

Serum prolactin status in primary infertile women

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Abstract

Background: Prolactin is a polypeptide hormone that is produced by the anterior pituitary gland. Prolactin stimulates milk production in women after the delivery of a baby. Physiologically during the first several months of breastfeeding, the high level of prolactin inhibits ovulation. But if women have abnormally high level of prolactin, it may cause infertility. Prolactin inhibits two hormones Follicle Stimulating Hormone (FSH) and Gonadotropin Releasing Hormone (GnRH) which are necessary for ovulation and these results in infertility. Hyperprolactinemia is the risk factor of hypogonadism, infertility and galactorrhoea of the women in reproductive age.

Objectives: To see the relationship between serum prolactin and primary infertility.

Method: This cross sectional comparative study was carried out in the Department of Obstetrics and Gynaecology, Dhaka Medical Collage Hospital, Dhaka and data were collected from sampling population, The infertile patients were selected from the out patients department of infertility center at DMCH. Control subjects were selected from personal contact. After selection of subjects the purpose of the study was explained to each subject with a cordial attitude given emphasis of the benefits they would obtain from the study. They were encouraged for the voluntary Participation. With all aseptic precaution 5.0 (five) ml of venous blood was drawn from the anticubetal vein by disposable plastic syringe in early morning. Blood was allowed to clot and then centrifuged at a rate of 3000 rpm and supernatant clear serum was separated and preserved at 2-8°C for further study. The serum prolactin measured by radioimmunoassay in the center for Nuclear Medicine and Ultrasound, Dhaka Medical Collage Hospital, Dhaka. Statistical analyses were carried out by using the Statistical Package for Social Sciences version for Windows (SPSS Inc., Chicago, Illinois, USA).

Results: Among 102 cases the mean age was found 28.13 ± 4.79 years in group A and 26.49 ± 4.14 years in group B. Mean BMI was found 25.28 ± 3.33 kg/m² in group A and 26.15 ± 2.49 kg/m² in group B. In group B, 39(76.47%) patients had menstrual abnormality followed by 20(39.22%) had acne/hirsutism, 15(29.41%) had dismenorrhoea, 11(21.57%) had dyspareunia, 10(19.61%) had asymptomatic and 2(3.92%) had galactorrhoea. Serum prolactin level 2-15 ng/ml among them 46(90.2%) in group A and 20(39.2%) in group B. Thirty (36) patients had serum prolactin level >15 ng/ml among them 31(60.8%) patients in group B. The difference was statistically significant ($p < 0.05$) between the groups. Mean serum prolactin level was found 10.66 ± 4.87 ng/ml in group A and 20.06 ± 8.22 ng/ml in group B ($p < 0.05$). Abnormal menstrual history was common in group B (76.47% vs 27.45%). Patients who had increased level of prolactin level their various from of abnormal menstrual history 27(87.1%) and normal menstrual history 04(12.9%). Mean serum prolactin level was found 15.62 ± 5.19 ng/mL in normal menstrual abnormality and 21.43 ± 8.55 ng/mL in abnormal menstrual abnormality. The mean serum prolactin level was found 40.68 ± 1.57 ng/mL in galactorrhoea and 19.22 ± 7.21 ng/mL in non galactorrhoea. Which were statistically significant ($p < 0.05$). Mean serum prolactin level was found 22.08 ± 9.05 ng/mL in duration of primary infertility ≤ 5 years and 18.53 ± 7.32 ng/mL in duration of primary infertility > 5 years. The difference was not statistically significant ($p > 0.05$).

Conclusion: In conclusion, that women with infertility had significantly higher serum prolactin than that of healthy parous woman. High level of prolactin may more prevalent in primary infertile women

Keywords: Infertility, serum prolactin level.

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Introduction

Throughout history, human societies were pre occupied by the process of procreation which they attempted described through art and religion. It is one of the major aspect of main- taining survival and perpetuation of the human race. In view of the entwined nature between sexuality, morality and reproduction. Fertility played a vital role in almost all religion on the earth. A global review of infertility from the world Fertility

Survey estimated rates of infertility both primary and secondary approximately 10% in South Asia, 8% in India, 10% in Paki- stan, 11% in Sri Lanka, 12% in Nepal and 15% in Bangladesh. Hormonal disorders of female reproductive system due to aberrant dysfunction of hypo-thalamic-pituitary-ovarian axis are relatively common disorders often lead to infertility. Prolactin is a polypeptide hormone that is produced by the anterior pituitary gland. Prolactin stimulates milk production in women after the delivery of a baby. Physi-ologically during the

first several months of breastfeeding, the high level of prolactin inhibits ovulation. But if women have abnormally high level of prolactin, it may cause infertility. Prolactin inhibits two hormones Follicle Stimulating Hormone (FSH) and gonadotropin releasing hormone (GnRH) which are necessary for ovulation and these results in infertility. The increased level of prolactin are associated with menstrual and ovulatory disorders like amenorrhea, oligomenorrhea, anovulation, ovulatory cycles with short or inadequate corpus luteal phase, and galactorrhea. So the present study was provided us information about cause of infertility and create awareness among the clinicians as well as with infertile women [1].

Materials and Methods

Type of study: This study was a cross-sectional analytical study.

Place of study: Department of Obstetrics and Gynaecology, Dhaka Medical Collage Hospital, Dhaka.

Duration of study: From January 2015 to December 2016

Sampling method: Consecutive purposive sample.

Study population: Primary infertile woman.

Sample size:

Estimation of sample size for cross-sectional study

$n =$

$n =$ sample size

$z = 1.96$ (Z value of standard normal distribution at 5% significance)

$p =$ Prevalence of primary infertility $76\% = 0.76$

$q = 1 - P$

$d = 0.05$ acceptable error

Using above formula the expected simple size:

$n = 280$

Estimated sample size is 280, but due to limitation of time 51 patients were taken in each group.

Grouping of the subjects

Group A (control group): Consisted of 51 apparently healthy fertile women.

Group B (study group): Consisted of 51 primary infertile women.

Inclusion criteria

Age between 20-40 years.

Exclusion criteria

Tubal factor abnormality.

Congenital anomaly of urogenital tract in female.

Obvious organic lesion or pelvic inflammatory diseases

Age of last child <3 years.

History of taking contraceptive for long time, history of TB and any major endocrine disease.

Patients with PCOS

Patients with thyroid disorder.

Site of sample collection and selection of the patient

The infertile patients were selected from the out patients department of infertility center at DMCH. Control subjects were selected from personal contact.

After selection of subjects the purpose of the study was explained to each subjects with a cordial attitude given emphasis of the benefits they would obtain from the study. They were encouraged for the voluntary Participation. They were also allowed to withdraw themselves as soon as they wish. The purpose of the study was explained to the subject and written informed consent was taken [2].

Data collection

A structured data collection sheet was prepared and designed. The data sheet was used for collection of information. Data was collected by the principle investigator (Appendix II).

Collection of blood sample

With all aseptic precaution 5.0 (five) ml of venous blood was drawn from the antecubital vein by disposable plastic syringe in fasting condition in early morning. Patients were council no to take any exercise, high-protein meals, sexual intercourse, breast examination or palpation, minor surgical procedures, physical or emotional stress because protein level can rise after these conditions. Blood was allowed to clot and then centrifuged at a rate of 3000 rpm and supernatant clear serum was separated and preserved at 2-8°C for further study (Appendix IV). The serum prolactin measured by radioimmunoassay in the center for Nuclear Medicine and Ultra-sound, Dhaka Medical Collage Hospital, Dhaka [3].

Main outcome variable

Serum prolactin

Operation definition

Serum prolactin: Prolactin is a hormone that is secreted by the anterior pituitary gland, a pea-sized gland found below the brain. Normal level of serum prolactin 2-15 ng/mL.

Primary infertility: Infertility is defined as the inability of a couple to achieve conception after one year of unprotected coitus. Infertility are two types-Primary infertility and Secondary infertility. Primary infertility or sterility is an absolute state of inability to conceive.

Data processing and data analysis: Statistical analyses were carried out by using the Statistical Package for Social Sciences

version 23.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. Chi-Square test with Yates correction was used to analyze the categorical variables, shown with cross tabulation. Student t-test was used for continuous variables. Pearson's correlation coefficient was used to test the relationship between the groups. P values <0.05 was considered as statistically significant [4].

Ethical consideration: Ethical clearance for the study was taken from the Institutional Review Board and Department of Obstetrics and Gynaecology DMCH. Prior permission for the study was taken from the authorities of the concerned place of study. The participants were fully informed about the nature, purpose and implications and benefits of the study. Safety and interest of the participants was protected at all times. Confidentiality was strictly maintained and participants had the freedom to withdraw from the study at any time.

Observation and Results

Table I: Distribution of the study population by age and BMI (N=102).

	Group A (n=51)	Group B (n=51)	p value
	Mean \pm SD	Mean \pm SD	
Age (in years)	28.13 \pm 4.79	26.49 \pm 4.14	0.067ns
BMI (kg/m ²)	25.28 \pm 3.33	26.15 \pm 2.49	0.138ns

Mean age was found 28.13 \pm 4.79 years in group A and 26.49 \pm 4.14 years in group B. Mean BMI was found 25.28 \pm 3.33 kg/m² in group A and 26.15 \pm 2.49 kg/m² in group B. The difference was not statistically significant (p>0.05) between the groups.

Result and Discussion

Infertility is a common problem all over the world. Statistics regarding infertility general population are difficult to come by since 40% of infertile couples do not attend hospital or clinic for treatment illustrating the potential for error in hospital based statistics. Among the cases of female infertility and prolactin plays a role but it is correctable that there should be a correct diagnosis and to provide best treatment option to the couple as early as possible.

In this study it was observed that mean age was found 28.13 \pm 4.79 years in group A and 26.49 \pm 4.14 years in group B. The difference was not statistically significant (p>0.05) between the groups. In study of Shown the mean age was found 27.5 \pm 3.0 years in primary infertile group and 23.525 \pm 2.48 years in control group. In study of Bheem et al. observed that the maximum infertile women population was found between the age group of 30-40 years. the mean age was found 23.525 \pm 2.48 years in primary infertile group, 27.575 \pm 1.94 years in secondary infertile group and 27.0 \pm 2.12 years in control group. studied group comprised of 54 women of which 32

women were infertile, age ranged from 20-40 years and 22 fertile women as control of the same age group.

In this current study it was observed that mean BMI was found 25.28 \pm 3.33 kg/m² in group A and 26.15 \pm 2.49 kg/m² in group B. The difference was not statistically significant (p>0.05) between the groups. (Shown 26% of infertile women with primary infertility were in overweight and obese groups. 3% with secondary infertility were overweight. In this study it was observed that in group B, 39(76.47%) patients had menstrual abnormality followed by 20(39.22%) had acne/hirsutism, 15(29.41%) had dysmenorrhea, 11(21.57%) had Dyspareunia, 10(19.61%) had asymptomatic and 2(3.92%) had galactorrhoea. In this present study it was observed that total 66 patients had serum prolactin level 2-15 ng/ml among them 46(90.2%) in group A and 20(39.2%) in group B. Thirty (36) patients had serum prolactin level >15 ng/ml among them 31(60.8%) patients in group B. The difference was statistically significant (p<0.05) between the groups [5].

Mean serum prolactin level was found 10.66 \pm 4.87 ng/ml in group A and 20.06 \pm 8.22 ng/ml in group B. Patients had serum prolactin level 2-15 ng/ml their mean prolactin level was 9.48 \pm 3.20 ng/ml in group A and 11.76 \pm 1.63 ng/ml in group B. The difference was statistically significant (p<0.05) between the groups. the mean serum level of Prolactin was 18.59 \pm 7.50 ng/ml in infertile women was higher than the mean serum level of Prolactin of 13.44 \pm 5.82 ng/ml in fertile women which was highly significant (p=0.0001). Similarly, increased levels of prolactin have also been reported by The prolactin levels are high in infertile women as compared to fertile women. These results are in agreement and who also found increased levels of FSH, LH and prolactin in infertile women. the mean prolactin level was found 11.7 \pm 5.9 ng/mL in control group and 29.07 \pm 9.7 ng/mL in

infertile group mean prolactin levels was found 63.09 \pm 61.78 ng/ml in hyperprolactinemic infertile women, 12.58 \pm 5.17 ng/ml in normoprolactinemic infertile women and 8.21 \pm 3.71 ng/ml in controls. The difference was statistically significant (p<0.05) among three groups the serum prolactin levels were found to be strongly correlated in primary infertile women and this correlation was statistically significant (P<0.001). Hymavathi et al. prevalence of hyperprolactinemia was 34% in study group with mean prolactin levels of 21.84 \pm 15.65. The mean prolactin levels in infertile patients were 17.7 \pm 25.8 ng/ml against the controls who had mean prolactin levels of 20.9 \pm 26.3 ng/ml (normal = 1.2-19 ng/ml) and both groups are showing not statistically significant difference to each other (p value = 0.570).

In my study it was observed that abnormal menstrual history was common in group B (76.47% vs 27.45%). Total 14 patients had abnormal menstrual history in group A among them majority 4(7.84%) had amenorrhoea. Out of 39 abnormal menstrual history in group B patients among them majority 11(21.57%) had intermenstrual bleeding. Study showed out of 32 patients 24 had hyperprolactinemia and 8 had hypothyroidism. showed an incidence of anovulation in hyperprolactinemia patients to be 73%.

In this study current study it was observed that patients who had increased level of prolactin level their various from of abnormal menstrual history 27(87.1%) and normal menstrual history 04(12.9%). The difference was statistically significant ($p < 0.05$). majority (83.9%) patients was found normal menstrual history in normal prolactin group and 7(53.8%) in hyperprolactinemia group. Four (12.9%) patients was found oligomenor-rhea/ ypomenorrhea in normal prolactin group and 4(30.7%) in hyperprolactinemia group. Hyperprolactinemia resulting from longstanding primary hypothyroidism has been implicated in ovulatory dysfunctions ranging from inadequate corpus luteal progesterone secretion when mildly elevated to oligomenorrhea or amenorrhea when circulating prolactin levels are high it is demonstrated by menorrhagia or oligomenorrhea, pregnancy loss and/or infertility. menstrual disturbances observed in the control and infertile groups were 18.7% and 61.2%, respectively. The majority of the cases (82.6%) as well as the controls (66.7%) who presented with menstrual disturbances had oligomenorrhea. Fifty percent of the subjects with hypothyroidism had menstrual irregularities, presented with amenorrhea. Maximum percentage of menstrual abnormality presented by the infertile group was oligomenorrhea (82%) whereas depicted the state to be smaller (50%).

Observed twenty nine (48%) patients was found Oligomenorrhea/Hypomenorrhea in normal prolactin level and 27(53%) in hyperprolactinemia. Three (5%) patients was found amenorrhea in normal prolactin level and 3(6%) in hyperprolactinemia. Two (4%) patients was found menorrhagia in hyperprolactinemia and not found in normal prolactin level. In this study it was observed that in group B, mean serum prolactin level was found 15.62 ± 5.19 ng/mL in normal menstrual function and 21.43 ± 8.55 ng/mL in abnormal menstrual function. The mean serum prolactin level was found 40.68 ± 1.57 ng/mL in galactorrhoea and 19.22 ± 7.21 ng/mL in non galactorrhoea. Which were statistically significant ($p < 0.05$). reported that galactorrhoea was present in 10(9%) of the total infertile patients, in five (5/67; 8%) with primary infertility and in five (5/44; 11%) with secondary infertility.

In this current study it was observed that in group B, mean serum prolactin level was found 22.08 ± 9.05 ng/mL in

duration of primary infertility ≤ 5 years and 18.53 ± 7.32 ng/mL in duration of primary infertility > 5 years. The difference was not statistically significant ($p > 0.05$). shows that mean duration of infertility in the patients with primary infertility was 4.58 years and in those with secondary infertility 3.39 years.

Conclusion

In conclusion, that women with infertility had significantly higher serum prolactin than that of healthy parous woman. High level of prolactin may more prevelant in primary infertile women.

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