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BIOCHEMICAL INFERTILITY AMONG FEMALES ATTENDING UNIVERSITY OF ILORIN TEACHING HOSPITAL, NIGERIA

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ABSTRACT

Background: Biochemical laboratory investigations potentially contribute to the diagnosis of over 50-75% of couples being investigated for infertility. Both hormonal and anti-hormonal treatments have achieved great successes in the treatment of infertility. Our aim therefore was to investigate the pattern of biochemical abnormalities in females diagnosed as infertile form anovulation.

Material and Methodology: One hundred and twenty women diagnosed clinically as primary or secondary infertility from anovulation referred from the gynecological clinic of UITH and private hospitals in Ilorin were investigated by routine fertility test profile.

Result: The age ranged between 20-40 years (mean = 32.9, sd±4.7) for the primary infertility and 23-47 years (mean = 34.4, sd±5.4) for the secondary infertility groups respectively. Ninety six (80%) subjects were found to have hormonal abnormalities. Pattern of biochemical diagnosis amongst the 33 (34.4%) primary infertility subjects included hypergonadotrophic hypogonadism 21 (63.6%), hypogonadotrophic hypogonadism 9 (27.3%), and hyperprolactinemia 3 (9.1%). Among the 63 (65.6%) cases of secondary infertility, there were 31 (49.2%) cases of hypergonadotrophic hypogonadism, 30 (47.6%) hypogonadotrophic hypogonadism, and 2 (3.2%) hyperprolactinemia. There was no statistical difference in the mean values in the various biochemical parameters.

Conclusion: Hormonal profile should be a goal standard in the diagnosis of anovulation.

Key Words: Infertility, Females, Biochemical (Accepted 22 January 2008)

INTRODUCTION

Infertility remains a common medical problem in developing countries[1]. Between 8-12% of couples around the globe have difficulty conceiving a child at some point in their lives despite regular unprotected sexual intercourse for more than 12 months[2]. Problems of infertility still remain the leading cause of gynecological clinics attendance in Nigeria[3].

The socio-cultural implications of infertility are grave, since childlessness is a major personal tragedy and a limitation for the individual concerned in this part of the world. It is an established cause of serious emotional disturbance, social and psychological pain for the couple especially the woman; and also a common cause of divorce.[4,5]

Various factors affecting either or both of the couple are known to cause infertility. Despite this knowledge, it is the woman that is always at the receiving end, blamed and held responsible for it. She is also the one to find solution to 'her problems' hence she is the one often seen in fertility clinic.

In Africa, female factors account for about 25 37% of infertility, while male factors contribute between 8-22% and the remaining are either due to combination of both male and female factors as well as unexplained factor[6]. This then suggests that female factors still contribute significantly to infertility problems. Unfortunately, 64% of infertile women in Sub-Sahara Africa have diagnosis that could be attributed to infectious causes most of which are from preventable conditions[7] as well as tubal problems and other related infections from post partum and abortion complications.

Even though about 26% of women in Chile[8] experienced delayed in conception that lasted more than 12 months, interestingly, experiences in fertility clinics from India[9] have shown that 38% supposedly infertile couples eventually conceive even without treatment, while 27% conceived before the completion of treatment.

Mayaud[10] stressed that in sub-Saharan Africa few studies have investigated the infertile couple, and most have focused only on the female partner. Tubal factor infertility plays a predominant role in female factor infertility in sub-Saharan Africa[10,11]. The major cause of tubal factor infertility is pelvic inflammatory disease (PID) resulting from an infection either from sexually transmitted diseases (STDs), such as gonorrhea and chlamydia, or from complications following an induced abortion, childbirth or

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invasive medical procedure. Ovulatory disorders are also common in Africa, but the prevalence varies widely.

Infertility due to endocrine dysfunction was previously thought to be uncommon in African women but with the introduction of immunoassay and other sophisticated technologies in gynecological practice in Africa, this problem has been found to constitute an important cause of infertility in African women[1,4,5]. The causes of infertility in women are many and approximately 40% of couples will have more than one cause for their infertility[3,6] Various ovulatory disorders ranging from luteal phase deficiency to anovulation are estimated to account for up to 15% of all infertility problems6. Recent advances in endocrinology points to the fact that the hypothalamus pituitary ovarian axis is essential for the smooth operation of the mechanism of the endocrine function which leads to ovulation,[2] and priming of the endometrium for implantation of the zygote which has to pass through a normal fallopian tube following fertilization.[12] Failure resulting in abnormally high or low gonadotrophin, sex hormones and cortisone like hormones can cause infertility.

The focus of this study therefore was therefore to investigate the pattern of biochemical abnormalities in females diagnosed as infertile.

MATERIALS AND METHODS

This was a cross sectional study of one hundred and twenty women diagnosed clinically as primary or secondary infertility form anovulation referred from the gynecological clinic of UITH and private hospitals in Ilorin were investigated by routine fertility test profile from January to December, 2005. The exclusion criteria included medications such as oral contraceptive pills and bromocriptine as obtained from the patients medical records.

Follicular stimulating hormone (FSH); Leutinizing hormone (LH), Prolactin, Progesterone and Estradiol was analyzed for each clinical group using micro well ELISA test kit for quantitative determination from Diagnostic automation Inc catalog no 4224, 4225, 4226, PG 96, and 2046Z respectively by resident doctors of the department of Chemical Pathology. 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 calibration curve as quality control instrument.

The profile tests in the two clinical groups were reported biochemical as either of the three: hypergonadotrophic hypogonadism (? FSH, LH, PROL, ?PROG, ?ESTRADIOL), hypogonadotrophic hypogonadism (?FSH,? LH, PROL, ?PROG, ?ESTRADIOL), hyperprolactinaemia (?FSH,? LH, ??PROLACTIN, ?PROG ?ESTRADIOL).

The data obtained was subjected to statistical analysis using the SPSS statistical soft ware package. The comparism of continuous variables was done using the Student t test while probability value of $p<0.05$ indicated a statistically significant difference.

RESULT

A total of 96 (80%) subjects comprising of 33 (34.4%) primary infertility and 63 (65.6%) secondary infertility cases out the 120 subjects analyzed had hormonal abnormalities. The age ranged between 20 and 40 years (mean = 32.9±4.7) for the primary infertility group and 23 and 47 (mean = 34.4±5.4) for the secondary infertility group respectively as contained in table 1

The biochemical pattern of infertility in this study as shown in table 2 showed that 52 (54.2%) of the cases had hypergonadotrophic hypogonadism profile and 39 (40.6%) had hypogonadotrophic hypogonadism profile. Only 5 (5.2%) showed the hormonal profile compatible with hyperprolactinemia.

Also shown on table 2, is the pattern of biochemical abnormalities in the two clinical groups. Majority (63.6%) of the primary infertility and 49.2% of secondary infertility cases respectively have hypergonadotrophic hypogonadism, while only a few 9 (23.3%) primary infertility cases had biochemical picture consistent with hypogonadotrophic hypogonadism. This was in contrast to the 30 cases (47.6%) with the same biochemical profile in secondary infertility. There were no statistical differences (p-values as shown on table 3) in the mean values of the biochemical parameters between the various biochemical diagnosis in the two groups, except for the LH values (p=0.01) in the hypergonadotrophic hypogonadism and PRL (p=0.03) and ESTR values (p=0.03) in the hypogonadotrophic hypogonadism diagnosis.

Table 1: **Mean Values of Age and Infertility Profile**

Variables	Primary Infertility	Secondary Infertility	p-value
Number of cases	33 (34.4%)	63 (65.6%)	
Age	34.4 ± 5.4	32.9 ± 4.7	0.4
Follicular Stimulating Hormone (FSH)	19.9	27.8	0.1
Luteinizing Hormone (LH)	23.7	21.4	0.6
Prolactin Hormone	29.1	33.9	0.6
Progesterone	3.9	4.3	0.9
Estrogen	29.1	26.2	0.6

Table 2**: Biochemical Diagnosis of Infertility by Group.**

	Primary Infertility n=33	Secondary Infertility n=63	Total	p-value
Hypergonadotrophic hypogonadism	21 (63.6%)	31 (49.2%)	52 (54.2%)	0.4
Hypogonadotrophic hypogonadism	9 (27.3%)	30 (47.6%)	39 (40.6%)	0.1
Hyperprolactinemia	3 (9.1%)	2 (3.2%)	5 (5.2%)	0.6
Total	33	63	96 (100%)	

Table 3: **P-values of the Biochemical Pattern in the Biochemical Diagnosis between Primary and Secondary Infertility.**

Diagnosis	Age	FSH	LH	PRL	PROG	ESTR
Hypergonadotrophic hypogonadism	0.45	0.06	0.01	0.40	0.90	0.50
Hypogonadotrophic hypogonadism	0.71	0.58	0.39	0.03	0.77	0.03
Hyperprolactinemia	0.06	0.60	0.60	0.60	0.60	0.60

DISCUSSION

Infertility is defined as the inability to establish a pregnancy within a specified period of time, usually one year despite regular, adequate unprotected sexual intercourse. Forty to fifty percent of all consultations in gynaecological clinics in Nigeria are due to cases of infertility as it affects 20-25% of married couples[13].

Infertility is reported to be common between the ages of 20 and 44years with an incidence of 8-12% in various parts of the world[14]. In Nigeria, the incidence of infertility was reported in a study [15] to be 14.8% with about three quarters (71.1%) between 25 and 34 years of age and mean duration of 3.38±1.65 years. Majority (78.3%) of the cases were reported due to secondary infertility. This agrees with the incidence of 8% with age of 32.9±4.7 years for the primary infertility and 34.4±5.4 years for the secondary infertility in our study. This observation is also consistent with another finding where the pregnancy rate at age 19-26 years is twice as those between 35-39 years of age and the probability of pregnancy at age 40 years to have declined to 67%.[15]

However, the mean age of primary infertility in this study may not be consistent with the African culture of early marriages in which one would have expected problems of child bearing to be exposed very early in marriage. However, many studies have shown that this could be due to the late presentation at the hospitals as many alternative measures may have been explored.

Our findings showed that there is a preponderance of the secondary infertility in a ratio of 2:1 compared to the primary infertility. This may be attributable to the high incidence of pelvic infections which may be contracted through intercourse, postnatally and after abortions. This is consistent with the findings in other Sub-Sahara Africa and Latin America reports where secondary infertility is more common[16,17].

Female factors have been shown in many studies to be responsible for more than half of the causes of infertility in Nigeria[13,15] In about 25% of cases of infertility, more than one factor is said to be responsible for the childlessness,[13] while in 4% the infertility is unexplained. The commonest cause of female infertility in Nigeria is the diseases affecting the Fallopian tubes. Other causes include anovulation (absence of ovulation), Uterine / Cervical factors and Endometriosis. Tubal factors are very common in Nigeria as in other parts of Africa due to a high incidence of pelvic infections.

In a combined data from over 5000 infertile couples, 30% of problems were related to ovulation and 22% to seminal defects. Biochemical laboratory investigation potentially contribute to the diagnosis of over 50% of couples investigated.[18] In Nigeria, ovulatory disorders, hormonal disorders, endometriosis and genital tuberculosis have been shown to be common causes of infertility[19].

The cause of infertility (including biochemical) was obvious in 279 (89%) of the 314 couples that completed their evaluation while 35 couples (11%) had unexplained infertility. The type of infertility (primary or secondary) had no influence on whether the aetiology is identified or not [20]. This was similar to our observation where more than 75% of the suspected anovulatory women had a known biochemical cause of their infertility. Various ovulatory disorders ranging from ovarian agenesis, failure and resistance leading to anovulation are estimated to be the second common cause and it accounts for up to 15-18% of all infertility problems in a previous study.[13] Female infertility treatment in Nigeria must now therefore place emphasis on tubal factors and also to an extent anovulation factors which we taught previously was not a common cause.

Hyperprolactinemia inhibits gonadotropin-releasing hormone (GnRH), thus inhibiting gonadal steroidogenesis, which is the cause of the inhibition of ovulation. Whereas, many previous studies whereas recorded 37% in Lagos, Nigeria, [21] 33% reported in Maiduguri and 31.6% was reported in Egypt, North Africa,[22] hyperprolactinaemia was seen in 5.2% of our subjects. Our study also demonstrated that hyperprolactinemia is more likely in the primary infertility though the difference was not significant when compared with secondary infertility. Many (88%) of the primary and secondary infertility cases presented clinical diagnosis of anovulation in our study in contrast to the women with secondary infertility who are more likely to presented with amenorrhoea (2% with primary and 34.6% with

secondary amenorrhoea).[23]

The mechanism by which hyperprolactinaemia leads to menstrual disorders and infertility have been described by several investigators.[22, 24] It is important to mention that studies have shown that increased prolactin may render the ovary less responsive to the effects of gonadotropin when given exogenously to induce ovulation.

The biochemical pattern of hypogonadtropic hypogonadism is characterised by the under production of follicular stimulating hormone (FSH) and Luteinizing hormone (LH) which prevent the development of functional ovaries. Severe post partum haemorrhage which has been documented to be a common complication of birth in Nigeria has been associated with thrombosis of the pituitary blood vessels from profound hypotension and hypovolaemia. This could be the most probably reason for the high percentage in secondary infertility. Other cause of this biochemical pattern that could be responsible for the 27.3% cases in primary infertility is the functional hypothalamic amenorrhoea (FHA). This is usually due to disturbance in the thyroid gland and hypothalamus-pituitary-adrenal (HPA) system. Eating disorders such as anorexia and bulimia are most often associated with FHA. Very rarely, the main cause of hypogonadotropic-hypogonadism in primary infertility is the pituitary infantilism which is characterized by primary amenorrhoea and low or absent serum levels of FSH and no Estrogen.

Polycystic ovarian syndrome has been reported to occur in about 6% of women with primary infertility and this is characterised by increased testosterone production and low FSH and progesterone levels.

In most cases, the cause of hypergonadotropic-hypogonadism is unknown. Unfortunately, this biochemical pattern accounts for the infertility in half of the cases as well as being the commonest pattern observed in both the primary and secondary infertility respectively. This was observed to be commoner (63.7%) in the primary infertility. This is characterised by high serum FSH and LH levels with a corresponding low levels of sex hormones (estrogen and progesterone). Premature ovarian failure which is the early depletion of follicles before age 40 and in most cases lead to premature menopause has been associated in some studies as a cause of secondary infertility. Women with this condition have only 5-10% chance to conceive without fertility treatments. Luteal phase defect is very common (25-60%) in recurrent miscarriages particularly in primary infertility. This is characterised by low serum progesterone.

Other factors that could cause biochemical infertility would include weight and excessive exercise, smoking, vaginal douching, hormone-distrupting chemicals, drugs, stress, chronic endocrinology illness and metabolic syndrome with an incidence rate of 25-30%. However, the influence of these factors on biochemical infertility could not be said to be more commoner in either type of infertility even though some studies have attributed vaginal douching and hormone-distruption to be more associated with primary infertility, while exercise, weight, smoking and chronic illness with secondary infertility.

In conclusion, hormonal profile should be a goal standard in the diagnosis of anovulation. This is because biochemical evaluation is the focus of a potential source of great successes in hormonal manipulation in the management of infertility.

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