

HORMONAL PROFILE IN EARLY MENOPAUSEEltayeb Tayrab*^{1&2}, Rasha Musa³ and Zeinab Abdalla¹¹Department of Chemical Pathology, National Riabt University, Faculty of Medical Laboratory Sciences, Khartoum, Sudan²Department of Medical Laboratories Sciences, College of Applied Medical Sciences, University of Bisha- Kingdom of Saudi Arabia.³Department of Laboratories and Blood Bank, Riabt University Hospital, Khartoum, Sudan.**Corresponding Author: Dr. Eltayeb Tayrab**

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ABSTRACT

Early cessation of the cycle in the reproductive age is harsh for women. The aim of this study was to evaluate the hormonal profile in infertile Sudanese women complaining of premenopausal amenorrhea, including serum luteinizing hormone (LH), follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), prolactin and estradiol (E2). This case control- cross sectional study was done in the 5 clinics of infertility in tertiary care hospitals in Khartoum-Sudan, from: May 2012 to December 2014. The study included 323 infertile premenopausal amenorrheic women and 198 ages matched women with proven fertility as control. ELISA method was used to measure serum levels of FSH, LH, TSH, prolactin and E2. Data was analyzed by IBM, SPSS version 20. The mean of the prolactin in the amenorrheic women was (121.5±1 265.12)ng/ml versus (15.09± 6.07)ng/ml in the control group; with *P. value* (0.000), FSH (50.33 ± 34.04) IU/ml versus (8.71 ± 31.29) IU/ml; with *P.value* (0.000), LH (34.89± 22.71) IU/ml versus (6.27± 2.55) IU/ml; with *P.value* (0.000), TSH (1.75± 2.02)IU/ml versus (1.27± 0.76) IU/ml; with *P.value* (0.004) and E2 (40.16± 34.30)pg/ml versus (50.68± 16.74)pg/ml ;with *P value* (0.029). The prevalence of secondary amenorrhea among the study group was 315 (97.5%). In premenopausal amenorrheic Sudanese; secondary amenorrheic is most common. Serum prolactin, FSH, LH, and TSH significantly increase; while estradiol significantly decreases.

KEYWORDS: Premenopause, amenorrhea, hormones, serum, Sudan.**INTRODUCTION**

Amenorrhea is the absence or abnormal cessation of menses.^[1,2] Primary amenorrhea is the failure to experience menarche by 13 to 15 years of age; with normal secondary sexual characteristics.^[3] Worldwide the prevalence of amenorrhea is approximately 3 to 4%.^[4] Primary amenorrhea is one of the common reproductive disorder affecting females in the reproductive age group^[5] this may be due to anatomical defects, when all or part of the uterus or vagina are absent in the presence of other normal female sexual characteristics.^[1,6] The most common etiologies of primary amenorrhea are the presence of gonadal dysgenesis.^[7] In primary amenorrhea there is a decrease in the initial primordial follicle number, high follicle-stimulating hormone (FSH) levels and hypoestrogenism.^[8] Secondary amenorrhea is characterized by cessation of previously regular menses for three months or cessation of previously irregular menses for six months.^[3] Lack of gonadal function is marked by high FSH levels, gonadal failure can occur at any age.^[1] Secondary amenorrhea affects approximately 6-10% of reproductive age women. Neuroendocrine

causes of amenorrhea and infertility, including functional hypothalamic amenorrhea and hyperprolactinemia, constitute a majority of these cases.^[9, 10, 11, 12]

Hyperprolactinemia is defined as higher-than-normal blood levels of the hormone prolactin.^[13] it is found in 0.3-17% of women presenting with hyperandrogenism and/or menstrual irregularities.^[14] it is also the most common cause of pituitary amenorrhea.^[15] The main cause of anovulation in hyperprolactinemic amenorrhea is impaired gonadotropin pulsatility and derangement of the estrogen-positive feedback effect on LH secretion in hyperprolactinemic patients.^[16] On the other hand, high prolactin levels are associated with anovulation or may cause directly or indirectly infertility. In young women, hyperprolactinemia is probably one of the most common endocrine disorders related to pituitary function.^[13,17] Hyperprolactinemia is associated with decreased estradiol concentrations and amenorrhea or oligomenorrhea.^[18] but prolactin concentrations are higher in women with amenorrhea than in those with oligomenorrhea.^[19] In premenopausal women, the ovaries are the principle source of estradiol, which

functions as a circulating hormone to act on distal target tissues.^[20] Estradiol concentration does not effectively distinguish between hypothalamic amenorrhea and polycystic ovary syndrome.^[21] Estradiol induces growth factors' activation, receptor activator of nuclear factor kappa B ligand production inhibition and is mainly referred to antiresorptive activity.^[22]

PATIENTS AND METHODS

This case control cross-sectional study assessed 323 infertile premenopausal women under 40 years and 198 ages matched apparently healthy volunteer women with proven fertility with no history of hormonal disturbance, served as control.

The purpose of this study was to assess the some endocrine hormones including serum luteinizing hormone (LH), follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), prolactin and estradiol in amenorrheic women, attending infertility centers. Blood specimens were collected under sterile conditions into sterile plain containers and the serum was separated by centrifugation into another plain container, and then stored at -70 °C till the time of analysis.

ETHEICAL CONSIDERATIONS

Ethical approval for the study was obtained from ethical committee of Federal Ministry of Health and National Ribat University. Informed written consents were taken from all the women participated in the study. The study was conducted in National Ribat University Hospital, Omdurman Maternity Hospital, Soba University Hospital, Reproductive Health Care Center (RHCC) and Sudan Reproductive Center (SARC) - Khartoum, Sudan. The study was done from May 2012 to December 2014. The precision and accuracy of all methods used in this study were checked by including commercially prepared control sera obtained from Biosystem- Spain.

STATISTICAL ANALYSIS

Data was analyzed using Statistical Package for Social Science (IBM- SPSS) version 20. *P. value* <0.05 was

considered significant. Student's *t*-test was used to compare means of the two independent groups.

RESULTS

The data of this study showed that among the amenorrheic group. The mean age of the amenorrheic women was (33.6± 6.2) years, while in the control group was (30.4± 6.1) years. The prevalence of primary amenorrhea among the study group was 8 (2.5%), while the secondary amenorrhea was 315 (97.5%). The mean age at menarche in the secondary amenorrheic women was 13.8(3.2) years, while in the control group was (14.2± 1) year (Table.1). In the amenorrheic group; panic hyperprolactinemia was observed in 10%, high TSH in 10.5%, high FSH in 74.5% and high LH in 73%. The study also showed that mean of the prolactin in the amenorrheic women was (121.51±265.12ng/ml versus (15.09± 6.07ng/ml in the control group; with *P. value* (0.000). The mean of the FSH in the amenorrheic women was (50.33±34.04)mIU/ml, versus (8.71 ± 31.29)mIU/ml in the control group; with *P.value* (0.000). The mean of LH in the amenorrheic women was (34.89±22.71)mIU/ml, versus (6.27±2.55)mIU/ml in the control women; with *P.value* (0.000). The mean of TSH in the amenorrheic women was (1.75± 2.02) mIU/ml versus (1.27±0.76)mIU/ml in the control group; with *P.value* (0.004). The mean of E2 in the amenorrheic group was (40.16± 34.30) pg/ml versus (50.68±16.74)pg/ml in normal fertile women; with *P.value* (0.029) (Table.1). The mean of the duration of marriage among amenorrheic women was (5.41± 0.63) years. When the study population was regrouped according to age; 88.7% of amenorrheic women were between 20-39years of age. The mean age in primary amenorrheic group was (21± 2.07) years. The mean of serum prolactin in the women with primary amenorrhea was (70.48±113.05)ng/ml, FSH (47.37± 31.81)mIU/ml, LH (40.71± 24.40)mIU/ml and TSH (1.13± 0.51)mIU/ml (Table. 2).

Table (1). T. test for comparison of different parameters between the amenorrheic women group and their control.

Items -*	Patients group (N**=323) (mean ±std)	Control group (N**=198) (mean±std)	<i>P. value</i>
Age (years)	33.6± 6.2	30.4± 6.1	
Menarche (years)	13.8± 3.2	14.2± 1	
Prolactin (ng/ml)	121.51± 265.12	15.09± 6.07	0.000
FSH (mIU/ml)	50.33± 34.04	8.71± 31.29	0.000
LH (mIU/ml)	34.89±22.71	6.27± 2.55	0.000
TSH (mIU/ml)	1.75±2.02	1.27± 0.76	0.004
Estradiol (pg/ml)	40.16±34.30	50.6±816.74	0.029

*Data was presented as (mean ±SD).

**N = number of cases

P. value <0.05 significant

Table (2). Descriptive study of the age, prolactin, FSH, LH and TSH in the women with primary amenorrhea.

Item	Minimum	Maximum	Mean	Std. Deviation
Age (years)	18.5	22.5	21.0	2.07
Prolactin (ng/ml)	3.30	334.50	70.48	113.05
FSH (mIU/ml)	4.80	91.70	47.37	31.81
LH (mIU/ml)	4.80	86.50	40.71	24.40
TSH (mIU/ml)	0.70	2.30	1.13	0.51

DISCUSSION

Early amenorrhea is a definitive cause of infertility and preventive factor for child production. Secondary amenorrhea is absences of menses for 3 cycles or six months in women with previous regular menstruation. In this study; approximately 96% of infertile Sudanese women with premenopausal amenorrhea have secondary amenorrhea; this finding raises many questions about the etiology of this condition; this phenomenon may associate with hormonal disturbance. In the present study prolactin is significantly elevated in the amenorrheic group, ten percent of these cases have panic hyperprolactinemia; similar finding was also reported by Touraine *et al* 2010^[19] this finding is in agreement with that reported by Allolio *et al* 1987^[23], Serri *et al* 2003^[24] and Patel *et al* 2007^[25]. Hyperprolactinemia is known as a common cause of amenorrhea according to the mechanism suggested by Matsuzaki *et al* 1994^[18]; in which hyperprolactinemia impairs estrogen-positive feedback on LH secretion and hence impairs gonadotropin pulsatility.

This study also shows significant increase in the gonadotropins -FSH & LH- in the infertile early amenorrheic Sudanese women; these finding are consistent to a Nigerian study reported by Adegoke *et al* 2007.^[26] FSH levels are higher in resistance ovarian syndrome, which occurs very rarely in younger menstruating infertile women; as written by Balen and Michelmores 2002.^[27] Hypersecretion of LH is associated with menstrual disturbances and infertility; that results in reduction of conception rates and increases in the rate of miscarriages as reported by Balen *et al* 1993.^[28] The variability in LH/FSH ratio is another important cause of ovarian dysfunction and infertility as written by ASRM 2008^[1]. The results of this study also reveal significantly high TSH in the premenopausal amenorrheic women compared to with their controls. The presence of high levels of TSH leads to low levels of thyroid hormones and interfere the ovulation. Hypothyroidism can affect fertility due to anovulatory cycle, luteal phase defect, hyperprolactinemia and sex hormone imbalance as reported by Poppe *et al* 2008.^[29]

The rate of depletion of the ovarian follicle store hastens at around the age of 37 years as reported by Yu and Yap 2003.^[30] but in this study the mean age of the study group is an only (33.5±6.0) year; which raises many questions again about the real causes of this early amenorrhea. In this study 8% of infertile amenorrheic Sudanese women have primary amenorrhea with the mean age of (21± 2.07) years. Hormone imbalances may

be due to exposure to some toxic chemicals that can lead to chronic anovulation or even amenorrhea, as reported by Olooto *et al* 2012^[31] and Cramer & Wise 2000.^[32]

CONCLUSION

Secondary amenorrheic is most common in the Sudanese women with premenopausal amenorrhea. In Sudanese women with premenopausal amenorrhea; serum prolactin, FSH, LH, and TSH significantly increase; while estradiol significantly decreases. The real cause of the early cessation of the cycle in the reproductive age should be widely searched especially in sub Saharan Africa like Sudan.

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CONFLICT OF INTEREST

The authors declared that they have no conflict of interest. The study was self-funded by the authors.

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