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SERUM FOLLICLE STIMULATING HORMONE AND LUTEINIZING HORMONE IN PATIENTS WITH ANOVULATORY DISORDERS WITH PRIMARY INFERTILITY

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Abstract:
Background: *Infertility is defined as the inability to conceive after one to two years of unprotected intercourse. It is of two types: primary infertility and secondary infertility [5]On the basis of etiopathology infertility is divided into five groups: unexplained (28%), male factor (24%), ovarian dysfunction (21%), tubal factor (14%) and others (13%). Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) are integral parts of the neural and endocrine interchange between the hypothalamus, pituitary, and gonads that control steroid hormone synthesis and gamete production.*
Method: *It's a Cross sectional (Descriptive Study) done from 24th May to 24th Nov 2014 for duration of six months in 143 patients of gynae department of Ayub Teaching Institute.*
Results: *A total of 143 female patients presenting with an ovulatory cycle with primary infertility. Average age of the patients was 29.14years+5.65SD with range 20-38 years. The deranged follicle stimulating hormone and deranged luteinizing hormone in IU/L among women presenting with an ovulatory cycle with primary infertility was observed in 85(59.44%) and 56(39.16%) respectively.*
Conclusion: *The deranged follicle stimulating hormone and deranged luteinizing hormone in IU/L are the considerable factors among women presenting with an ovulatory cycle with primary infertility*
Key Words: *Follicle stimulating hormone, luteinizing hormone, an ovulatory cycle, primary infertility*

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INTRODUCTION:

Infertility is defined as the inability to conceive after one to two years of unprotected intercourse [1]. WHO in 1991 estimated that 8-12% of couples experience some form of infertility in their reproductive life, thus affecting 50-80 million of couples worldwide [2]. It is of two types: primary infertility, when there is no preceding pregnancy and secondary infertility when couple previously had pregnancy irrespective of its outcomes [3]. Infertility is a major problem affecting women's health and quality of life [4]. In Pakistan the prevalence of infertility is reported as 21.9% [5]. On the basis of etiopathology infertility is divided into five groups: unexplained (28%), male factor (24%), ovarian dysfunction (21%), tubal factor (14%) and others (13%) [1].

Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) are integral parts of the neural and endocrine interchange between the hypothalamus, pituitary, and gonads that control steroid hormone synthesis and gamete production [6]. Both LH, and FSH are required for follicle development and estrogen production and hence low levels of these hormones mean fewer numbers of follicle will develop, and no graffian follicle will develop[2]. The pattern of GnRH pulses changes during ovarian cycle. The pulse frequency and amplitude gradually increases during follicular phase.FSH causes recruitment and maturation of follicles, and subsequent enlarge in estradiol level stimulates an accelerated GnRH pulse frequency triggering the LH mid-cycle surge which initiates ovulation [7]. A normal follicular growth is the result of complementary action of both FSH and LH hormones [8]. FSH level can be as low as 0.5 IU/L at the luteal phase nadir and as high as 20 IU/L at the midcycle peak. However, values below 1 IU/L are associated with hypothalamic pituitary failure and values above 20 IU/L or above indicate ovarian failure as in menopause. LH value can be as high as 20 IU/L at bicycle, and in polycystic ovaries its value can be raised to 13-25 IU/L with normal values of FSH [9].

Anovulation is the common cause of infertility. WHO classified an ovulation in 3classes.[10] I. hypogonadotropic hypogonadism [10]. II Hypothalamic pituitary dysfunctions [10] and III. hyper gonadotrophic hypogonadism [10]. Infertility resulting from ovulatory dysfunction account for about 21% or a fifth of all of infertility and 30% of female infertile patients. Studies carried out in Pakistan quote this figure between 16–48%. It was placed at a much higher figure in India in a community based study [11][1]In most mammalian species; spontaneous ovulation is preceded by a surge of both FSH and LH. This combined gonadotropin surge is thought to be necessary for final oocyte nuclear maturation (meiosis) and initiation of follicular rupture [12]. In one study, the frequency of abnormal FSH levels among infertile women was 39.1% and abnormal LH levels were 67.4%. In the same study, abnormal LH/FSH ratio was seen in 45.7% of women [13].

Infertility is not uncommon in our population and there is a strong need to generate local and fresh evidence about the deranged levels of FSH and LH among those infertile women who have anovulatory cycles. Infertility puts a serious threat to the existence of a married woman in a family and it also poses serious problems since our population seeks Hakeem and other non allopathic treatments as first choice [14]. After doing this study, we will get a fresh local data about the deranged FSH and LH levels among women who present to our settings with infertility and have anovulatory cycles. The results of this study will be useful to local health professionals in adjusting the management protocols for patients with primary infertility.

MATERIAL AND METHOD:

It is a Cross sectional study which is conducted in patients presented to Gynae unit B of Ayub Teaching Institute for the duration of six months from 24th May to 24th Nov 2014.Sample size was 143 calculated by using WHO software for sample size determination, using 39.1%[10] proportion of infertile women with deranged FSH levels. with 95% confidence level and 8% margin of error. Sample technique was Non-probability consecutive sampling. Women presenting with primary infertility presented with anovulatory cycles, and Reproductive age group (15-39 years) and duration of marriage more than 1 year were included in study. Women with secondary infertility or male factor infertility or unexplained infertility were excluded from study. All women who fail to achieve conception (as per operational definitions above) meeting the inclusion criteria were enrolled in the study through OPD. The purpose and benefits of the study were explained to the patients and they were assured about the confidentiality of data. An informed consent was obtained from all patients. Detailed history was taken and clinical examination was carried on all patients. Fasting sample of 5cc of blood were obtained under strict aseptic techniques and on day 03 of the menstrual cycle and were sent immediately to hospital laboratory to determine the levels of FSH and LH. Deranged levels of LH and

FSH were determined in patients of anovulatory cycles presented with primary infertility. All the above mentioned information including name, age, address etc. were recorded on a pro forma. All the laboratory investigations were done under supervision of an expert pathologist having minimum of five year of experience. Ultrasounds were performed by expert ultrasonologist. Data were analyzed using SPSS version 10.0. Mean ± SD were calculated for quantitative variables like age, FSH and LH levels. Frequencies and Percentages were calculated for categorical variables like deranged LH and FSH levels. Deranged levels were stratified among age to see the effect modification. All results were presented in the form of tables and graphs.

RESULTS:

A total of 143 female patients presenting with anovulatory cycles with primary infertility were included in the study. Average age of the patients was 29.14years ± 5.65SD with range 20-38 years. Patient's age was divided in four categories, out of which most common age group for anovulatory cycles with primary infertility was above 31 years in our study. There were 14(9.8%) patients were of the age less than or equal to 20 years. Twenty-six (18.2%) patients were in the age range of 21-25 years, 32 (22.4%) were of age range 26-30 years, 71(49.7%) presented at age more than 31 years of age. (Table1)**.**

TABLE NO: 1 AGE WISE DISTRIBUTION OF THE PATIENTS

	FREQUENCY	**PERCENT**	**CUMULATIVE PERCENT**
<= 20.00	14	9.8	9.8
21.00 - 25.00	26	18.2	28.0
26.00 - 30.00	32	22.4	50.3
31.00+	71	49.7	100.0
Total	**143**	**100.0**	

The deranged follicle stimulating hormone in IU/L among women presenting with an ovulatory cycle with primary infertility was observed in 85(59.44%) while in 58(40.56%) women show no deranged follicle stimulating hormone. Similarly, deranged luteinizing hormone in IU/L among women presenting with an ovulatory cycle with primary infertility was observed in 56(39.16%) while in 87(60.84%) women show no deranged luteinizing hormone.

Age wise distribution of FSH was high in older ages as that of younger age. The patients having age less than or equal to 20 years of age have deranged FSH of 35.7%, age group 21-25 years 46.2%, 26-30 years' age groups 62.5% and patients having more than 30 years of age have 69% deranged FSH in women presenting with an ovulatory cycle with primary infertility. (Table 2) Age wise distribution of LH also shows same findings as that of FSH. The patients having age less than or equal to 20 years of age have deranged LH of 14.3%, age group 21-25 years 23.1%, 26-30 years' age groups 37.5% and patients having more than 30 years of age have 50.7% deranged LH in women presenting with an ovulatory cycles with primary infertility. (Table 3)

TABLE NO: 2 AGE WISE DISTRIBUTION OF FSH (TABLE 2) AND LH (TABLE 3) AMONG PRESENTING WITH ANOVULATORY CYCLES WITH PRIMARY INFERTILITY

		DERANGED FSH		TOTAL	P-VALUE
		YES	NO		
age (in years)	<= 20.00	5	9	14	
		35.7%	64.3%	100.0%	
	21.00 - 25.00	12	14	26	
		46.2%	53.8%	100.0%	
	26.00 - 30.00	20	12	32	**0.046**
		62.5%	37.5%	100.0%	
	31.00+	49	22	71	
		69.0%	31.0%	100.0%	
Total		**86**	**57**	**143**	
		60.1%	**39.9%**	**100.0%**	

TABLE NO: 3

		DERANGED LH		TOTAL	P-VALUE
		YES	NO		
age (in years)	<= 20.00	2	12	14	
		14.3%	85.7%	100.0%	
	21.00 - 25.00	6	20	26	
		23.1%	76.9%	100.0%	**0.015**
	26.00 - 30.00	12	20	32	
		37.5%	62.5%	100.0%	
	31.00+	36	35	71	
		50.7%	49.3%	100.0%	
Total		**56**	**87**	**143**	
		39.2%	**60.8%**	**100.0%**	

DISCUSSION:

Infertility is defined as the failure to conceive after one year of regular intercourse in women < 35 years not using contraception and after six months in women > 35 years[15]. Epidemiological data suggest that about 10% to 15% of all couples will experience difficulties to conceive (primary infertility). Based on a survey performed in developed countries, the World Health Organization (WHO) estimates that female infertility accounts for 37% of causes in infertile couples, male infertility for 8% and both – male and female infertility – for 35%. Five percent of couples have unexplained infertility and 15% became pregnant during the study. The most common identifiable factors that accounted for female infertility were ovulatory disorders (25%). Other reports describe ovulatory disorders as responsible for more than half of the causes of female infertility[16]. Hormone levels in infertile women had been evaluated by many researchers. Higher level of FSH and LH is rarely found in infertile women with a proper menstrual cycle but lower concentrations are observed [17]. Early follicular phase (2nd-5th day): FSH and inhibin B levels may show the likelihood of ovulation, especially in older women candidates for in vitro fertilization (IVF). FSH levels > 10 IU/L are considered predictive of poor pregnancy outcome, and >18 IU/L were reported as resulting in no live

births[18].Mid cycle: LH peaks before ovulation, achieving two to fourfold above baseline levels. Ovulation usually occurs 28-36 hours after the beginning of LH rise, and 8-20 hours after the LH peak. Estrogen levels, as well as those of FSH and progesterone, rise steadly from the follicular phase and reach an ovulatory peak. For monitoring purposes, LH peak can be measured in the blood, together with estrogen levels in assisted reproduction cycles of low complexity.

Our study coincides with study of K. Mohan & Mazher Sultana & suggests that decrease level of LH in the midcycle clearly indicates that there is a possibility of anovulation. Low levels of FSH and LH which may further explain the abnormal or delay ovum maturation.[19] FSH can influence the development of preantral follicles via paracrine factors[20]. However, growth of antral follicles becomes critically dependent on FSH support, making a preovulatory follicle capable of ovulation and forming a corpus luteum in response to the mid-cycle surge of LH[21].The separate but complementary roles of FSH and LH in stimulating folliculogenesis and ovulation are well established. However, it is not known if there are levels under which low LH concentrations may be equally or suboptimal for oocyte quality and subsequent embryonic development competence. On the other hand, there are some conflicting data related to the high levels of LH promoting follicular atresia and early miscarriage. This has lead to the concept of a 'therapeutic window' of LH for successful conception in ART and ovulation induction. As can be seen from the opposing results presented by various groups, the controversy surrounding the role of LH in ovarian stimulation has certainly not been resolved.

CONCLUSION:

The present study on FSH, LH levels in infertile women evaluates the hormonal profile of infertile women. Both luteinizing hormone (LH) and follicle-stimulating hormone (FSH) are required for follicle development and oestrogen production. Although FSH is universally recognized as the key driver of ovarian follicle growth and maturation, the role of LH in these processes is more controversial. Future studies are needed to better identify those who would benefit from the addition of LH and FSH.

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