A three-year review of reproductive hormonal profiles of infertile women attending gynaecological clinics at UITH, Ilorin

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Abstract

Background: Reproductive hormonal profile is an invaluable tool in evaluation of infertile women. It aids the diagnosis of biochemical causes of infertility and monitoring of patients on treatment for infertility of various causes. This study highlights the various patterns of hormonal profile results obtained from female patients being evaluated for infertility and seeks correlations between these patterns, age at presentation and anovulation.

Methodology: This was a retrospective cross-sectional study of 555 women who carried out hormonal profile as part of their evaluations for infertility, over a 3-year period between 1st of January 2013 and 31st of December 2015.

Results: Of the 555 women whose results were reviewed, 188 (33.9%) had primary infertility and 367 (66.1%) had secondary infertility. The mean age of the participants was 33.7±5.3 years. Two hundred and twenty one (38.1%) were anovulatory, 229 (41.3%) had adequate ovulatory cycles and 105 (18.9%) had ovulatory cycles with luteal phase insufficiency. The pattern of hormonal abnormalities included 15 (2.7%) with hypogonadotrophic hypogonadism, 29 (5.2%) with normogonadotrophic normogonadism, 57 (10.3%) with hypergonadotrophic hypogonadism, 78 (14.1%) with hypergonadotrophic normogonadism. Three hundred and seventy six (67.7%) had normogonadotrophic normogonadism with 80 (14.4%) being hyperprolactinemic and 16 (2.9%) had hyperandrogenism.

Conclusion: Secondary infertility, hypergonadotrophism, anovulation and hyperprolactinemia are relatively common findings among our patients.

Keywords: Reproductive, Hormonal patterns, Infertile, Women.

Introduction

Infertility is defined as the inability of a couple to achieve conception after at least one year of regular, unprotected sexual intercourse.[1] About 10-15% of couples are infertile.[2] Primary infertility is infertility in a couple who have never achieved conception. Secondary infertility is failure to conceive following a previous pregnancy.

Female infertility accounts for about 40-50% of causes of infertility among couples.[1] Causes of female infertility can be classified

aetiopathologically into acquired and genetic causes or classified based on sites of pathology into hypothalamo-pituitary, ovaraian, tubal, uterine, cervical and vaginal causes.

Reproductive hormonal disorders cut across various classifications of causes of female infertility, either as aetiological factors or humoral responses to other causes of female infertility. The hypothalamo-pituitaro-gonadal axis plays a central role in synthesis, release and regulation of reproductive hormones. Measurement of the hormones synthesized or released from the different component of this axis aids the specific diagnosis of reproductive hormonal disorders causing infertility.

Reproductive hormones including follicle stimulating hormone (FSH), luteinizing hormone (LH), oestradiol (E_2), progesterone (P), prolactin (PRL) and testosterone (T), regulate all aspects of a woman's reproductive development and functions such as germ cell development, ovulation, copulation, fertilization, pregnancy, lactation, menstruation and development of external genitalia.

Reproductive hormonal assay is a routine investigation in the evaluation of females with infertility. It aids the diagnosis of hormonal causes of infertility and monitoring of therapeutic interventions in infertility. Patterns of reproductive hormonal profile abnormalities include: hypergonadotrophic hypogonadism (end-organ resistance/ failure), hypogonadotrophic hypogonadism (hypothalamic/ pituitary insufficiency), hyperprolactinaemia (common cause of menstrual abnormalities and anovulation), anovulation, luteal phase insufficiency and hyperandrogenism etc.

This study highlights the prevalence and various patterns of reproductive hormonal profiles obtained from female patients being evaluated for infertility.

Methodology

This was a retrospective cross sectional study of five hundred and fifty five women who were referred for reproductive hormonal profile as part of their evaluations for infertility over a 3-year period. They were referred from the gynaecological clinics in UITH, Ilorin. Ethical approval was sought and obtained from the University of Ilorin Teaching Hospital Ethical committee. Data was retrieved from laboratory records of infertile women with a complete reproductive hormonal request performed on samples collected on day 21 of their menstrual cycles. Patients on hormonal replacement therapy and bromocriptine were excluded. Serum Follicular Stimulating Hormone (FSH); Luteinizing hormone (LH), Prolactin (PRL), Progesterone (P), Oestradiol (E_2) and

Testosterone (T) were analyzed using AccuBind ELISA Microwell test kits (Monobind Inc, Lake Forest, CA 92630, USA) by resident doctors of the Department of Chemical Pathology between 1st of January 2013- 31st of December 2015. The absorbance value for each test was used to determine the corresponding concentration of the hormone from the standard curve developed using the kit standards. Internal controls levels 1 and 2 were run with each standard curve as quality control.

Reference intervals of the reproductive hormones[3] are:

FSH: 2-12mIU/ml

LH: 0.5-10.5mIU/ml

E_2: 44-196pg/ml

P: 2-25ng/ml

PRL: 1.2-19.5ng/ml

T: 0.25-0.9ng/ml

Progesterone was considered as a marker of ovulation and its serum levels aid in diagnosis of ovulatory disorders.

Levels < 3ng/ml → Anovulation

Levels 3-9 ng/ml → Ovulation with luteal phase insufficiency

Levels ≥ 10ng/ml → adequate ovulation

The profile tests were reported biochemically as follows: hypogonadotrophic hypogonadism (decreased FSH, decreased LH, decreased P, and decreased E_2), hypergonadotrophic hypogonadism (elevated FSH and LH, with decreased PROG and E_2), hypergonadotrophic normogonadism (elevated FSH and LH with PROG and E_2 within reference limits) normogonadotrophic normogonadism (all analytes within reference intervals), hyperprolactinaemia (elevated serum PRL), hyperandrogenic state (elevated serum testosterone).

Data analysis

Data was compiled and computed using Microsoft Excel 2010 and analysed using its inbuilt basic tools. The means and standard deviations were calculated for the two classes of infertility. Percentages were calculated for various patterns of biochemical diagnosis of infertility and patterns of ovulation.

Results

Of the 555 women whose results were reviewed, 188 (33.9%) had primary infertility and 367 (66.1%) had secondary infertility. (Table 1) The mean age of the study was 33.7 ± 5.9 years. The mean age of women with primary infertility was 31.0 ± 5.7 years, and those with secondary infertility was 35.1 ± 5.5 years. (Table 2) Two hundred and twenty one women (39.8%) were anovulatory, 105 (18.9%) women had ovulatory cycles with luteal phase insufficiency and 229 (41.3%) had adequate ovulatory cycles. (Table 3)

The pattern of reproductive hormonal abnormalities revealed the following: 15

(2.7%) with hypogonadotrophic hypogonadism, 29 (5.2%) with

Table 1: Classification and mean values of age of infertility normogonadotrophic hypogonadism, 57 (10.3%) with hypergonadotrophic hypogonadism, 78 (14.1%) with hypergonadotrophic normogonadism and 376 women (67.7%) had normogonadotrophic normogonadism.(TABLE 2) Eighty (14.4%) were hyperprolactinaemic and 16 (2.9%) had hyperandrogenism. (Table 4)

Variables	Primary infertility	Secondary infertility	Total
Number of cases	188	367	555
Percentage (%)	33.9	66.1	100
Age (years)	31.0 ± 5.7	35.1 ± 5.5	33.7 ± 5.9

Discussion

Among 555 women who presented for evaluation within the period of review, secondary infertility cases predominate with incidence rate of 66.1%. This is comparable to similar studies in the Northern part of the country with incidence rates of 63.3% [4] and 67.2 [5] but lower than the 80% [6] in another similar study done at south western part of the country. This may be due to relatively high literacy level which encourages presentation at healthcare facility in the southern part of the country.

The mean age at presentation was 33.7 ± 5.9 years, with 31.0 ± 5.7 years and 35.1 ± 5.5 years for primary and secondary infertility respectively, this may be due to delay in marriage because of education or delay in presentation at the healthcare centre for management.

Two hundred and twenty-nine patients (43.1%) were ovulating adequately in our study, this differs from another study done in Lagos, south west Nigeria [7] where 82.6% were found to be ovulating adequately. Also 39.8% of our patients were anovulatory while 18.9% had luteal phase insufficiency (LPI) higher than 11.5% and 5.9% respectively in the same comparable study.[7] LPI has been implicated in female infertility, recurrent pregnancy loss and unsuccessful assisted reproduction.[8]

Hypergonadotrophic normogonadism and Hypergonadotrophic hypogonadism suggestive of end-organ resistance/ failure are 14.1% and 10.1% respectively. This Hypergonadotrophic state found in 24.2% of our patients is considerably lower than the prevalence of 53% found in a similar study by Kuku et al [7] in Lagos, where at least one of the gonadotrophins is elevated. Hypogonadotrophic hypogonadism,

Table 2: Patterns of biochemical diagnosis of infertility

Pattern	Number	Primary infertility (%)	Secondary infertility (%)	Percentage (%) of infertile patients
Hypogonadotrophic hypogonadism	15	4 (0.7%)	11 (2.0%)	2.7
Normogonadotrophic hypogonadism	29	8 (1.4%)	21 (3.8%)	5.2
Hypergonadotrophic hypogonadism	57	17 (3.1%)	40 (7.2%)	10.3
Hypergonadotrophic normogonadism	78	29 (5.2%)	49 (8.8%)	14.1
Normogonadotrophic normogonadism	376	130 (23.4%)	246 (44.3%)	67.7
Total	555	188 (33.9%)	367 (66.1%)	100

Table 3: Patterns of ovulation

Ovulatory pattern	Number	Primary infertility (%)	Secondary infertility (%)	Percentage (%)
Anovulation	221	68 (12.3%)	153 (27.5%)	39.8
Luteal phase insufficiency	105	42 (7.6%)	63 (11.3%)	18.9
Adequate ovulation	229	78 (14.1%)	151 (27.2%)	41.3
Total	555	188 (33.9%)	367 (66.1%)	100

Table 4: Other aetiologic patterns of infertility

Aetiologic pattern	Number	Primary infertility (%)	Secondary infertility (%)	Percentage (%) of infertile patients
Hyperprolactinaemia	80	33(5.9%)	47(8.5%)	14.4
Hyperandrogenic state	16	9(1.6%)	7(1.3%)	2.9

suggesting hypothalamo-pituitary disorder, resulting in decreased serum gonadotrophins level and consequently decreased gonadal hormones, was found in 2.1% of our patients. This was the least common pattern of reproductive hormonal disorder in our patients.

Hyperprolactinemia is a known cause of infertility resulting from menstrual abnormalities and anovulation.[9] This maybe because it causes hypogonadotrophic hypogonadism by either directly or indirectly inhibiting the secretion and release of gonadotrophins, resulting in menstrual abnormality and infertility.[10] Hyperprolactinemia was found in 14.4% of patients in this study. This is consistent with 18% found by Avasthi Kumkum et al [11] but

comparably lower than 28% by Olooto et al [12] and 26.2% found by Kuku et al. [7]

2.9% of our patients had hyperandrogenism, a major diagnostic criterion in diagnosis of polycystic ovarian syndrome, which is a major cause of infertility.[13] The other criteria include chronic anovulation and polycystic ovaries.

Conclusion

Secondary infertility, end-organ resistance leading to hypergonadotrophic state, anovulation and hyperprolactinemia are relatively common findings among our patients. The importance of biochemical investigation of the infertile couples cannot be over emphasized.

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Conflict of interest: Nil