

Frequency of Hyperprolactinemia and Hypothyroidism in Infertile Women

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Hyper-
Prolactinemia
and
Hypothyroidism
in Infertile
Women

ABSTRACT

Objective: To determine the frequency of hyperprolactinemia and hypothyroidism in infertile women

Study Design: Descriptive / Cross Sectional study

Place and Duration of Study: This study was conducted at the Department of Obstetrics & Gynecology, Federal Government Services Hospital, Islamabad, from 7th July 2017 to 6th January 2018.

Materials and Methods: After hospital ethical committee approval the study was conducted and informed written consent was taken. All infertile women with duration of marriage >2 years were selected after fulfilling of inclusion criteria between 20 to 40 years and women with pituitary tumor (assessed on medical record), polycystic ovarian disease, known hyperthyroidism and drug history of dopamine depleting, dopamine receptor blocking, H-2 blocker and verapamil intake were excluded. After taking relevant history, an ultrasound abdomen and pelvis was performed. Then 3 ml of blood sample was taken and sent to the institutional pathology laboratory for measuring the serum prolactin levels and serum TSH, T3 & T4 levels. All the data was recorded on a predesigned proforma. Collected information was analyzed by using SPSS 23 version.

Results: Total 72 patients were selected and the age range in this study was from 20 to 40 years with mean age of 29.26 ± 4.65 years. Majority of the patients 37 (51.39%) were between 20 to 30 years of age and mean duration of marriage was 4.17 ± 1.10 years. Hyperprolactinemia in infertile women was found in 22 (30.56%) patients, whereas there was no hyperprolactinemia in 50 (69.44%) patients and Hypothyroidism in infertile women was found in 25 (34.72%) patients, whereas there was no hyperprolactinemia in 47 (65.28%) patients.

Conclusion: This study concluded that frequency of hyperprolactinemia and hypothyroidism in infertile women is quite high. So, we recommend that in every patient of infertile women, hyperprolactinemia and hypothyroidism should be taken into consideration and its early recognition and management should be done in order to reduce the morbidity of the community.

Key Words: Infertility, Hyperprolactinemia, Hypothyroidism

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INTRODUCTION

By definition infertility is defined as inability of a female to conceive after 12 months of regular intercourse without any contraception measures, within period of 6 months 75% of normal healthy couple conveys, about 85% within one year and 93% within 2 years.

Infertility may be referred as primary (no previous conceptions) or secondary (with a history of previous

conception but having difficulty currently to conceive). Globally approximately 8 to 12 % of couple's are affected due to infertility.¹ Altered function of Hypothalamic- Pituitary-Ovarian (HPO) axis is relatively common among the female factors contributing to infertility.²

Many sources contribute to infertility, most likely nutrition, some diseases, and uterine malformations. Women's worldwide are effected by infertility and cases varies regarding culture taboos and stigma. Almost 85% of infertile pairs have a recognizable cause. Of the approximately 5 million infertile women in the United States, it is estimated that 2 million (40%) have medical or hormonal infertility; 2 million (40%) have mechanical infertility; and 1 million (20%) have idiopathic infertility.³

Infertility factors of females mostly divided into several categories: e.g. cervical or uterine, ovarian, tubal, and other. Although stress and distress (anxiety or depression) have been considered factors in reducing pregnancy chances with assisted reproductive technologies (ART), the number of studies has been limited.⁴ Hyperprolactinemia is one of the most common endocrine disorder of the hypothalamic-

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pituitary-ovarian axis affecting the reproductive function. Despite the significant role of hyperprolactinemia in infertility, serum prolactin estimation is still not universally done as a part of the evaluation of infertility,⁵ while the literature review is also not clear regarding the frequency of this morbidity in infertility.

Hyperprolactinemia, the presence of abnormally high levels of prolactin in the blood, is the most common endocrine disorder of the hypothalamic-pituitary axis. Clinical and experimental studies have suggested a close relationship between the hypothalamic-pituitary-thyroid axis and the hypothalamic-pituitary-ovarian axis.⁶ Hypothyroidism and hyperprolactinemia are found to be closely interlinked.⁷ Failure in regular ovulation is mostly effected due to hypothyroidism in women of the reproductive age group. Hypothyroidism is found in some females with high prolactin levels which is characterized by raised serum TSH levels.⁸ In a study, prevalence of hyperprolactinemia was 24.67% and hypothyroidism was 27.33% in infertile women.⁹ Many aspects of reproduction and pregnancy in females are disturbed by thyroid dysfunction. Therefore measurement of prolactin and thyroid hormones, especially thyroid stimulating hormone (TSH), has been considered an important component of infertility workup in women. I had planned to conduct this study to evaluate the frequency of hyperprolactinemia and hypothyroidism in infertile women in local population. The results of this study will be a useful addition in local as well as international data. Also this study will help us to design our routine practice guidelines for early recognition and management of hyperprolactinemia and hypothyroidism in these particular patients in order to reduce the morbidity of community. Also on the basis of this study, public awareness programs on national and regional levels can be arranged for early screening and treatment of these conditions in these particular patients.

MATERIALS AND METHODS

This Descriptive, Cross Sectional study was conducted at the Department of Obstetrics & Gynecology, Federal Government Services Hospital, Islamabad for six months from 7th July 2017 to 6th January 2018 after approval from the hospital’s ethical committee. Sample size of 72 cases had been calculated by using WHO calculator with 95% confidence level, 10% margin of error and taking expected frequency of hyperprolactinemia as 24.67%⁹ by using following formula. $sample\ size = n = (Z_{(1 - \alpha/5 P(1 - P))}^2) / d^2$

Detailed history was obtained from each patient. A complete clinical examination was performed by the trainee researcher. Informed consent was taken from the patients. All infertile women with duration of marriage

>2 years were selected after fulfilling of inclusion criteria between 20 to 40 years and women with pituitary tumor(assessed on medical record), polycystic ovarian disease, known hyperthyroidism and drug history of dopamine depleting, dopamine receptor blocking, H-2 blocker and verapamil intake were excluded.

Data was analyzed by SPSS version 23. Age, duration of the marriage and BMI were presented as mean and standard deviation. Type of infertility (primary/secondary), hyperprolactinemia (present/absent) and hypothyroidism (present/absent) were presented as frequency and percentage. Effect modifiers like age, duration of the marriage, and type of infertility (primary/secondary) were controlled through stratifications. Post-stratification Chi square was applied to see their effects on the frequency of hyperprolactinemia and p value ≤ 0.05 was considered as significant.

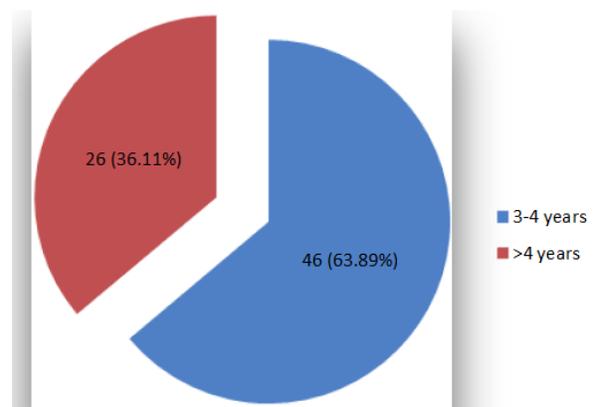
RESULTS

Total of 72 patients were selected and the adult female with age of 20 to 40 years with mean age of 29.26 ± 4.65 years and most of the patients 37 (51.39%) were between 20 to 30 years of age as shown in Table 1, and mean duration of marriage was 4.17 ± 1.10 years Figure 1.

Table No.1: Age distribution of patients (n=72).

Age (in years)	No. of Patients	%age
20-30	37	51.39
31-40	35	48.61
Total	72	100.0

Mean ± SD = 29.26 ± 4.65 years



Mean ± SD = 4.17 ± 1.10 years

Figure No.1: Distribution of patients according to duration of marriage (n=72)

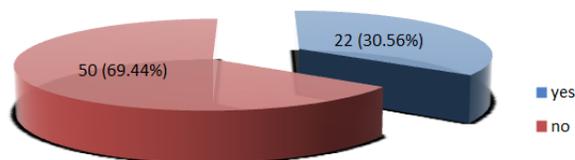


Figure No.2: Frequency of hyperprolactinemia in infertile women (n=72)

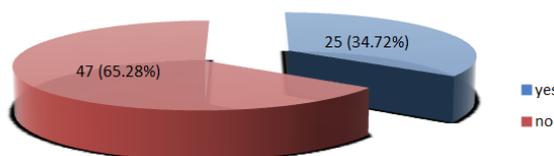


Figure No.3: Frequency of hypothyroidism in infertile women (n=72).

Hyperprolactinemia in infertile women was found in 22 (30.56%) patients, whereas there was no hyperprolactinemia in 50 (69.44%) patients as shown in Figure 2 and Hypothyroidism in infertile women was found in 25 (34.72%) patients, whereas there was no hyperprolactinemia in 47 (65.28%) patients as shown in Figure 3.

DISCUSSION

In infertile couples 37% infertility is due to female factor & ovulatory disorders are most common, and is often associated with hormonal irregularities.¹⁰ Presence of abnormally high values of prolactin, $>25\mu\text{g/L}$ is considered as hyperprolactinemia referred to as one of the most common endocrinological disorder of the hypothalamopituitary axis affecting fertility.¹¹ Fertility is affected by high prolactin levels which results in impaired pulsatile secretions of GnRH that interfere with gonadotrophins response at ovarian level results in altered ovulation. Hyperprolactinemia causes galactorrhea along with menstrual and ovulatory disturbances. It is present in two-thirds of women with both galactorrhea and amenorrhea. So estimation of serum prolactin levels should be advised in all unexplained infertilities, any menstrual irregularity with or without hirsutism, galactorrhea with or without amenorrhea, luteal phase defects and anovulation.¹² Mild hyperprolactinemia can cause infertility even with regular menstruation.¹³ Women with hyperprolactinemia and galactorrhea might have primary hypothyroidism. Hypothyroidism stimulates increased secretion of TRH which stimulates thyrotrophs and lactotrophs, causing increase in the levels of both TSH & prolactin.¹⁴

I have conducted this study to determine the frequency of hyperprolactinemia and hypothyroidism in infertile women. The selected age of females in this study was from 20 to 40 years with mean age of 29.26 ± 4.65 years. Majority of the patients 37 (51.39%) were between 20 to 30 years of age. Hyperprolactinemia in

infertile women was found in 22 (30.56%) patients, whereas there was no hyperprolactinemia in 50 (69.44%) patients. Hypothyroidism in infertile women was found in 25 (34.72%) patients, whereas there was no hyperprolactinemia in 47 (65.28%) patients. In a study, prevalence of hyperprolactinemia was 24.67% and hypothyroidism was 27.33% in infertile women.¹⁵

According to various studies the prevalence of hyperprolactinemia, as in Avasti et al¹⁶ study 46% (111 patients), in Goswami et al¹⁷ study 41% (160 patients), in Indu Verma et al¹⁸ study 13.7% (54 out of total 394 patients). In Chowdhury and Goswami et al¹⁷ study 16.6%, Indu Verma et al¹⁸ study 4.57% (total 394 patients), in an other study 57%, In an other study 46.1% (total 160 patients). From the above data, in infertility evaluation both TSH and prolactin levels estimation are important. Increased levels of TRH secretion in primary hypothyroidism stimulates both TSH and prolactin secretion. In infertile females if hypothyroidism is associated with hyperprolactinemia, hypothyroidism should be treated first and TSH should be maintained at lower limit.

In a local study, of 100 cases 30(30%) were between age of 16-25 years, 26(26%) between age of 26-30 years, 21 (21%) between 31-35 years, 19 (19%) between age of 36-40 years and only 4% (n=4) were between 40-45 years of age, 93 (93%) between 1-10 years and only 7 (7%) had >10 years of duration, frequency of type of was recorded 56 (56%) as primary and 44 (44%) as secondary infertility, hyperprolactinemia was present in 39 (39%) infertile females while 61% (n=61) were having normal prolactin levels, out of 41 cases of hyperprolactinemia, in 11(26.83%) galactorrhea was there and 30(73.17%) had no galactorrhea.¹⁹

In study of 394 infertile women for the prevalence of hypothyroidism i.e. Indu Verma et al, hyperprolactinemia was present in 54 women (13.7%) whereas hypothyroidism and hyperprolactinemia in 18 patients (4.57%).¹⁸ In an other study on 160 women with primary infertility results showed 41% of infertile women were having hyperprolactinemia and 46.1% of hypothyroid women were associated with hyperprolactinemia.²⁰ Mechanism for raised PRL levels is considered as, the production of TRH is stimulated due to hypothyroidism which results in increased production of TSH and prolactin. GnRH secretions are impaired due to hyperprolactinemia leading to anovulation and infertility.

A study conducted in USA considered the requirement of TSH with Prolactin levels in infertile women. Non promising results were obtained regarding carrying out both tests together, 2.48% of patients (21 out of 846 patients) had abnormal levels of TSH, and 1.77% (15 out of 844 patients) had elevated levels of PRL.²⁰

Results showed Incidence of hypothyroidism in hyperprolactinemia was 25.5%. There was high incidence of hyperprolactinemia in infertile women, with positive correlation of 1:4 was found in hypothyroidism and hyperprolactinemia.²¹ For the first time, Luboshitzky R. et al an increase of serum prolactin was reported in woman with carpal tunnel syndrome and subclinical hypothyroidism.²² Study of Bahar A et al. had shown high incidence of hyperprolactinemia in sub-clinical hypothyroidism in female (21.7%) as compared to male (11.3%). Estrogen is considered mainly the main reason, because Meier et al have found that women on estrogen before or after menopause have greater level of prolactin.²³

CONCLUSION

This study concluded that there is high frequency of hyperprolactinemia and hypothyroidism in infertile women. So, we recommend that hyperprolactinemia and hypothyroidism should be taken into consideration in every infertile female and their timely recognition and treatment should be done in order to decrease the morbidity of the community.

Author's Contribution:

Concept & Design of Study:	Sumbal Andleeb Choudhary
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Final Approval of version:	Syed Saif Ur Rehman

Conflict of Interest: The study has no conflict of interest to declare by any author.

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