Prevalence of hyperprolactinemia in Afghan women with infertility

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Abstract: *Hyperprolactinemia is one of the common endocrinological disorders among women of reproductive age, inducing infertility by several mechanisms acting on the Hypothalamus-Pituitary-Ovarian axis. Despite the high incidence of hyperprolactinemia in infertile women, serum prolactin level is not done as part of Afghanistan's infertility investigation. Therefore, this study aims to evaluate hyperprolactinemia frequency among infertile Afghan women and demonstrate that hyperprolactinemia is a quietly common but not rare finding in women with infertility. The study examined 346 women with primary and secondary infertility between 19-39 years for serum prolactin levels and other assessments for fertility check-ups in Ahdya Noor obstetrics and gynaecological clinic in Mazar-I-Sharif, Afghanistan from March 2019 to March 2020. All hyperprolactinaemic infertile female patients without any other infertility factors were included. It has been revealed that 61 (17.6%) of infertile female patients had hyperprolactinemia. Furthermore, secondary infertility incidence was higher than primary infertility in the hyperprolactinaemic population (88.5%) in which (45.9%) of women were between 25-34 years. Similarly, the majority of hyperprolactinaemic secondary infertile patients were also aged 25-34 meanwhile, women with para 1-3 made the largest proportion 60.7% of the hyperprolactinaemic infertile patients.*

Key Words: *Hyperprolactinemia, primary infertility, secondary infertility, Afghanistan.*

1. INTRODUCTION:

Hyperprolactinemia is one of the common endocrine disorders found in 9-17% of women with reproductive disorders and 15-20% of women with a history of infertility [1], [2] which is considered when prolactin level is higher than 25µg/l [3]. Hyperprolactinemia acts on the Hypothalamus-Pituitary-Ovarian axis, perturb it at several levels, which causes hypogonadotropic hypogonadism that results in infertility. At the hypothalamus, prolactin binds to its receptors in Kiss1 neurons at the arcuate nucleus (ARC) and anteroventral periventricular nucleus (AVPV), reducing the level of kisspeptin, a neuropeptide expressed in Kiss1 neurons. When the formation of kisspeptin is suppressed, it decreases the release of GnRH and, subsequently, the secretion of gonadotropins in the hypophysis[4]. Besides, PRL increases the dopaminergic tone, which reduces the GnRH release and, consequently, the LH secretion [5]. At the pituitary, PRL reduces LH response to pulsatile secretion of GnRH [6]; also, PRL afflicts estrogen positive feedback on gonadotrophs and subside the pulsatile release of LH but not FSH [5], [7]. At the ovarian level, prolactin inhibits synthesis of hCG induced plasminogen activator, which degenerate surface epithelia of mature graffian follicle, follicular rupture, and ovulation, thus contributing to anovulation [8], [9] Moreover, it inhibits aromatase activity in the ovary's granulosa cells to reduce the E2 level at follicular fluid, which affects follicular development, oocyte maturation, and fertilizability of the ovum [10], [11].

This work is conducted to identify the frequency of hyperprolactinemia in Afghanistan's infertile population since it is assumed that hyperprolactinemia may have a different extent in the local infertile population of Afghanistan. Besides, research on high prolactin levels in women with infertility has never done before in this local population, with many infertile women remaining undiagnosed, which would help manage infertility.

Nomenclature	
ARC	Actuate Nucleus
AVPV	Anteroventral Periventricular Nucleus
PRL	Prolactin
GnRH	Gonadotropin-releasing hormone
hCG	Human chorionic gonadotropin
E2	Estrogen
TSH	Thyroid-stimulating hormone

2. LITERATURE REVIEW:

In developing countries, including Afghanistan, hyperprolactinemia is not considered a cause of infertility than other causes. Various studies on the hyperprolactinaemic cause of infertility among women show a high incidence among infertile patients. In a retrospective study by Dr. PO on 199 infertile women at fertility clinics in Kogi State University Teaching hospital, Neighbour Multicare hospital and Women Welfare Centre in Anyigba, Kogi State and North Central Nigeria between March 2016 and February 2019, the prevalence of hyperprolactinemia was found 21% [12]. Likewise, in a cross-sectional study by Agrawal on 200 infertile women at Acharya Vinoba Bhave Rural Hospital, Wardha, in 2011-2013 reported 11.5% cases of hyperprolactinemic cases.[13] Whereas in a Descriptive Cross-Sectional study from the outpatient department of obstetrics & gynecology, DHQ Hospital, Faisalabad, among 75 infertile women, the frequency of hyperprolactinemia was recorded 28%.[14] Furthermore, research in Ahmadu Bello University Teaching Hospital (ABUTH), Zaria, Northern Nigeria 120 infertile female patients aged 15–45 years attended the infertility clinic at ABUTH over 9 months, which sixty-two of them (51.7%) had hyperprolactinemia [15]. Table (1) shows the prevalence of hyperprolactinemic infertility in developing countries.

Table 1. Prevalence of hyperprolactinemic infertility

Author	Sample size	Research Design	Findings	Ref
A. S. PO, A. M. U. 2016-2019	199	Retrospective study	42 female patients had high level of PRL level >25ng/L with 33 cases of primary infertility and 9 cases of secondary infertility among them.	[12]
M. Agrawal, S. Samal, C. Hariharan, S. Agrawal 2011-2013	200	Cross sectional study	The incidence of hyperprolactinemic infertility was 23 out of 200 (11.5%).	[13]
W. Shabab, S. Firdous, a. Seemab 2010	100	Cross sectional study	39 female patients (39%) had hyperprolactinemia with 11(26.83%) cases of galactorrhea among them.	[16]
M. F. Afzal, S. Saeed, M.U.Youns 2018	75	Descriptive Cross Sectional study	21(28%) female patients are found with high prolactin level as a cause of their infertility.	[14]
I.CHAUDHRY 2014 to 2015	100	Cross sectional study	Hyperprolactinemia was reported in 41% of the 100 female patients while 59% of the cases had no high level of prolactin.	[17]
U. B. AKPAN 2012	152	Comparative cross sectional study	57 female patients (37.5%) had high level of PRL with 3.89 + 3.433 years of infertility.	[18]
H. E. Elbashir, A. A. M. Garais, K. M. Hamaza. 2005 to 2010	14129	Retrospective study	The prevalence of hyperprolacatinemia found in 4096 (29%) of cases.	[19]
I. A. Isah, I. S. Aliyu,R. Yusuf, H. S. Isah, A. J. Randawa, A. G. Adesiyun 2018	120	Descriptive cross-sectional study	62 (51.7%) patients had a mean serum prolactin level of 31 ng/ml (range, 2.5–109 ng/ml)	[15]

3. METHODOLOGY:

This research is a descriptive based cross-sectional study conducted during the 1-year interval at one of the outpatient OBGY private clinics in Mazar I Sharif, Balkh, from March 2019 to March 2020. Out of 12230 patients, 346 women were found with primary and secondary infertility between the age of 19-39 years. Cases excluded were Male infertility factor, female tubal factors, urinary and genital tract abnormalities, and women who had apparent organic lesions in the pelvis or a history of thyroid disease/surgery. Detailed clinical history, Clinical examination, and laboratory investigations, including ultrasonography of abdomen and pelvis, hysterosalpingography, husband's semen

analysis, serum TSH, free T4 levels, and serum prolactin levels are carried out. Women with PRL level PRL level >25µg/l are considered as hyperprolactinemia[20].

Study design: Descriptive cross sectional
Study period: March 2019-March 2020
Population: 346
Inclusion criteria: Primary and Secondary infertility
Exclusion criteria: Female tubal factors ,Male infertility factors, , urinary and genital tract abnormalities, pelvic lesions and thyroid disease.
Proforma: *Detailed clinical history including*; Age, menstrual cycles, marital history, drug history, galactorrhea and any visual disturbances. *Investigations:* USG abdomen and pelvis, hysterosalpingography, serum TSH and free T4 levels by and serum prolactin levels. *Clinical examination including*; measurements of weight, heigh, breast, abdomen and pelvic examination.
Ethical considerations: Prior using this data, informed consent was received from patients with infertility problem in a written form.

4. ANALYSIS AND RESULT:

The total number of infertile women who attended the clinic was 346, of which (17.6%) were with hyperprolactinemia, and (82.4% were normoprolactinemic, as shown in Table (2).

Table 2: Prevalence of hyperprolactinemia among the infertile females

Infertile women	N	%
Hyperprolactinemia	61	17.6%
Normoprolactinemia	285	82.4%
Total infertility	346	100%

Most of the hyperprolactinemic infertile women were with secondary infertility (88.5%) compare to primary infertility (11.5%), as presented in Table (3).

Table 3: Types of infertility in female patients with hyperprolactinemia

Type of infertility	N	%
Primary infertility	7	11.5%
Secondary infertility	54	88.5%
Total	61	100%

According to the age group, hyperprolactinemia incidence was higher in 25-34 years (45.9%), while it was low in ages 25-34 (32.8%) and lower (21.3%) in 35-44 years. Table (4) shows the age distribution of infertile hyperprolactinemic women.

Table 4: Age distribution of infertile hyperprolactinemic women

Age (years)	N	%
15-24	20	32.8%
25-34	28	45.9%
35-44	13	21.3
Total	61	100

The majority (40.9%) of hyperprolactinaemic secondary infertile patients were aged 25-34, while 27.9% were between 15-24 years and 19.8% were 35-44 years. In primary infertility cases, the percentage of hyperprolactinemic women at 15-24 and 25-34 age groups were the same (4.9%), but lower (1.6%) in 35-44 years of age Table (5).

Table 5: Relation of age to the infertility type

Age (years)	(%) of primary infertility	(%) of secondary infertility	Total
15-24	4.9	27.9	32.8
25-34	4.9	40.9	45.8
35-44	1.6	19.8	21.4
Total	11.4	88.6	100

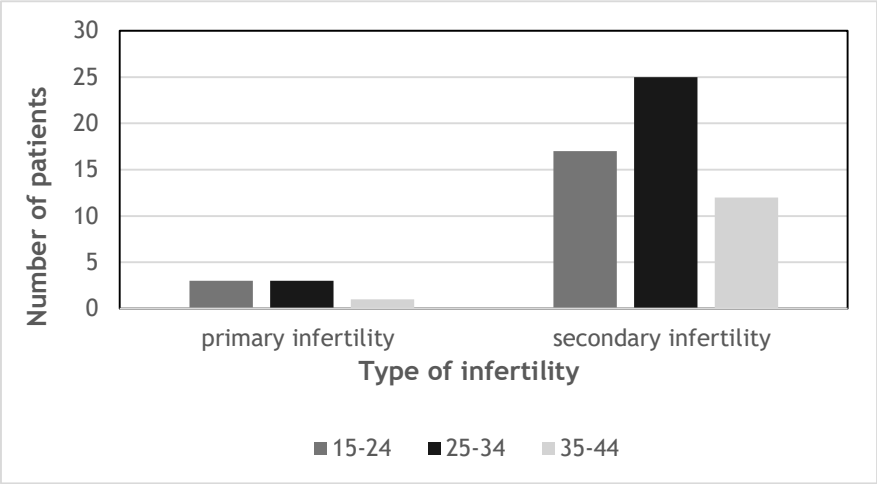

Figure 1. Relation of age and the infertility type in hyperprolactinemia

Women with para 1-3 made the largest proportion (60.7%) of hyperprolactinemic infertile patients, 15 (24.6%) women were nulliparous , and (14.7%) had Para 4 ≤ Table (5).

Table 5: parity distribution of hyperprolactinemic infertile women

Parity	**N**	**%**
Nulliparous	15	24.6%
Para (1-3)	37	60.7%
Para 4 ≤	9	14.7%
Total	61	100%

5. DISCUSSION:

This study is conducted to show the frequency of hyperprolactinemia in the infertile population in our society since it is assumed that hyperprolactinemia might have a different extent in the Afghan local infertile population. Besides, there is lack of research on high prolactin levels in women constituting infertility in this local population that might be helpful for managing infertility. The result reveals that the incidence of hyperprolactinemia was 17.6% among infertile women who are closely similar to the prevalence obtained from Anyigba, North Central Nigeria by PO. S. A.[12], [21]. Which shows a higher rate in developing countries, while as per Souter I. study in Boston, Massachusetts [21], it has been found 5.2%. These similarities and differences might be due to the stress level, etiological factors, and demographics.

In the present study majority of the patients, 54 (88.5%) between 25-34 year found with secondary infertility; this coincides with Isah et al. [15] study conducted in a tertiary health facility in Northern Nigeria where 72% of hyperprolactinemic patients were secondary infertile, this is probably due to women in this age group seek for specialist consultation to complete their family number. Additionally, most hyperprolactinemic infertile women were aged (25-34), which agrees with Lee, D, Y that reported hyperprolactinemia is more frequent in 21-30 age groups [22]. This finding shows that most infertile hyperprolactinemic women were in their mid-reproductive life. Because in this age group, women always start their marriage life.

6. CONCLUSION:

Hyperprolactinemia is prevalent in the infertile population; thus, it is necessary to evaluate serum prolactin levels in all primary and secondary infertility cases and include prolactin assay as a part of an infertility workup.

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