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The Role of Anti Mullerian Hormone (AMH) Levels as Predictive and Diagnostic Biomarker of Age at Menopause Among Infertile Sudanese Women

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Abstract: *Infertility is a global health problem with an increasing incidence rate among Sudanese women. The study aimed to compare serum anti-mullerian hormone (AMH), folic stimulating hormone (FSH) and luteinizing hormone (LH) between primary infertility and secondary infertility. Furthermore, also to study the effect of woman's age on these hormones. The study was carried out in Khartoum State, Sudan during the period from January to March 2017. A cross sectional hospital included 260 infertile women [169 with primary infertility (mean age 32.7 ± 7.26 years) and 91 with secondary infertility (mean age 35.02 ± 6.25 years). Three ml of venous blood were collected in plain container and serum were obtained by centrifugation, all serum samples were analyzed for AMH, FSH and LH concentration using ELISA techniques. The results were showed significant difference in LH and AMH between primary infertility and secondary infertility (P value = 0.017, 0.001 respectively) and insignificant differences in FSH between them (P value = 0.606). Furthermore, the serum AMH level decreased in elder ages (P value = 0.000; r = - 0.4564) and increased of FSH level (P value = 0.001; r = - 0.199). In addition, the serum FSH levels increase in elder ages (P value = 0.001: r = -0.2036). In conclusion, the results of this study showed that hormones play a crucial role in diagnosis infertile women and serum AMH concentration has created more promising results to predicting age at menopause.*

Keywords— Sudanese infertile women, AMH, FSH, LH, menopause age.

1. INTRODUCTION:

Infertility is defined as the inability to become pregnant after at least one year of unprotected sex (1). It is still a global health problem with an increase in rate. An estimated 70 to 80 million couples worldwide suffer from infertility, mainly from developing countries, including the Middle East (2). The main health problem in these countries is severe social and psychological suffering (3).

Impaired fecundity is a condition associated with infertility and applies to women who have difficulty in pregnancy or pregnancy for a while the complex biological processes such as follicular development, maturation, division of oocytes, ovulation, and yellow body formation are coordinated by autocrine, paracrine, and endocrine factors and by the hypothalamic, pituitary axis, ovarian gland (4).

Follicles development depend on the interrelationship between many hormones such as folic stimulating hormone (FSH), luteinizing hormone (LH) and anti-mullerian hormone (AMH).

Follicle stimulating hormone (FSH) is main promoter of the organization and differentiation of follicular development in granulose cells of pre-ovulatory follicles (5). While LH plays a key role in initiating the ovulation process in follicles by activating multiple cellular signaling pathways (6).

Anti-Mullerian hormone (AMH) is a dimeric glycoprotein, which is a member of the transforming growth factor family. It is secreted exclusively by granulosa cells of primary, pre-antraland small antral follicles. Its secretion gradually diminishes in the subsequent stages of follicle development (7). Serum AMH concentrations have been correlated with the number of small follicles and hence ovarian reserve. The size of the pool of small follicles remains relatively constant during the menstrual cycle and consequently circulating AMH concentrations show minimal fluctuation throughout the menstrual cycle. The AMH gradually falls with advancing age owing to a depletion of the number of follicles as menopause approaches (8) an effect that are important for normal folliculogenesis. During follicular growth, as one follicle reaches a certain size, the AMH expression decreases resulting in an increased sensitivity of that follicle to circulating FSH, thus allowing it to continue growth with low levels of FSH until ovulation (7) (9). Thus the serum AMH concentration has may assist to predict age of women at menopause.

2. METHODOLOGY:

This is a hospital based cross sectional study conducted in Dr. Elsir Abu-Elhassan Fertility Center, Khartoum State, Sudan during the period from January to March 2017. Every patient was counseled and gave an informed consent prior to participating in the study after approval by the Minstry of Health in Khartoum State and Fertility Center. The study included 260 infertile women (169 with primary infertility and 91 with secondary infertility). Full history and information were collected by using questionnaire. Three ml of venous blood from each women was collected in plain container, then serum was obtained by centrifugation of blood at 3000 rpm for 10 minutes. The serum FSH, AMH and LH levels were measured by using ELSIA technique. The data were analyzed by SPSS(V 16.0) and Microsoft office (V 13).

3. Results:

The study include 260 infertile Sudanese women (mean age 33.5 ± 6.8 years; range between 20 to 50years) attended Dr. Elsir Abu-Elhassan Fertility Center. 169 with primary infertility (mean age 32.7 ± 7.26 years) and 91 with secondary infertility (mean age 35.02 ± 6.25 years). Most age group was 31 – 40 years (48.5%). The majority of the women were from urban regions (69%), while mostly were housewives (67.7%) (Table 1).

The serum LH and AMH levels were increased in primary infertility compared to secondary infertility (*P value* = 0.017, 0.001 respectively) and insignificant differences in FSH between them (*P value* = 0.606) (Table 2).

The serum FSH levels increased with age (*P value* = 0.035) while serum AMH levels was decreased with age (*P value* = 0.000) (Table 3).

The serum AMH levels were negatively correlated with serum levels of FSH women with infertility (*P value* = 0.001; r = -0.199) and women age's (*P value* = 0.000; r = -0.456) (Figure 1). The serum FSH was negatively correlated with women age's (*P value* = 0.001; r = - 0.462). Furthermore, the serum LH levels was positively correlated with serum levels of FSH (*P value* = 0.001: r = +0.462).

Table (1): Demographic characteristics for the study population.

Property	Frequency (N =260)	Percentage (%)
Age/year		
20 – 30 years	84	32.3%
31 – 40 years	126	48.5%
41 – 50 years	50	19.5%
Residence		
Urban	180	69%
Rural	80	31%
Occupational Status		
Work	79	30.3%
Housewife	176	67.7%
Student	5	2.0%

Table (2): Comparison of LH, FSH and AMH between primary and secondary infertility.

Hormones	Infertility types	N	Mean	SD	P value *
LH (IU/L)	Primary Infertility	169	11.80	12.1	**0.017**
	Secondary Infertility	91	10.64	12.9	
FSH (IU/L)	Primary Infertility	169	16.60	21.6	0.606
	Secondary Infertility	91	17.52	26.1	
AMH (IU/L)	Primary Infertility	168	6.18	10.2	**0.001**
	Secondary Infertility	90	3.54	7.0	

* P value > 0.05

Table 3. Comparison of LH, FSH and AMH between age group of infertile women.

Hormones	Age group	N	Mean	SD	P value *
LH (IU/L)	20 – 30 Years	84	9.72	7.4	0.108
	31 – 40 Years	126	11.32	13.6	
	41 – 50 Years	50	14.41	15.4	
FSH (IU/L)	20 – 30 Years	84	12.66	19.8	**0.035**
	31 – 40 Years	126	17.20	23.3	
	41 – 50 Years	50	23.37	27.0	
AMH (IU/L)	20 – 30 Years	83	10.42	12.3	**0.000**
	31 – 40 Years	125	3.48	6.9	
	41 – 50 Years	50	1.16	3.5	

* P value > 0.05

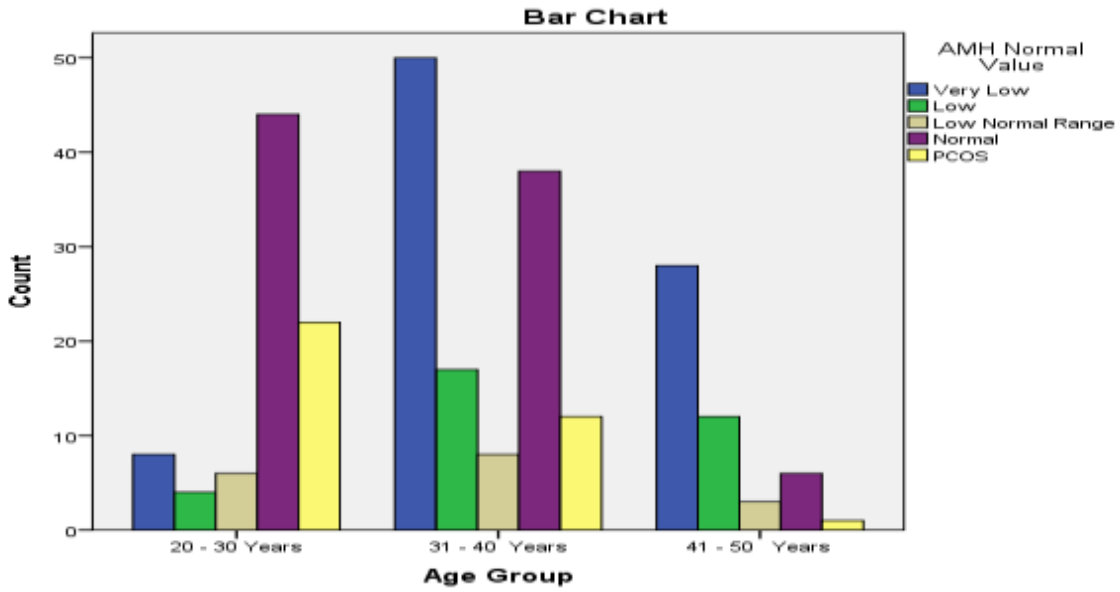

Figure (1): Coloration between AMH and Age group among population study.

4. Discussion:

Fertility is highly valued in most cultures and the wish for a child is one of the most basic of all human motivations. According to WHO (2015), the reproductive health including infertility take second problem, and affects 15 % of couples in the world, and more than 30% of marriage women their ages 25 – 49 years suffering from infertility in Africa WHO (2004). The aims of this study to compare serum anti-mullerian hormone (AMH), folic stimulating hormone (FSH) and luteinizing hormone (LH) between primary infertility and secondary infertility; in addition to study the effect of woman's age on these hormones. The present study is a hospital based cross sectional study carried out in Khartoum State, Sudan. In accordance to the socio-demographic data, the majority of the infertile women in this study were from urban regions (69%), and mostly were housewives (67.7%). This result is agree with study done in Iraq that indicated 81.18% infertile women lived in urban area (10) (unpublished data); and disagree with study done in Egypt that indicated 31.4% infertile women lived in urban area (11). Such differences may be attributed to the variations of the population community and the sample taken.

The study results showed significant increasing in serum LH levels of primary infertility compared to secondary infertility (*P value* = 0.017); this finding agreed with study done in Nigeria (12) and Sudan (13) who both noticed that serum LH was higher in women with primary infertility. Higher levels of serum LH more than normal levels in woman may mean the ovaries are absent or not functioning (14).The study also showed that there was insignificant difference in serum LH levels between age group (*P value* = 0.108); this finding consistence with study done in Sudan (15) and disagree with Lee *et al*. study that showed the mean concentration of LH wasn't changed with age (16).

Regarding to FSH levels, there were insignificant difference in serum FSH levels between primary and secondary infertility (*P value* = 0.606); this agree with Leach *et al*. study that demonstrated higher basal FSH levels in unexplained infertility compared with fertility-proven women (17). This finding may suggesting a subtle diminution of ovarian reserve as one of the etiologic factors in unexplained infertility. Furthermore, there was significant increasing in serum FSH levels with age (*P value* = 0.001, r = - 0.204); this result agreed with another study carried by Aroma *et al*. which showed that FSH and LH values above the normal limits suggests a problem arising from another component of the reproductive system, probably a defect in the negative feedback regulation mechanism in the hypothalamus by estrogen and progesterone (12). This can be supported with related similar study that indicated the significant increase levels of FSH with age, this results may be related to disturbances in the ovarian functions which are directly correlated with infertility (18).

Our results demonstrated a significant association between serum AMH levels and women fertility status (*P value* = 0.001). This finding consistance with the Eljak *et al*. study in which serum AMH was significantly lower in women with unexplained infertility as compared to controls (19).

The present study illustrated that powerful marker of ovarian reserve, namely serum AMH levels was falling with age (*P value* = 0.0001: r = - 0.456). These results consistence with de Vet *et al*. study that reported the serum AMH levels related with increase in age (20). Probably result was due to relative follicular attrition that characterizes the decline of ovarian function, with a noticeable reduction in the number of early antral follicles (21).

There was significant negative correlation between the serum AMH levels and the serum levels of FSH in women with infertility (*P value* = 0.001; r = - 0.199). De Vet *et al.* reported the serum AMH levels declined significantly whereas serum levels of FSH increase (20).

In this study, the average age of PCOS patients was significantly younger than non-PCOS patients. This finding is consistent with study done by Russell *et al*. who reported that the proportion of women with PCO decreased with age (6). This can be caused by a decrease in the number of antral follicles throughout the reproductive years that occurs in normal women (20).

5. Conclusion:

The results of this study showed that hormones play a crucial role in diagnosis infertile women and serum AMH concentration has created more promising results to predicting age at Menopause. Our results suggested that AMH is primarily a marker of ovarian function and not associated with other organ pathologies or metabolic disturbances. Study recommended AMH must be included in routine tests for women complain of infertility, and expand this study to include all hormones and increase study group.

6. Competing interests:

The authors declare that they have no competing interests.

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