



A Retrospective Study to Determine Infertile Sudanese Women with Hyperprolactinemia

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ABSTRACT

This study aimed to determine prevalence rate of Sudanese infertile women with hyperprolactinemia attended Reproductive Health Care Center. The selected period of the study started from 2005 to 2010. The data was obtained from the statistical records available in the center to determine the prevalence rate of target group .Prolactin, FSH and LH serum levels were determined using Enzyme Immunoassay Technique (EIA). A total of 14129 infertile women attended the center during the study period, 4096 of them with hyperprolactinemia (prolactin < 400 IU / L) and a prevalence rate of 29% . Among the hyperprolactinemic subjects, 39.4% with FSH > 12.9 IU/ L and 12.2 % with LH > 9.6 IU/L Two groups were selected from hyperprolactinemic subjects. Group A which composed of 2333 (16.5% of total infertile women or 57% of hyperprolactinemic patients) were hyperprolactinemic with regular menstrual cycle . Group B which composed of 491 (3.5% of total infertile women or 12 % of hyperprolactinemic subjects) amenorrhic hyperprolactinemic patients. In conclusion, high prevalence of infertile Sudanese women with hyperprolactinemia was observed . Prevalence of women with hyperprolactinemia associated with high FSH was more common compared to those with hyperprolactinemia and high LH. Higher prevalence of Infertile hyperprolactinemic women with regular menstrual cycle compared to infertile hyperprolactinemic women with a menorrhea was observed.

المستخلص

هدفت هذه الدراسة لتحديد معدل شيوع النساء العقيمات المترددات على مركز رعاية الصحة الإنجابية. ولديهن إرتفاع في هرمون اللين. تم إختيار فترة الدراسة من العام 2005 حتى 2010 تم الحصول على البيانات الإحصائية المتوفرة في المركز لتحديد معدل شيوع الفئة المستهدفة . تم قياس هرمون اللين والهرمون المنبه للجريبات والهرمون الملتنوني بإستعمال طريقة الإنزيم المناعية . عدد النساء العقيمات المترددات على المركز في فترة الدراسة = 14129. اللاتي لديهن إرتفاع في هرمون اللين = 4096 بمعدل شيوع = 29 % .معدل شيوع النساء اللاتي لديهن إرتفاع في هرمون اللين < (400 IU/L) والهرمون المنبه للجريبات < (12.2

IU/L) يساوي 39.4% من مجموعة النساء الآتي لديهن إرتفاع في هرمون اللين . معدل شيوع النساء الآتي لديهن إرتفاع في هرمون اللين < 400 IU/L) والهرمون الملتنوني (< 12.2 IU/L) يساوي % 12.2 من مجموعة النساء الآتي لديهن إرتفاع في هرمون اللين . تم إختيار مجموعتين من النساء . المجموعة (أ) لديها إرتفاع في هرمون اللين مع إنتظام الدورة الشهرية . المجموعة (ب) لديها إرتفاع في هرمون اللين وانقطاع الطمث. عدد نساء المجموعة (أ) يساوي 2333 بمعدل شيوع يساوي % 16.5 من المجموع الكلي للنساء وبمعدل شيوع يساوي % 57 من مجموع النساء اللاتي لديهن إرتفاع في هرمون اللين عدد نساء المجموعة (ب) يساوي 491 بمعدل شيوع يساوي % 3.5 من المجموع الكلي للنساء وبمعدل شيوع يساوي % 12 من مجموع النساء اللاتي لديهن إرتفاع في هرمون اللين . خلصت الدراسة الى إرتفاع في معدل شيوع النساء العقيمات ولديهن إرتفاع في هرمون اللين. معدل شيوع النساء الآتي لديهن إرتفاع في هرمون اللين والهرمون المنبه للجريبات مرتفعاً مقارنةً بمعدل شيوع النساء الآتي لديهن إرتفاع في هرمون اللين والهرمون الملتنوني. معدل شيوع النساء الآتي لديهن إرتفاع في هرمون اللين مع إنتظام الدورة الشهرية مرتفعاً مقارنةً بمعدل شيوع النساء الآتي لديهن إرتفاع في هرمون اللين وانقطاع الطمث.

KEYWORDS: Prolactin ,a menorrhoea, infertility.

INTRODUCTION

Infertility is a lack of pregnancy within two years after marriage by regular coital exposure ⁽¹⁾. Infertility can also be defined as inability of getting pregnant at least 6 months to one year for women after 35 years old ,without using birth control means and while having normal sexual intercourse ⁽²⁾. There are 4 major factors causing infertility which include : female factor, male factor, combined factor and unexplained factor. In some West-African communities ,infertility rate is approximately 50% , in less developed countries , infertility ranged between 6.9% to 9.3% . The most common risk factor of infertility in Africa is sexually transmitted diseases (STD) ^(2,3,4) Human prolactin (PRL) is a polypeptide hormone composed of 199 amino acid synthesized and secreted by pituitary lactophors ⁽⁵⁾. PRL is also produced by mammary glands , placenta , uterus prostate gland and the brain ⁽⁶⁾. Factors inducing PRL synthesis include, secretion of estrogen, thyrtropin- RH and dopamine antagonist PRL is suppressed by hypothalamic dopamine

receptor antagonists ⁽⁵⁾. The most important prolactin inhibiting factor (PIF) is dopamine which is synthesized by the tuberoinfundibular dopaminergic neurons of the arcuate nucleus ⁽⁷⁾. PRL exerts a negative feedback by its own release, by stimulating hypothalamic dopamine synthesis (Ben-Jonathan and Hnasko⁽⁸⁾). Hyperprolactinemia is the presence of PRL in the blood higher than 22- 400 IU/L in females and 10-208 IU/L in males ⁽⁹⁾. Hyperprolactinemia is one of the most common endocrine disorders of hypothalamic – pituitary axis ⁽¹⁰⁾ . Hyperprolactinemia is a frequent cause of amenorrhoea , infertility and galactorrhea in women particularly young women ⁽⁹⁾. Most symptoms of hyperprolactinemia involves the decrease in gonadotropin secretion that leads to gonadal dysfunction ⁽¹¹⁾.

MATERIAL and METHODS

This is a retrospective study conducted in Reproductive Health Care Center to determine the prevalence of Infertile women with hyperprolactinemia attended the Center during the period from 2005 to 2010. Age of participants

ranged between 18 to 45 years. Existing statistical records and demographic data of the study group were obtained from Statistical Department of Reproductive Health Care Research Center, Khartoum. Prolactin, FSH and LH serum levels were determined using Enzyme Immunoassay Technique (EIA). Magnetic antibody washing buffer, diluted enzyme labeled were added to each sample at room temperature. Colored product was read in a calorimeter at 550 nm wavelength. Two groups from hyperlactinemic population were selected, group (A) were hyperprolactinemic with regular menstrual cycle, group (B) were hyperprolactinemic and a menorrhic (subjects with oligomenorrhea were excluded). After approval by Reproductive Health Care Center authorities – a written consent was obtained from each subject before sample collection. Quality control samples were standards from calibrated agent WHO IRP 84/ 500. Specific reagents standard magnetic antibody, labeled antibody, washing

buffer, substrate and assay buffers were obtained from Immunometrics (UK), Ltd, London.

RESULTS

Total number of infertile women attended the Center during the study period were 14129, those with hyperprolactinemia were 4096, (29%) and those with serum prolactin within normal range (22- 400 IU/ L) = 10033 (71%). Hyperprolactinemic subjects with high FSH (>12.9 IU/ L) were 1614 (39.4 %) from hyperprolactinemic population, high LH (> 9.6 IU/L) was observed in 499(12.2 %) from hyperprolactinemic population. FSH and LH within normal range(3.3 – 12.9 IU/L and 1.6 – 9.6 IU/L) was observed in 15.6 % (638) and 27.8 % (1138) from hyperprolactinemic populations respectively. Subjects with hyperprolactinemia and regular menstrual cycle (group A) were 2333 (57%) subjects with hyperprolactinemia and a menorrhic were 491 (12%).

Table 1: Prevalence of Sudanese Infertile Women with Hyperprolactinemia (2005-2010).

Year	Prolactin \geq 400mIU/L	
	NO	Percentage
2005	738	18.0%
2006	465	11.4%
2007	429	10.5 %
2008	452	11.0 %
2009	1079	26.3%
2010	933	22.8 %
Total	4096	100.0%

The number of infertile women attended Reproductive Health Care Center was 14129 (71.0 %) with normal prolactin level compared to 4096 (29%) with hyperprolactinemia.

Highest prevalence of women with hyperprolactinemia was observed in the year 2009 was 26.3% . Prevalence ranged between 10.5 % and 26.3% in

the years 2007 and 2009 respectively (table 1). $\frac{4096}{14129} = 29.0\%$

Prevalence of infertile hyperprolactinemic subjects attended the center during the study period =

Table 2: Prevalence of Sudanese Infertile Women with Hyperprolactinemia and regular menstrual cycle (2005-2010). (Group A)

Year	Prolactin \geq 400mIU/L (Total = 4096)	
	NO	Percentage
2005	155	3.8 %
2006	184	4.5%
2007	278	6.8 %
2008	266	6.5 %
2009	784	19.0%
2010	666	16.2 %
Total	2333	-

According to table (2), the prevalence rate of group A throughout the study period ranged between 3.8 5% in the year 2005 and 19.0 % in the year 2009. Number of Infertile hyperprolactinemic women with regular menstrual cycle was 2333 with prevalence from total population (14129) was 16.5 %, and from hyperprolactinemic subjects was 57.0%. Prevalence of infertile hyperprolactinemic subjects with regular menstrual cycle (from the total population) attended the center during the study period =

$$\frac{2333}{14129} = 16.5\%$$

Prevalence of infertile hyperprolactinemic subjects with regular menstrual cycle (from hyperprolactinemic population) attended the center during the study period =

$$\frac{2333}{4096} = 57.0\%$$

Table 3: Prevalence of Sudanese Infertile a menorrhic Women with Hyperprolactinemia

(Group B)(2005-2010).

Year	Prolactin \geq 400mIU/L Total = 4096	
	NO	Percentage
2005	72	1.8 %
2006	63	1.5 %
2007	82	2.0%
2008	97	2.4%
2009	90	2.2 %
2010	87	2.1%
Total	491	-

Prevalence of infertile women with hyperprolactinemia and a menorrhagia was 3.5 % from total population and was 12% from hyperprolactinemic subjects. Throughout the study period, the prevalence ranged between 1.8% in the year 2005 and 2.4% in 2008 (table 3). Prevalence of infertile hyperprolactinemic and a menorrhic subjects (from the total population) attended the center during the study period =

$$\frac{491}{14129} = 3.5 \%$$

Prevalence of infertile hyperprolactinemic and a menorrhic subjects (from hyperprolactinemic population) attended the center during the study period =

$$\frac{491}{4096} = 12.0 \%$$

DISCUSSION

The results of the present study revealed that the prevalence of hyperprolactinemia among infertile women visiting Reproductive Health Care Center during the period from 2005 to 2010 = 29% , a study in Central Sudan (Wad Medani)

concluded that the prevalence was 33.3 %⁽¹²⁾. Kars et al⁽¹³⁾ reported an overall prevalence of 29.5 per 100.000 among treated hyperprolactinemic women in Japan. However the prevalence of hyperprolactinemia worldwide varies from 0.4% to 70% in different patient populations⁽¹⁴⁾. Level of prolactin exceeding 1429 IU/ L is an indication of prolactinoma⁽¹⁵⁾, since prolactinoma was reported to be more common among women⁽⁹⁾. Moreover, breast stimulation can cause dopamine release via autonomic nervous system, which reduces dopamine inhibition of prolactin secretion, thus increasing prolactin production⁽⁹⁾. In addition, stress can cause hyperprolactinemia through inhibition of dopamine secretion⁽¹⁶⁾, since prolactin acts as an endogenous anxiolytic agent⁽¹⁷⁾. Other cause of hyperprolactinemia may be related to the relatively high expression of estrogen receptors⁽¹⁸⁾. Abdelghani et al⁽¹²⁾. observed a significant increase in FSH and LH serum levels of women with irregular menstrual cycle. Greenspan⁽¹⁹⁾ stated that primary gonadal failure results in elevation of FSH and LH. The present results revealed that subjects with

hyperprolactinemia and high FSH were 39.4%, and those with hyperprolactinemia and high LH were 12.2% from hyperprolactinemic population. Speroff and Fritz⁽²⁰⁾ concluded that high FSH and LH indicates ovarian abnormalities (hypergonadotropic hypogonadism), but normal or low levels of FSH and LH indicates pituitary – hypothalamic abnormalities (hypogonadotropic – hypogonadism), the authors observed lower concentrations of FSH and LH associated with high prolactin in primary infertile women, which further explain the abnormal or delayed ovum maturation. The prevalence of women with hyperprolactinemia and regular menstrual cycle in the present study was higher (57%) compared to the prevalence of infertile hyperprolactinemic females in Gezira State (33.3%)⁽¹²⁾. This may be a transient hyperprolactinemia due to increased serum prolactin concentration on the late follicular phase⁽²¹⁾. Alternatively this may be due to the presence of macroprolactin due to the presence of endogenous anti-prolactin antibodies, that acting like a binding protein which prolonged the half life and block receptor binding site⁽²²⁾. Macroprolactin is the main circulating form and it have been reported by several authors to be present in more than 15% of patients with hyperprolactinemia⁽²³⁾. Results of the present study showed that the prevalence of a menorrhic women with hyperprolactinemia was 12% compared to 6.7 % in Gezera State as reported by AbdElghani et al.⁽¹²⁾ One of the causes of hyperprolactinemia in this study may be due increase of pituitary hormones such as thyroid stimulating hormone, growth hormone, prolactin which act synergistically with follicle stimulating hormone and luteinizing hormones to enhance the entry of non-growing follicles into the

growth phase⁽²⁴⁾. Ezzat, et al⁽²⁵⁾ estimated the rate of women with a menorrhhea was 9% , while 70% were amenorrhic with galactohrrea . Studies by Serri et al.⁽⁹⁾ concluded that hyperprolactinemia in one-third of women with amenorrhhea, and in 75% of women who have both a menorrhhea and glactorrhea. According to Sunita et al.⁽²⁶⁾ hyperprolactinemia adversely affects the fertility potential by impairing the pulsatile secretion of Gn RH and hence interfering with ovulation. This disorder has been implicated in menstrual cycle and ovulatory dysfunctions like a menorrhhea and oligomenorrhhea.

CONCLUSION

High prevalence of infertile Sudanese women with hyperprolactinemia attended Reproductive Health Care Center was observed. Prevalence of infertile hyperprolactinemic subjects with high FSH was higher compared to hyperprolactinemic infertile subjects with high LH. The prevalence of infertile women with hyperprolactinemia and regular menstrual cycle was higher compared to infertile women with hyperprolactinemia and a menorrhhea.

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