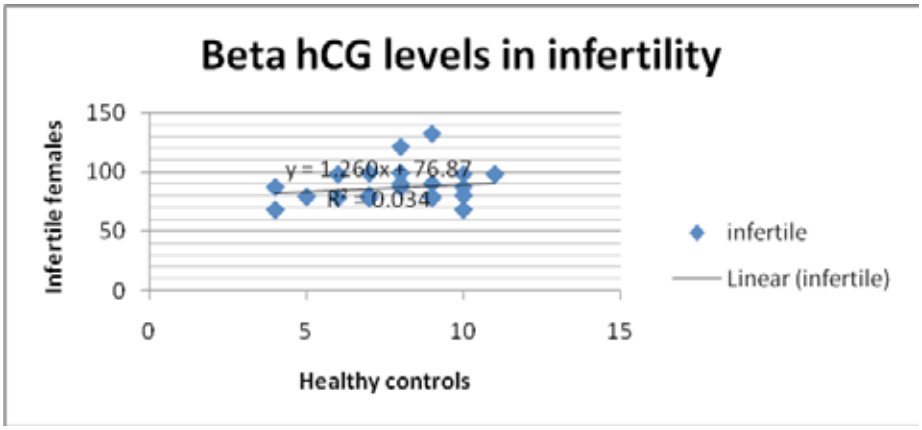
$P < 0.05$

The levels of Prolactin and beta hCG was increased in infertile female as compared to healthy control. In Infertile females the levels of prolactin was 33.96±11.46 and in healthy controls the levels was 8.92±2.87 with a p value of <0.0001 which a significantly indicating Hyperprolactinemia. Serum beta hCG levels was also increased in infertile women's with a p value of <0.0001



Graph 1: Scatter graph showing prolactin levels.

The above scatter graph depicts the levels of prolactin in infertile womens and normal healthy controls.



Graph 2: Scatter graph showing beta hCG levels.

The above scatter graph depicts the levels of beta hCG in infertile womens and normal healthy controls.

Discussion

Human chorionic gonadotropin (hCG), also known as the "pregnancy hormone," plays a significant role in human reproduction. Serum hCG has a circulating half-life of 24 hours. Female infertility accounts for 37% of all infertile couples and most of them are attributed to ovulatory dysfunction and are also correlated with dysregulation of the hormonal network.[17] The existence of abnormally high prolactin values is considered hyperprolactinemia, which is one of the most common endocrinological disorders of the hypothalamopituitary axis affecting fertility.[18-20] Hyperprolactinemia is one of the fertility-influencing endocrinological disorders most severe. The perception that hyperprolactinemia is not only expressed as galactorrhea and amenorrhea but also induces gonadal dysfunction and infertility has contributed to prolactin estimation in infertile females. Hyperprolactinemia influences the reproductive capacity by impairing pulsatile GnRH secretion and interferes with the function of ovarian-level gonadotropins so as to interfere with ovulation.[21,22] Hyperprolactinemia triggers galactorrhea together with menstrual and ovulatory disorders. It is present in females with both galactorrhea and amenorrhea in two thirds. Thus, serum prolactin levels should be estimated in unexplained infertility, any menstrual abnormalities with or without hirsutism, galactorrhea with or without amenorrhea, luteal phase defects, and anovulation.[23] Mild hyperprolactinemia may cause infertility even with normal menstruation.[24] Women with galactorrhea and hyperprolactinemia may be predominantly hypothyroidism. Hypothyroidism induces increased TRH secretion that induces thyrotrophin and lactotrophs, causing both TSH & prolactin levels to rise[25]. Hyperprolactinemia decreases the pulsatile release of the GnRH and impairs the secretion of FSH, LH. It also affects ovarian follicle steroidogenic activity and induces insufficient luteal-phase progesterone secretion[26]. These all result in luteal phase defects, inconstant ovulation, and chronic anovulation. Luteal insufficiency impairs endometrial development and inhibits embryo implantation.[27] It accounts for 3–10 percent of infertility and two-thirds of these women have hyperprolactinemia.[28] In hyperprolactinemic infertility, reduced prolactin secretion with dopaminergic drugs is the best therapy for raising the risk of conception[29].

Conclusion

For nonpregnant people, HCG in the serum rises with age. Consequently, it is concluded that hyperprolactinemia is a major contributing hormonal factor in infertility among infertile women and, as such, prolactin and hCG should be measured in infertile women. Even with normal menstruation, moderate hyperprolactinemia can cause infertility. Hyperprolactinemia is one of the most common female infertility endocrinological disorders and is often associated with hypothyroidism. Present study concludes that all infertile women should be offered serum prolactin estimation at an early stage of infertility checkup rather than going for more costly tests or invasive procedures.

Ethical Clearance: Taken from institutional ethics committee.

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Conflict of Interest: Nil.

References

1. Balen A et al. Management of infertility. J. Mol. Biol.,2007; 335: 60811.
2. Sanders B. Uterine factors and infertility. J. Reorod. Med., 2006;51: 169-76.
3. Gronovski Aet al. Use of serum FSH to identify pre-menopausal women with pituitary hCG, Clin. Chem.,2008; 54: 652-56.
4. Heinonen P et al. Primary infertility and uterine anomalies. Fertil. Steril., 1983; 40, 311-17.
5. Evers MC. The infertile couple. Am Fam Physician. 2002;54(3):1001-10.
6. Wright KL. Defining infertility: what infertility means for clinicians and clients. Network. 2003;23(2):4-6.
7. Audu D et al. Infertility and gender difference in reaction among couples and family and community treatment: a study of patients attending N.K.S.T. hospital Mkar in Benue state, Nigeria. ESJ. 2013;9(32):96106.
8. Majumdar A et al. Hyperprolactinemia. J Hum Reprod Sci. 2013;6(3): 168–75.
9. Chawla Ret al. Detection of Macroprolactinemia and molecular characterization of prolactin isoforms in blood samples of hyperprolactinemic women. In: Journal of medical biochemistry, 2012; 31:19.

10. Y-p Zet al. Impact of transitory hyperprolactinemia on clinical outcome of in vitro fertilization and embryo transfer. In: Journal of medical biochemistry. 2012; 31: 27.
11. Boyers Set al. Serum prolactin response to embryo transfer during human in vitro fertilization and embryo transfer. J In Vitro Fert Embryo Transf. 1987;4(5):269–72.
12. Braunstein Get al. Serum human chorionic gonadotropin levels throughout normal pregnancy. Am J Obstet Gynecol 1976;126:678–681.
13. Hay DL, Lopata A. Chorionic gonadotropin secretion by human embryos in vitro. J Clin Endocrinol Metab 1988;67:1322–1324.
14. Kletzy Oet al. Dynamics of human chorionic gonadotropin, prolactin and growth hormone in serum and amniotic fluid throughout normal human pregnancy. Am J Obstet Gynecol 1985;151:878–883.
15. Obiekwe Bet al. Placental proteins in late pregnancy: relation to fetal sex. Br J Obstet Gynaecol 1983;3:163–164.
16. Steier Jet al. Human chorionic gonadotropin in maternal serum in relation to fetal gender and uteroplacental blood flow. Acta Obstet Gynecol Scand 2004;83:170–174.
17. Unuane Det al. Endocrine disorders & female infertility. Best Prac Res Clin Endocrinol Metab. 2011;25(6):861-73.
18. Rosato F, Garofalo P. Hyperprolactinemia: from diagnosis to treatment. Minerva pediatrica. 2002;54(6):547-52.
19. Ratner Let al. Short-term pharmacological suppression of the hyperprolactinemia of infertile hCG-overproducing female mice persistently restores their fertility. Endocrinology. 2012;153(12):5980-92.
20. Berinder Ket al. Parity, pregnancy and neonatal outcomes in women treated for hyperprolactinaemia comparedwith a control group. Clin Endocrinol. 2007;67(3):393-7.
21. Poppe Ket al. Thyorid disorders in infertile women. Ann Endocriniol (Paris). 2003;64(1):45-50.
22. Zollner Uet al. Assessment of endocrine status in patients undergoing in-vitro fertilization treatment. Is it necessary? Arch Gynecolo obstet. 2001;265(1):16-20.
23. Kaur A et al. Hyperprolactinemia and its correlation with hypothyroidism in infertile women J obstet gynecol India. 2006;56:68-71.
24. Eldin S et al. Hyperprolactinemia as a cause of female infertility and its prevalence in central Sudan. Egypt Acad. J.Biolog. Sci. 2013;5(1):31-6.
25. Shoupe D et al. Hypoprolactinemia: Diagnosis and treatment. In: Mishell‘s textbook of Infertility, Contraception and Reproductive Endocrinology.. Massachusetts. Blackwell Science. 1997;4:323-41.
26. Muhammad O, Bushra J. Physiological study of some Hormonal Parameters in Infertile Hyperprolactinemic Women in Pre and Post Treatment with Cabergoline and Bromocriptine. Medical journal of Babylon. 2012;9(2):349-61
27. Dizerega G et al. Luteal phase dysfunction. Clin Obstet Gynecol. 1981;8:733-51.
28. Shibli-Rahhal A, Schlechte J. Hyperprolactinemia and infertility. Endocrinol Metab Clin N Am. 2011;40:837-46.
29. Crosignani P. Management of hyperprolactinemic infertility. Middle East Fertility Society Journal. 2012;17:63–69.