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Research Article

Pattern of Hormonal Imbalance among Women of Child-bearing Age in a Tertiary Healthcare Centre in Southern Nigeria

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Abstract

Background and Objectives: Infertility is a common social problem among women and it is linked to many etiologies. This study was done to assess the pattern of hormonal imbalance among infertile women of child-bearing age attending a tertiary health facility in Calabar, Nigeria. **Materials and Methods:** A total of 119 women with infertility were assessed for quantitative fertility hormone values to determine if hormonal imbalance was implicated in the cause of infertility in them and the pattern of hormonal abnormality/imbalance they have. **Results:** The study involved a total of 119 female adults of child-bearing age, whose ages ranged between 20 and 49 years with an average age of 31.95±6.87 years. Women aged between 25-29 years had the highest prevalence of infertility due to hormonal imbalance. Of the 119 women the distribution with hormonal imbalance caused infertility was 96.6%. Reduced luteinizing hormone levels accounted for the highest pattern of infertility (71.6%), while prolactin excess was next (42.9%). Low levels of day 21-progesterone/luteal phase insufficiency accounted for the highest singular hormonal causative factor in women aged 40-44 years. However, there was no significant difference in the ages of the women and the progesterone values as a criterion in determining the cause of infertility ($p < 0.305$), same applied to prolactin, luteinizing hormone and follicle stimulating hormone levels, respectively. **Conclusion:** This study shows that hormonal imbalance is a major cause of infertility among women and that the pattern of imbalance varies widely. Reduced luteinizing hormone levels with consequent anovulation was the commonest presentation in the population studied.

Key words: Infertility, hormonal, child-bearing, prolactin, anovulation

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Infertility is defined as a medical condition characterized by inability to conceive after a year of regular unprotected sexual course. It is a common social problem and usually affects more than 10-15% of marriage couples^{1,2}. This condition can arise from various etiologies which range from localized to systemic problems. Both males and females are equally affected^{3,4}. In Africa and indeed Nigeria, because of the varied level of literacy, infertility is often linked to superstitious beliefs by some people. This goes a long way to aggravate the situation in the affected couple who may not even know the reason for their childlessness. Globally, Common causes of infertility may include premature ovarian failure, fallopian tube blockade, endometriosis, leiomyoma, obesity and hormonal imbalance^{5,6}. Many researches done in our environment have not been able to identify the commonest causes of infertility among our childless women. Most of the cited articles in this regard by authors, are from researches done outside our African environment. Thus, this study aims to explore the hormonal causes of infertility among our women, with emphasis on our environment.

Hormonal imbalance, as a cause of infertility in women could present as hypogonadism (with resultant low estrogen), hyperprolactinemia, polycystic ovary syndrome (PCOS), thyroid dysfunctions among others^{7,8}. Low levels of female sex hormones are associated with infertility for example, low or insufficient Luteinizing Hormone levels could lead to failure to anovulation and subsequent decreased day 21 progesterone levels. The PCOS is a common of female infertility in our environment. It is indeed the most common cause of infertility due to anovulation. It is believed to occur in 40% of women with infertility⁹. Infertility is a public health issue and is deeply associated with stigma to the women folk. Despite all possible investigations, infertility may also be due to unexplained reasons or idiopathic accounting for about 30% of infertility cases. The PCOS, a common cause of infertility in women is also associated with hormonal imbalance¹⁰. This study assesses the pattern of hormonal imbalance commonly presenting in patients with infertility presenting at the University of Calabar Teaching Hospital in South Southern part of Nigeria.

MATERIALS AND METHODS

Experimental site: The research was done at the fertility clinic and the Department of Chemical Pathology of the University of Calabar Teaching Hospital over a 6-month period between February, 2019 and August, 2019.

Materials and research tools: Women of child-bearing age between the ages of 20 and 49 years who were being investigated for infertility were recruited for this study. These were selected randomly from the lot of women who were referred from the Gynaecology clinics to the Chemical Pathology laboratory of the University of Calabar Teaching Hospital. Selected women were counseled after which written consents were obtained.

Data collection: Records of detailed history and physical examinations in addition to non-hormonal investigations were obtained from their hospital medical records to rule out other causes of infertility in them. A total of 119 women were eventually recruited after a 60-day sampling period. 5 mls of venous blood was then drawn from the ante-cubital fossa under aseptic procedure into plain sample bottles and allowed to clot after which they were spun to separate serum from the clot. The serum was then assayed using Enzyme Linked Immunosorbent Assay (ELISA) technique to quantify the levels of the reproductive hormones.

Parameters measured: The serum levels of luteinizing hormone (LH), oestradiol (E₂), testosterone, prolactin, progesterone and follicle stimulating hormone (FSH).

Statistical analysis: Statistical analysis was done using SPSS for windows version 18. All variables were reported as mean value \pm standard deviation for the valuables. A p-value of more than 0.5 was concluded to be statistically significant. Appropriate statistics were used to analyze the data. Data were represented in both tabular form and pie chart.

RESULTS

Biostatistics: Majority of the women studied (29.4%) were between 25 and 29 years. Only 4.2% were aged between 45 and 49 years (Table 1, 2). Of the 119 women the distribution with infertility attributed to hormonal abnormalities was 96.6% (Fig. 1). Hormonal abnormality in this study was defined

Table 1: Age distribution of participants

Variables	Frequency (n =119)	Percentage
Age group (years)		
20-24	14	11.8
25-29	35	29.4
30-34	30	25.2
35-39	19	16.0
40-44	16	13.4
45-49	5	4.2
Mean \pm SD	31.958 \pm 6.868	
Median \pm Interquartile range	31.00 \pm 11.00	

Table 2: Association between sex hormone abnormalities and age of participants

Variables	Infertility status based on all criteria						Test statistic	
	Yes		No		Total		Chi-square test	p-value
	Number	Percentage	Number	Percentage	Number	Percentage		
^a Age group (years)								
20-24	14	100	0	0.0	14	100	7.719 ^f	0.048*
25-29	35	100	0	0.0	35	100		
30-34	30	100	0	0.0	30	100		
35-39	17	89.5	2	10.5	19	100		
40-44	14	87.5	2	12.5	16	100		
45-49	5	100	0	0.0	5	100		

^aGeneral infertility using the combined criteria, ^fFisher's exact test, *Statistically significant

Table 3: Association between day 21 progesterone only with infertility

Variables	Infertility status based on all criteria						Test statistic	
	Yes		No		Total		Chi-square test	p-value
	Number	Percentage	Number	Percentage	Number	Percentage		
^a Age group (years)								
20-24	3	21.4	11	78.6	14	100	5.932 ^f	0.305
25-29	11	31.4	24	68.6	35	100		
30-34	9	30.0	21	70.0	30	100		
35-39	4	21.1	15	78.9	19	100		
40-44	9	56.3	7	43.8	16	100		
45-49	1	20.0	4	80.0	5	100		

^aInfertility based on progesterone profile only, ^fFisher's exact test, no significant between ages of child bearing age women and infertility based on progesterone alone criterion at $p \leq 0.05$

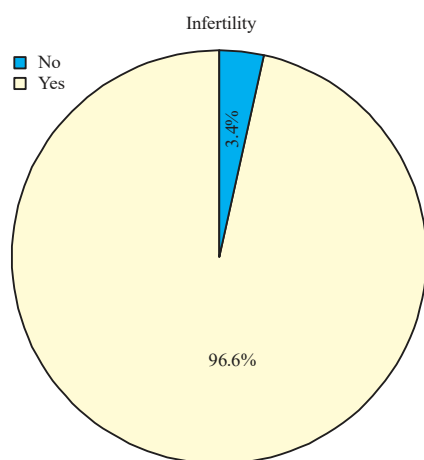


Fig. 1: Pie chart showing the distribution of respondents whose infertility was attributed to hormonal imbalance

as women who had either a high serum prolactin levels, a low serum FSH (reference range 1.5-30 ng mL⁻¹), a low serum LH level (reference range 5-20 ng mL⁻¹) or a low day 21 serum progesterone level which signifies luteal phase insufficiency (reference range 2.5-32 ng mL⁻¹). These could occur singly or in any combination, reduced LH accounted for the highest pattern of hormonal abnormality causing infertility (7%), followed by elevated serum prolactin levels (Hyperprolactinemia) which accounted for 43% of cases.

Hormonal findings: Women aged between 25-29 years had the highest prevalence of hormonal abnormalities, generally hormonal abnormalities were seen to be commoner in women aged 25-29 years using all criteria ($p < 0.048$) (Table 2). Low levels of day 21 progesterone (luteal phase insufficiency) accounted for the highest singular hormonal cause of infertility in women aged 40-44 years (56.37%). Though, there was no significant difference in the ages in of the women and the progesterone values as a criterion in determining the cause of infertility ($p < 0.305$) (Table 3). The same applies to prolactin, LH and FSH levels.

DISCUSSION

This study reveals that among the causes of infertility, hormonal imbalance stands out among the causes in our own environment. This finding is of great importance as it guides the managing physician about the areas to give attention when managing patients with infertility. This study corroborates with previous work^{8,11,12}. Fertility declines with age in both men and women, but effects are greater in women than in men¹². More than 15% of human couples are infertile and out of this, about 50% of infertility are linked to the female factors^{13,14}. Many studies have studied hormone levels in the treated groups with hormonal infertility to understand responses to these treatments in this regard^{15,16}.

Table 4: Distribution of individual sex hormone as cause of infertility

Variables	Frequency (n =119)	Percentage
Hormone		
Progesterone	37	31.1
Luteinizing hormone	84	70.6
Follicle stimulating hormone	21	17.6
Prolactin	51	42.9

Infertility affects 10-20% of reproductive-age couple and ovulatory dysfunction accounts for 29% of infertility in women¹². Studies have shown that 12-15 and 10% of couples are unable to achieve conception after one and 2 years of adequate unprotected sex respectively¹⁷. Hormones play great roles in the overall fertility output of both men and women¹⁸. Hormonal causes of infertility account for a large number of infertile women¹⁸. In this study, a large number of the reproductive women (42.9%) had hormonal imbalance as the cause of their infertility. This is in agreement with the findings of other authors that support the notion of high hormonal-caused infertility¹⁹. Hormonal imbalance is a common cause of female infertility. Exaggerated or reduced levels of prolactin, follicle stimulating hormone and luteinizing hormone and reduced levels of oestradiol in addition to high unchallenged testosterone levels may affect fertility in women. Hormonal imbalance in women could cause ovulatory dysfunction such as anovulation, in addition to preventing the thickening of the uterine lining in preparation for implantation of fertilized ovum. These imbalances/abnormalities may be caused by drugs, diet, lifestyle modes, pathologies along the pituitary-ovarian axis, endocrinopathies and some metabolic conditions⁶. There is a delicate balance of several hormones affecting fertility in female adults. Assessment of these hormones (prolactin, LH, FSH, progesterone, oestradiol and testosterone) have been used to evaluate infertility in women^{15,16}. Excess prolactin, as demonstrated by 42.9% of subjects in this study suppresses gonadotrophin releasing hormone (GnRH) secretion which may eventually end in anovulation (Table 4). The day 3 testing of the ovarian hormones were assessed. These include FSH, LH and oestradiol. Ovulation and hormonal problems can be from defects in the hypothalamus, the pituitary, or the ovary. Alteration of the gonadotrophic sex hormones (LH, FSH) affects the fertility rate of most women, also alterations or disturbances in the normal secretion or release of gonadotropin releasing hormone can lead to an ovulatory cycle with subsequent infertility⁹.

Two other endocrine causes of are hyperprolactinemia and thyroid diseases. Excess prolactin can account for one

third of women experiencing amenorrhea. It also causes subfertility in both men and women. Common causes of hyperprolactinemia are pituitary tumors especially adenomas, polycystic ovary syndrome, chronic kidney failure and medications such as alpha methyl dopa (aldomet), opioids, metoclopramide and phenothiazines. These would usually present with irregular/absent menstruation, headache, visual disturbances, loss of libido and loss sexual potency with resultant low levels of follicle stimulating hormone and luteinizing hormone and oestradiol⁹.

Diminished secretion of LH and FSH as observed in 70.6 and 17.6% of our subjects, respectively has been known to cause gonadal failure with eventual infertility. LH is also known to stimulate oestradiol secretion, so low levels as seen in this study is likely to result in low levels of oestradiol. Leach *et al*/noted that some women with infertility whose hormonal levels were monitored had diminished levels of sex hormones²⁰. The commonest age with the highest number of infertility were women aged between 25-29 years (Table 2). Tulandi *et al*. in their study considered age 36 years and above in females as a common age range for infertility to occur and most the women studied had tubal-based factors as the cause of infertility²¹. Again, the effect of age on female fertility was further explained by Maheshwari *et al*.²² They concluded that causes of infertility in infertile women were different in different age groups. Women over 35 years of age are said to be usually twice as likely to have unexplained infertility. Infertility is as serious social problem with a prevalence as high as 6.1-32.6% in some studies²³.

In summary, many causes of infertility exist and the commonest cause of hormonal-based infertility in our environment is reduced luteinizing hormone levels and hyperprolactinemia, a fact demonstrated by this study (70.6 and 42.9%, respectively). It is possible that the reduced levels of LH in this subjects may be due to hyperprolactinemia, as raised levels of prolactin may be associated with suppression of LH and with consequent inhibition of ovulation and eventual infertility^{14,15,16,17}.

CONCLUSION

This study assesses hormonal imbalance as a cause of infertility among women of child-bearing age. Information from this study raises awareness to the managing physician to have a high index of suspicion of hormonal imbalance as a possible cause of infertility since it is a common finding from this study.

SIGNIFICANCE STATEMENT

This study discovered that, in our environment, a major cause of infertility was linked to hormonal imbalance. This study will help researchers to uncover the fact that hormonal imbalance as a cause of infertility should be given a high priority when managing women with this condition.

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