

Hormonal Imbalance and Infertility Among Females

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ABSTRACT

Objective: Determine the association of hormonal imbalance and infertility and any other endocrine disorder in the causation of infertility among female patients.

Study Design: Observational / descriptive study.

Place and Duration of Study: This study was conducted at the Govt. Aziz Bhatti Hospital (NSMC) for one year 2014-2015.

Materials and Methods: Female patients who presented with primary and secondary infertility among patients who were married and in the reproductive age group (15-49). The hormone profile was advised on the day-2 of the menstrual cycle especially F.S.H, L.H and prolactin. The patients who presented with amenorrhea were given hormones for withdrawal bleeding and then profile done and at random in irregular bleeding. Thyroid hormones were advised depending upon the history and positive symptomatology. The study was not funded. The duration of infertility was not considered.

Results: Majority of the patients who presented with infertility were in the reproductive age group, 51.8% from 20 to 29 and 44.44% from 30 to 39. Majority of the patients had normal hormone profile (64.81%). About 11.11% presented with polycystic ovarian syndrome (P.C.O's), the same numbers with premature ovarian failure and about 7.4% with disturbed thyroid profile. Hyper-prolactinemia was not found as an important cause of infertility in this study.

Conclusion: Hormone profile is an important investigation in cases of infertility in addition to the history, examination and ultrasonography, especially in cases that are also having associated menstrual abnormalities. Polycystic ovarian syndrome and premature ovarian failure were important causes of infertility and to some extent disturbed thyroid functions among the study group.

Key Words: Infertility, P.C.O's, Premature Ovarian Failure, Hyperprolactinemia

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INTRODUCTION

If a couple is unable to conceive after one year of complete consummation of the marriage, could be labeled as infertile.

Both male and female factors are important in cases of infertility although this period may be reduced to 6 months in a woman of 35 and above because of less ovarian reserve.

In primary infertility, the couples have never been able to conceive while in secondary infertility there is a difficulty in conceiving having once conceived, conditionally that it was a confirmed pregnancy, whether it reached to the term or not. Secondary infertility is not present if there has been a change of the partner within one year period.

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O.S. Philippov Et in their study found that infertility in Tamsk (Siberia) was 16.7%, the female reproductive cause was 52.7% and male reproductive disease in 6.4%. In 38.7% of couples, both spouses suffered from Infertility. In 2.2% of the cases the cause was not determined.¹

In another study² the incidence was 14.8% with a mean duration of 3.38 ± 1.65 years. Male factor was present in 26.8%, female factor in 51.8% and both male and female factor were contributing in 21.4% cases.

Majority of the infertile females are nulliparous (56.6%). About 73.3% of the patients were having secondary infertility. More than 70% were between 25-34 years of age and only a few (6%), were below the age of twenty five.²

Obesity is associated with hormonal derangements which may be responsible for infertility hence it should be primarily targeted in the management of the individuals before starting any therapy to correct their hormonal imbalance. The patients should be educated to adopt a healthy body weight by life style intervention before they undertake any medical or surgical management of infertility.¹⁹

The disturbances in thyroid gland functions, multicystic ovaries, and disturbances in prolactin secretion may affect the ovulation and thus causing subfertility.

Out of 394 infertile women 23.9% were hypothyroid (T.S.H) > 4.2 Micro Liter U/ml. After treatment for hypothyroidism 76.6% of infertile women conceived within 6 weeks to one year.³

In infertile women the prevalence of autoimmune thyroid disease is significantly higher compared to parous age matched women. This is especially the case in women with endometriosis and polycystic ovarian syndrome. During the first trimester, however pregnant women with AITD carry a significantly increased risk of miscarriage compared to women without AITD.¹⁷

Hyperprolactinemia was found in 33.3%, irregular menstrual cycle 66%, amenorrhea 6.7% and oligomenorrhea 59.3%.⁴ Normal menorrhea 33.3% and galactorrhea in 3.3% primary infertile women.

Ovarian factor contributes about 20% cases of infertility. It could be because of the congenital absence of the ovaries, or failure to ovulate.

Female infertility occurs in about 37% to 40% of all the cases. The infertile patients with ovulatory dysfunction usually present with primary infertility. They usually have higher than required BMI (>30) oligomenorrhea, amenorrhea, hirsutism and other associated hormonal abnormalities. However, the patients with normal or low BMI may present with anovulation.⁵

Pcos is not a single entity, rather a syndrome; there are two agreed definitions of P.C.O.S. In 1990 consensus workshop by NIH and NICHD suggested, that a person has PCOS if they have the following criterion.

i. Oligoovulation

ii. Signs of androgen excess. (Chemical or bio chemical).

iii. Exclusion of other disorders that can result in menstrual irregularity and hyperandrogenism.

Another definition is that PCOS is present if any out 2 out of 3 criteria are met. In the absence of any other entities that might cause these findings oligoovulation and anovulation, excess androgen activity, polycystic ovaries by gynecological ultrasound.

Clinical hyperandrogenism is characterized by acne, male pattern of baldness and the elevated androgen levels. There are also minor criterion of PCOS e.g. insulin resistance and disturbed ratio of LH and F.S.H. >2.5 - 3. PCOS is present in 15-20% of cases of infertility and 95% cases must be further investigated to exclude other causes e.g. free insulin, DHEAS, morning 17 hydroxyprogesterone, 24 urine for cortisol. These patients should also be investigated for undiagnosed diabetes which is present in 10% of the cases and by GTT, which is disturbed in 35% of the cases. The long term consequences of PCOS are cardiovascular diseases and endometrial cancers, however it protects the patients from osteopenia and osteoporosis. The short term consequences are increased prevalence of diabetes, PIH and recurrent pregnancy losses.

There is no definite definition of PCOS however there are major criterions and minor ones. The major includes

menstrual irregularity due to oligo and anovulation. Clinically and biochemically these patients should be investigated for undiagnosed diabetes, in 10% of the cases and by GTT, which is disturbed in 35% of the cases.

An ovulatory infertility may be the result of ovarian failure, gonadotropin failure resulting from hyperprolactinemia, normoprolactinemia cases with tumors or low gonadotropin secretion, polycystic ovarian syndrome and thyroid disease.¹⁸

There is hyperandrogenism in PCOS a study on mice it was found that orally administered rhFSH restored estradiol level and reduce the percentage of cystic follicles. Further studies are needed although the present data supports the concept that orally administered FSH could attenuate some of the characteristics of the PCOS in the mouse model.

The causes of premature ovarian failure are chromosomal aberrations, e.g. 47xxy. There is a high risk of malignancy and they must be treated by gonadectomy. The other causes may be turner syndrome xx/xo mosaic pattern. It could be because of resistant ovarian syndrome. The premature menopause is less than 45 years of age. The incidence is 1:250 by the age of 35 and one in 100 by the age of 40. It usually presents with irregular periods and infertility and the symptoms are similar to menopause. There is high FSH, and LH 10-20% has a family history. It may be iatrogenic and treatment option is IVF with a donor eggs.

Premature ovarian failure is another important cause of infertility especially in young women who presented with amenorrhea. Current evidence suggests that DHEA administration appears to objectively improve ovarian reserves.

Artificial reproductive techniques have given relief to such patients in the form of cryopreservation in females who are prone to have premature ovarian failure and who have to go under radiation therapy for certain malignant conditions.

However sometimes the only option for many such women is ova donation.⁶

Serum T3, T4 and TSH level were statistically highly significant among infertile woman. High incidence of hypothyroidism was found in infertile patients who presented with menstrual irregularities,⁷ the hyperthyroidism patients presented with amenorrhea or oligomenorrhea.

Thirty eight (38%) of the PCO's patients presented with infertility, primary or secondary and 85.3% presented with menstrual irregularities. Abnormal uterine bleeding was the most common presentation and 48.2% had weight disorders. Type II or gestational diabetes were diagnosed in 13.9%.⁸ Hyper prolactinemia is the presence of abnormally high prolactin levels in the blood, values lesser than 580 mille international unit/L were considered normal for woman, up to 2400, they

were because of micro adenomas and values greater than 4000 may be because of macro adenomas of the pituitary glands which may present with other physical symptoms also. The P.C.O's patients may present with amenorrhea (30-40%), oligomenorrhea, (75-90%) and an ovulatory infertility in about 70% of the patients. The BMI is usually more than normal in such patients; however 20-30% of the patients may be asymptomatic or have normal weight or even less than normal. Insulin resistance is the main pathology and it is inherited by an autosomal dominant mode. It also causes subfertility by causing early losses and recurrent miscarriages. Unexplained infertility is found in about 25 to 30 % of the cases. In a study it was found that data do not support the hypothesis that unexplained infertility is caused by an abnormality in pulsatile GnRH secretion or abnormal pituitary sensitivity to GnRH.²¹

MATERIALS AND METHODS

The observational descriptive study was done in Govt. Aziz Bhatti Hospital (NSMC) for one year 2014-2015. Infertile female patients who presented with primary and secondary infertility among patients who were married and in the reproductive age group (15-49). The hormone profile was advised on the day 2 of the menstrual cycle especially F.S.H., L.H and prolactin, the patients who presented with amenorrhea were given hormones for withdrawal bleeding and then profile done and at random in irregular bleeding. Thyroid hormones were advised depending upon the history and positive symptomatology. The study was not funded. The duration of the fertility was not considered. Data analysis was done on SPSS 16

RESULTS

About 108 patients were included in the study, majority of the patients were in the reproductive age group. Majority of the patients (51.8%) were in the 20-29 years age group. Forty four percent (44.44%) patients were in the 30 to 39 years age group. It is obvious in table one that there are only a few females in the 40 to 44 years age group and also 45 to 50 years, because either they have completed the family or they have accepted the eventuality. (Table I)

Table No.I: Age as a determinant of infertility (n=108)

Age in years	No. of patients	Percentage
< 20	0	0
20-29 years	56	51.8%
30-39 years	48	44.44%
40-44	Zero	Zero
43-50	04	3.7%

The various hormonal imbalances and their percentages are explained in the table 2.

As is obvious in table II, 64.81% of the patients were having normal hormonal profile; the reason is that either the couple is having psychological, male factor, other female factors, unexplained infertility and other reasons for secondary infertility.

Table No.2. Hormones Profile with infertility among the patients (n=108)

Category of the Patients	No of Patients	Percentage
Normal F.S.H & L.H	70	64.81
Patients of P.C.O's	12	11.11
Premature ovarian failure	12	11.11
Hypo gonadotrophic hypogonadism	02	1.85
Menopausal	04	3.7
With Thyroid disorders	08	
Hyperthyroidism	04	3.70
Hypothyroidism	04	3.70
Hyperprolactinemia		
< 400	08	7.4
> 400	00	

About 12(11%) of the patients presented with the hormone profile indicating PCO's with increased L.H and normal F.S.H. It was strange to see that about the same number 11.11% patients presented with premature ovarian failure, they presented with primary and secondary infertility but majority were with secondary infertility. About 3.7% presented with a profile in the range of menopause and 3.7% each presented with hyper and hypothyroidism and 7.4% of the patients with hyper prolectinemia. About 7.4% of the patients presented with hyper prolactinemia which was less than 4000 international units.

DISCUSSION

Age is an important determinant of the fertility, due to changing social scenario more women opting to have career present in the 3rd and fourth decade for infertility treatment. In a study by Korula George and Mohan S.Kamath.⁹ It was found that fertility and aging are closely linked and age of the female partner remaining the single most important factor in the treatment of infertility, although the tests for this are the poor predictors. The same was evident in this study, that there was no patient < 20 years who presented with infertility. Majority of the patients were in the 3rd and fourth decade and a little number from 40 to 50 years. It was found in this study that about 30% of the patients presented with hormonal imbalance. The various categories which were detected were patients with P.C.O's, premature ovarian failure, premenopausal and

a sizeable number with thyroid disorder. However none of the patients was found with significant hyperprolactinemia.

In a study by Kausta E and associates¹⁰ found that prevalence of P.C.O. was significantly higher in each of the infertility groups than in controls and a similar tendency was found among women with un-explained infertility. The similar trend was found in this study, the incidence of P.C.O's was 11%. However the patients with P.C.O's were the majority among the patients with hormonal imbalance, 12 out of 30.

The same number of patients was with premature ovarian failure which presented with primary, but majority were with secondary infertility, twelve patients out of thirty were with premature ovarian failure.

In his study by Paolo Beck – Pecoz and Luca Persani¹¹ it was found that this defect affects about 1% of the patients. It may present with primary or secondary amenorrhea. Beyond infertility, hormone defect may cause severe neurological, metabolic or cardio vascular consequences, and lead to early onset of osteoporosis.

About 7.4% patients presenting with infertility were having thyroid disorders equally as hyper and hypothyroidism.

However in their study by Priya DM, Akhtar N. and Ahmad J, it was found the incidence of hypothyroidism was 53.7% (TSH > 4.6 Micro Litter Units / ml). After treatment with thyroxin, 33.3% of the subclinical hypothyroid women conceived within six months to two years period and thus they concluded, that thyroid should be included in infertility profile work up.¹²

However no significant hyper prolectinaema was found in this study and only two patients of (1.85%) hypo gonadotrophic, hypogonadism presented with infertility, and 3.7% of the patients were menopausal but still seeking for conception. Sharma N. & Associates concluded in their study that high incidence of hyperprolectinemia was found in fertile women and a positive correlation was found between hyperprolectinemia and hypothyroidism¹³.

Emokpae MA & Associates found in their study that 33.7% had hyperprolactinemia among infertility patients. Subclinical hypothyroidism was observed in 29.9% and 70.1 % in primary and secondary infertility respectively. Mean levels of thyroid stimulating hormones and prolactin were higher in secondary infertility than primary infertility. The ratio of proportions between hypothyroidism and hyperprolactinemia 1:7¹⁴

The hypo gonadotrophic hypogonadism patients are treated with exogenous hormones. They found that 12/14 women 80% achieved one or more live births after treatment¹⁵

CONCLUSION

In this study the patients who presented with infertility and associated hormonal imbalance, 64.8% of the

patients had normal hormone profile. The patients with PCO's and premature ovarian failure were among the patients with disturbed hormone profile presenting with infertility.

Unuane and associates (16) found in their study that female infertility occurs in 37% of all infertile couples and ovulatory disorders account for more than half of these.

The various endocrine disorders, found were, hypo gonadotrophic, hypogonadism, hyper prolactinemia, acromegaly and Cushing's disease, thyroid disorder and primary ovarian disorders such as, polycystic ovarian syndrome and primary ovarian infertility and they proposed an algorithm to investigate such patients.

Thyroid disorder was among the others whose patients presented with infertility. It is concluded that patients who presented with infertility and menstrual disturbances must be investigated regarding hormone profile. The normal hormone profile gives a psychological advantage and to search for other reasons of infertility. The causes of the hormonal imbalance were treatable, hormonal imbalance was one of the major reasons of anovulation and even if not treatable saves the patients from undue investigations, psychological trauma and looking for other causes. Hormonal imbalances presenting with menstrual irregularities is one of the reasons for ovulatory infertility also which if treated properly ends up in reassuring results.

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

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