British Journal of Medicine & Medical Research
4(5): 1269-1278, 2014

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Reproductive Hormonal Profile of Post-menopausal Women in Ebonyi State, Nigeria

Ewenighi Chinwe O.[1], Dimkpa Uchechukwu[2], Adejumo Babatunde I.[3], Onyeanusi Joel C[1]., Onoh Linus U. M.[4], Onoh Gladys O.[5], Uzor Simon[1], Ikegwuonu Ifeoma C.[6], Udemba M. O. A.[7] and Anojulu Amarachukwu[1]

[1]Department of Medical Laboratory Science, Ebonyi State University, Abakaliki, Ebonyi, Nigeria.
[2]Department of Physiology, Nnewi Campus, Nnamdi Azikiwe University, Awka, Anambra, Nigeria.
[3]Department of Medical Laboratory Science, Faculty of Health Science, University of Benin, Edo, Nigeria.
[4]Departement of Community Medicine, Enugu State University of Science and Technology, Enugu, Nigeria.
[5]Department of Nursing Science, Ebonyi State University, Abakaliki, Ebonyi, Nigeria.
[6]Department of Medical Laboratory Science; Nnewi Campus, Nnamdi Azikiwe University, Awka, Anambra, Nigeria.
[7]Department of Medical Laboratory Science, Mother of Christ Specialist Hospita, Ogui Enugu, Nigeria.

Authors' contributions

"This work was carried out in collaboration between all authors. Author ECO designed the study, managed the analysis and literature searches and wrote the first draft of the manuscript; author DU performed the statistical analysis, edited the manuscript and managed the literature searches. Authors ABI, OLUM, OGO, US, OJC, IIC, UMOA and AA assisted in the analyses of the study and the literature searches. All authors read and approved the final manuscript.

Original Research Article

Received 5th September 2013
Accepted 10th October 2013
Published 21st November 2013

ABSTRACT

Background: Assessment of the concentrations of reproductive hormones during post-menopause has been suggested as a confirmatory test for menopause due to

**Corresponding author: Email: ectabiel@yahoo.com, coewenighi@gmail.com;*

irregularities in rise and fall of sex hormones in menopausal transition. In this study, we assessed the concentrations of estrogen, progesterone, follicle stimulating hormone (FSH) and luteinizing hormone (LH) in post-menopausal women in Ebonyi state, Nigeria. In addition we tried to establish if relationships exist between the pituitary hormones and the ovarian (sex) hormones and between the reproductive hormones and age and body mass index (BMI).

Method: The study population comprised forty post-menopausal women of mean age 59.6 years and forty young female adult controls of mean age 27.8 years. Blood samples were collected into heparin container and the serum used for the analysis of estrogen, progesterone, FSH and LH using ELISA method.

Result: Post-menopausal women had significantly ($P<0.001$) higher mean serum FSH and LH concentrations compared to their controls. In contrast, the control group had significantly ($P<0.001$) higher progesterone and estradiol levels compared to the post-menopausal women. There was inverse correlation ($P<0.01$) between estradiol and FSH levels, but no significant correlations were observed between FSH and Progestrone; LH and Progestrone; and LH and Estradiol respectively. In addition, after adjusting for BMI, the concentrations of LH was significantly associated with age ($P<0.01$) but FSH, estradiol and progesterone levels were not. Furthermore, estradiol and FSH levels were significantly associated ($P<0.001$ and $P<0.05$) with BMI after controlling for age.

Conclusion: The present findings underscore the importance of understanding the reproductive hormonal profile of post-menopausal women and the need to consider age and body mass when studying hormonal changes of menopausal women. These data may help clinicians make optimal therapeutic decisions for hormone replacement therapy and life-style changes that may reduce the risk of some of the conditions associated with menopause.

Keywords: Follicle stimulating hormone; luteinizing hormone; progesterone; estradiol; menopause; post-menopause.

1. INTRODUCTION

Menopause is the cessation of monthly cycle. It announces the end of reproductive phase of a woman's life when the ovaries start decreasing their production of estrogen and progesterone on a permanent basis [1]. Hormonal fluctuation starts about 2 years before menopause and stabilizes from 12 months-2years post-menopause [2,3,4]. Post menopause can be defined as cessation of menstrual flow for a period of 12 months and above [2]. It is therefore more appropriate to declare a woman as menopausal at post-menopause stage. This is because menstrual cycles are usually extremely erratic at early stage thus making hormonal assessment at the early stage of menopause futile. The assessment of reproductive hormones at postmenopausal stage therefore would serve as a confirmatory test for menopause.

Epidemiological studies have reported hormonal involvement in sexual dysfunction during post-menopause. During this period of a woman’s life, there is a decline in sexual interest accompanying relative decline in production of ovarian hormones [5]. A prolonged deprivation of estrogens has been associated with cervical atrophy, reduced production of mucus, atrophic changes, and reduced vaginal lubrication, which can bring about dyspareunia, vaginitis, or vaginismus. These changes can reduce sexual satisfaction and lead to secondary sexual dysfunctions [6].

Changes in sensory perception, systemic blood flow and muscular contractility, are among the extragenital manifestations of postmenopause. A decline in the production of androgens often negatively affects sexual desire, sexual fantasies, excitation, and sexual satisfaction [6-10]. Furthermore, a decline in estrogen levels has been implicated in other changes such as brittle nails, thinning of the skin, hair loss and generalized aches and pains [11]. The factors that contribute to the sexual changes that take place during climacterium, and the suspected role of hormones in these changes, have not yet been elucidated [12,13].

Serum sex hormones have also been linked with the risk of several diseases in postmenopausal women. For example, estrogen deficiency has been linked with coronary artery disease, stroke and peripheral vascular disease due to vascular endothelial dysfunction [14]; osteoporosis, and breast and endometrial cancer [15,16,17]. The role of endogenous sex hormones in these disease conditions makes the understanding of factors that influence levels of these hormones increasingly important. This therefore calls for more studies to elucidate the roles reproductive hormones and other factors such as age and body weight play in the postmenopausal stage of a woman's life.

The endocrine feedback loops that provide for integrated function among the organs of the hypothalamic-pituitary-gonadal axis are paramount to reproductive potentials in reproductive aged women [18]. However, the interactions between the pituitary hormones and the ovarian hormones during the post-menopause stage are not well defined. Similarly there is paucity of information on the hormonal profile of post-menopausal Nigerian women. Furthermore, we believe that the roles which reproductive hormones and other factors such as age and body weight play in the postmenopausal stage of a woman's life need to be elucidated. In view of these facts, we aimed at estimating the concentrations of reproductive hormones- estrogen (estradiol), progesterone, follicle stimulating hormone and luteinizing hormone in postmenopausal women in the present study. In addition we tried to establish if there are significant interrelationships between the pituitary hormones and the ovarian (sex) hormones on one hand, and whether relationships exist between these reproductive hormones and age and body mass index (BMI) on the other hand.

2. METHODOLOGY

2.1 Subjects

The study population comprises forty apparently healthy post-menopausal women (mean age of 59.6 years) and forty healthy reproductive controls (mean age of 27.8 years). These participants were randomly selected from residents of Onicha Local Government Area of Ebonyi State, Nigeria. Subjects were selected based on the results of a structured questionnaire, body mass index measurement (computed as weight in kilogram divided by height in meters squared), resting blood pressure measurements and blood chemistry tests. Subjects were included in the study if they were non-smokers, non-alcoholics, non-obese (BMI < 30 Kg/m^2), non-diabetics, non-hypertensive, apparently without chronic systemic disorders or secreting pituitary tumors and not taking medications that could affect hormonal functions or taking hormonal treatment in the previous three months. Their consents were sought, ethical issues were referred accordingly and they participated voluntarily. Withdrawal at any time was permitted. The post-menopausal group included those within 12 months and above into menopause, while the control group included those not menstruating or ovulating at the time of sample collection and who were sure of their last menstruation date. The

ovulation period was then calculated based on the date of when the last menstruation started (usually between 12-16th day). Since all women do not follow similar menstrual pattern, we allowed a space of 11-21st day of their last menstrual period to accommodate variations in menstrual patterns. Women who were not up to 12 months into menopause were excluded from the postmenopausal group, while reproductive women who were not sure of the date of their last menstrual period (LMP) were excluded from the control group.

2.2 Sample Collection and Laboratory Analysis

5ml of blood was collected into a heparin bottle, centrifuged and the serum was used for laboratory analysis. The serum samples were obtained and analyzed during morning hours. The entire hormonal assay was done using the principle of peroxidase-conjugated sandwich ELISA (enzyme linked immunosorbent assay) by Diagnostic Automation, Inc, Calabasas. The final colour developed was measured spectrophotometrically at 450 nm using IPHIPPERION-3.0

2.3 Statistical Analysis

Data was expressed as mean and standard deviation. Comparative analysis involving two continuous variables was done using independent sample T-test and analysis of covariance (ANCOVA). Correlation between two variables was done using multivariable linear regression analysis. Statistical significance was set at $p<0.05$. All statistics were done using SPSS for windows (version 16.0)

3. RESULT

Table 1 shows the age and anthropometric measurements of the post-menopausal women and their controls. Independent sample t-test indicated that postmenopausal women were significantly ($P<0.001$) older than the controls. Similarly, postmenopausal women indicated higher body weight and body mass index compared to their controls. No significant difference was observed in height of both groups.

Table 1. Demographic and anthropometric measurements of the study population

Characteristics	Control (n=40)	Post-menopausal women (n=40)	*P*-value
Age (yrs)	27.80 ± 5.83	59.60 ± 8.41	0.000
Height (meters)	1.69 ± 0.07	1.70 ± 0.07	0.431
Weight (Kg)	57.63 ± 5.68	64.73 ± 8.47	0.000
Body Mass Index (Kg/m2)	20.05 ± 1.08	22.23 ± 2.74	0.000

Table 2 indicates the mean serum progesterone, estradiol, follicle stimulating hormone and luteinizing hormone concentrations in post-menopausal women and their normal control. Independent sample t-test indicated that post-menopausal women had significantly higher ($P<0.001$) mean serum FSH and LH concentrations but significantly lower ($P<0.001$) progesterone and estradiol levels compared to their controls. The significant differences observed between postmenopausal women and their controls persisted even after controlling for age and BMI using analysis of covariance (ANCOVA). Our data further revealed that postmenopausal women had progesterone level declined by 74%, estradiol

level decreased by 93%, FSH increased by 86% while LH increased by 81% compared to the control subjects.

Table 2. Reproductive hormone levels compared between post-menopausal women and their controls

Variables	Control	Post-menopausal women	P-value (unadjusted)*	P-value (adjusted) **
Progesterone (ng/ml)	1.9 ± 2.23	0.5 ± 0.41	0.000	0.000
Estradiol (Pg/ml)	111.1 ± 14.4	7.7 ± 3.76	0.000	0.001
FSH (MIU/ml)	9.6 ± 4.43	68.1 ± 40.62	0.000	0.000
LH (IU/L)	10.2 ± 6.16	53.1 ± 11.95	0.000	0.000

**Independent sample t-test; ** Analysis of covariance (ANCOVA).*

Table 3 shows relationships between pituitary hormones and sex hormones in post-menopausal women. After controlling for age and BMI, Pearson's multivariable regression analysis indicated lack of significant associations between FSH and Progestrone; LH and Progestrone; and LH and Estradiol respectively. In contrast, significant inverse correlation (P<0.01) was observed between FSH and estradiol.

Table 3. Age and BMI adjusted relationships between pituitary hormones and ovarian (sex) hormones in post-menopausal women

Variables	Correlation coefficient	P-value
FSH vs. Progesterone	-0.226	0.214
FSH vs. Estradiol	-0.572	0.001**
LH vs. Progesterone	0.245	0.176
LH vs. Estradiol	0.042	0.818

***Significant (P<0.01).*

Linear regression analysis indicated significant correlation between age and estradiol (P<0.01) and LH (P<0.001). In contrast, no significant associations were observed between age and progesterone and FSH. After controlling for BMI, the initial correlation observed in age vs. estradiol disappeared, while that of age vs. LH persisted (Table 4).

Table 4. Relationship between age and reproductive hormones in post-menopausal women

Age vs.	Unadjusted linear correlation		Bmi-adjusted correlation	
	Coefficient	P-value	Coefficient	P-value
Progesterone	-0.120	0.499	-0.081	0.652
Estradiol	-0.471	0.005**	-0.096	0.594
FSH	0.270	0.123	0.015	0.933
LH	0.570	0.000***	0.480	0.005**

****Significant (P<0.001); ** P<0.01.*

Linear regression analysis indicated significant correlation between BMI and estradiol (P<0.001) and FSH (P<0.05) and LH (P<0.05). However, no significant association was observed between BMI and progesterone. After controlling for age, the correlation

disappeared in BMI vs. LH but remained in BMI vs. estradiol (P<0.001) and in BMI vs. FSH (P<0.05; (Table 5).

Table 5. Relationship between BMI and reproductive hormones in post-menopausal women

Bmi vs.	Unadjusted linear correlation		Age-adjusted correlation	
	Coefficient	P-value	Coefficient	P-value
Progesterone	0.092	0.606	0.025	0.891
Estradiol	0.691	0.000***	0.579	0.000***
FSH	-0.430	0.011*	-0.348	0.047*
LH	-0.350	0.042*	-0.012	0.949

****Significant (P<0.001); * P<0.05.*

4. DISSCUSSION

In this study, post-menopausal women had significantly lower estrogen and progesterone levels while follicle stimulation hormone and luteinizing hormone levels were significantly higher when compared to the control group. This result was expected since it has been established that during menopause, there are very low levels of sex hormone (estrogen, testosterone and progesterone) and high levels of FSH and LH in the blood stream in response to depleted ovarian follicles [19]. During this period, the ovaries stop responding to FSH and LH but the anterior pituitary keeps releasing FSH and LH. Our findings agree with previous studies [3,20-24] which showed a significantly higher FSH and LH levels and significantly lower estradiol and progesterone levels in postmenopausal older women compared to their younger reproductive controls.

Our finding also established that estradiol level decreased by 93%, progesterone decreased by 74% while LH increased to 5-folds and FSH increased to 7-folds in post-menopausal women compared to control subjects. Our finding is in strong agreement with the work of Henrich et al. [25] which showed that mean FSH was seven times higher in post-menopause compared to the reproductive stage. The present data also agrees with some studies [26,27] which showed that estradiol in menopausal women decreased by more than 90% and LH levels increased 4- to 5-fold compared with those of younger, reproductive controls. The present findings underscore the importance of understanding the hormonal levels of the hypothalamic-pituitary-gonadal axis in postmenopausal stage of a woman's life in order to make optimal therapeutic decisions for hormone replacement therapy and life-style changes that may reduce the risk of some of the conditions associated with menopause in women.

The interactions between the pituitary hormones and the ovarian hormones during the postmenopausal stage are not well defined. Similarly there is paucity of information on the interrelationships between the hormones of these two endocrine organs. In the present study, there was significant inverse correlation between FSH and estradiol after adjustment for age and BMI. However, no significant correlations were observed between FSH and progesterone, LH and estradiol, and between LH and progetsterone respectively. A previous study by Ausmanas et al. [22] showed an inverse correlation between estradiol and FSH levels in postmenopausal Asian women thus agreeing with the present finding. The inverse correlation of estradiol and FSH levels suggests that estradiol still affects the pituitary FSH output at the postmenopausal state. It also suggests the possibility that FSH may be used to indicate the total estrogen status of postmenopausal women. Furthermore, the observation of significant relationship between FSH and estradiol and the lack of such association

between LH and estradiol emphasizes the complexity of the hypothalamic-pituitary-ovarian regulatory system and suggests that LH and FSH are modulated independently at the level of pituitary.

We assessed the extent of relationship between age and the reproductive hormones. A linear regression analysis indicated that age positively correlated with LH but inversely correlated with estradiol, whereas progesterone and FSH levels were not significantly associated with age. However, after controlling for BMI, the correlation between age and estradiol disappeared thus suggesting that the influence of age on estradiol is accounted for by changes in BMI. On the other hand, the correlation between age and LH persisted after controlling for BMI. A previous study [22] has reported significant relationships between age and LH and estradiol but not FSH in post menopausal women, thus agreeing with the present data. Vermeulen et al. [28] reported inverse correlation between age and estradiol in postmenopausal women. However, other studies [29,30,31] indicated lack of significant relationship between age and estradiol (estrogen). In contrast to our findings, Reyes *et al* [31] have demonstrated significant correlation between age and FSH in post-menopausal women. We could not find any study on the relationship of progesterone and age in postmenopausal women. The present findings underline the need to consider age when determining hormonal changes and its associated disease risks and sexual changes in post-menopausal women.

Our data further revealed that body mass index was independently related to estradiol and FSH. Estradiol increased, while FSH declined with increase in BMI. These findings concurred with a previous study [32] which reported positive correlation between BMI and estrogen in post-menopausal women. Similarly, Ausmanas et al. [22] reported significant associations between BMI and three of the hormones estradiol, FSH and LH in post-menopausal women. Furthermore, Vermuelin et al. [28] reported that estradiol was significantly correlated with the degree of adiposity and fat mass. In another study involving both normal and obese post-menopausal women, Klinga *et al.* [33] reported that FSH inversely correlated with body weight while estradiol did not change with changes in body weight. The present data which showed positive correlation between estrogen and body mass index is compatible with the hypothesis that after menopause, excess fat mass increase estrogen concentration through the aromitisation of androgens in adipose tissue. These findings further reiterate the need to put into consideration body mass when determining the role of reproductive hormones in sexual changes and disease conditions associated with post-menopausal state in women.

5. CONCLUSION

In conclusion, the present study indicated that post-menopausal women had significantly lower estrogen and progesterone levels and higher FSH and LH levels compared to the control group. There was inverse correlation between estradiol and FSH levels, but no significant correlations were observed between FSH and Progestrone; LH and Progestrone; and LH and Estradiol respectively. In addition, after adjusting for BMI, the concentrations of LH was associated with age but FSH, estradiol and progesterone levels were not. Furthermore, estradiol and FSH levels were significantly associated with BMI after controlling for age. These findings underscore the importance of understanding the reproductive hormonal profile of menopausal women and the need for more detailed studies on the biological significance of hormonal changes with age and body weight. These data may help clinicians to make optimal therapeutic decisions for hormone replacement therapy

and life-style changes that may reduce the risk of some of the conditions associated with menopause in women.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. World Health Organization. Research on the Menopause in the 1990s. Technical report Scr 1996; 866 Geneva, Switzerland.
2. Burger HG, Dudley EC, Robertson DM, Dennerstein L. Hormonal changes in the menopause transition. J Clin Endocrinol Metab. 2002;81:1401–1405.
3. Burger HG, Dudley EC, Hopper JL, Groome N, Guthrie JR, Green A, Dennerstein L. Prospectively measured levels of serum FSH, estradiol and the dimeric inhibins during the menopausal transition in a population-based cohort of women. J Clin Endocrinol Metab. 1999;84:4025–4030.
4. Harlow SD, Gass M, Hall JE, Lobo R, Maki P, Rebar RW, et al. Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. J Clin Endocrinol Metab. 2012;97(4):1159-68.
5. Moghassemi S, Ziaei S, Haidari Z. Female sexual dysfunction in Iranian postmenopausal women: prevalence and correlation with hormonal profile. J Sex Med. 2011;8(11):3154-9.
6. Liuveras JL, Duran RS, Alvarez CT, Barbosa FT. Sexual function and sex hormones in women with premature menopause. Cuban Medical Research. 2002;4(1).
7. McCoy NL. Estrogen levels relation to self-reported symptoms and sexuality in perimenopausal woman. In: Multidisciplinary Perspectives on Menopause. Ann NY Acad Sc. 1990;592:450-452.
8. Dennerstein L, Dudley EC, Hopper TL, Burger H. Sexuality, hormones and the menopausal transition. Maturitas, 1997;26:83-93.
9. Bachmann GA. Influence of menopause on sexuality. Int J Fertil Menopausal Stud 1995;40(Supp 1):16-22.
10. Sarrel PM. Sexuality and Menopause. Obstet Gynecol, 1990;75:26s-30s
11. Hall G, Phillips TJ; Estrogen and skin: the effects of estrogen, menopause, and hormone replacement therapy on the skin. J Am Acad Dermatol. 2005;53(4):555-68; quiz 569-72.
12. Meston CM. Aging and sexuality. West J Med. 1997;167:285-290.
13. McKinlay SM, Brambilla DJ, Posner JG. The normal menopause transition. Maturitas. 1997;14:103-115.

14. Kalantaridou SN, Naka KK, Bechlioulis A, Makrigiannakis A, Michalis L, Chrousos GP. Premature ovarian failure, endothelial dysfunction and estrogen-progestogen replacement. Trends Endocrinol Metab. 2006;17(3):101-9.
15. Van Hemert AM, Birkenhäger JC, De Jong FH, Vandenbroucke JP, Valkenburg HA. Sex hormone binding globulin in postmenopausal women: a predictor of osteoporosis superior to endogenous oestrogens. Clin Endocrinol (Oxf). 1989;31(4):499-509.
16. Kaaks R, Rinaldi S, Key TJ, Berrino F, Peeters PH, Biessy C, et al. Postmenopausal serum androgens, oestrogens and breast cancer risk: the European prospective investigation into cancer and nutrition. Endocr Relat Cancer. 2005;12(4):1071-82.
17. Allen NE, Key TJ, Dossus L, Rinaldi S, Cust A, Lukanova A, et al. Endogenous sex hormones and endometrial cancer risk in women in the European Prospective Investigation into Cancer and Nutrition (EPIC). Endocr Relat Cancer. 2008;15(2):485-97.
18. Couse JF, Yates MM, Walker VR, Korach KS. Characterization of the hypothalamic-pituitary-gonadal axis in estrogen receptor (ER) null mice reveals hypogonadism and endocrine sex reversal in females lacking ERα but not ERβ. Molecular Endocrinology. 2003;17(6):1039-1053.
19. Nelson H. Menopause. Lancet. 2008;1:371,760-70.
20. Sherman BM, West JH, Korenman SG. The menopausal transition: analysis of LH, FSH, estradiol, and progesterone concentrations during menstrual cycles of older women. J Clin Endocrinol Metab. 1976;42(4):629-36.
21. Trevoux R, De Brux J, Castanier M, Nahoul K, Soule JP, Scholler R. Endometrium and plasma hormone profile in the peri-menopause and postmenopause. Maturitas. 1986; 8:309–326.
22. Ausmanas MK, Tan DA, Jaisamrarn U, Tian XW, Holinka CF. Estradiol, FSH and LH profiles in nine ethnic groups of postmenopausal Asian women: the Pan-Asia Menopause (PAM) study. Climacteric. 2007;10(5):427-37.
23. Navarro D, Acosta A, Robles E, Díaz C. Hormone profile of menopausal women in Havana. MEDICC Rev. 2012; 14(2):13-5.
24. Geller S, Scholler R. FSH and LH pituitary reserve and output in the postmenopause. Maturitas. 1980;2(1):45-52.
25. Henrich JB, Hughes JP, Kaufman SC, Brody DJ, Curtin LR. Limitations of follicle-stimulating hormone in assessing menopause status: Findings from the National Health and Nutrition Examination Survey (NHANES 1999-2000). Menopause. 2006;13:171-7.
26. Greendale GA, Soers M. The menopause transition. Endocrinol Metab Clin North Am. 1997;26(2):261–277.
27. Burger HG. The endocrinology of the menopause. J Steroid Biochem Mol Biol. 1999;69:31–35.
28. Vermeulen A, Verdonck L. Sex hormone concentration in post-menopausal women: relation to obesity, fat mass, age and years of post-menopause. Clinical Endocrinology. 2008;9(1):59-66.
29. Cauley JA, Gutai JP, Kuller LH, LeDonne D, Powell JG. The epidemiology of serum sex hormones in post-menopausal women. Am J of Epidemiol. 1989;129 (6):1120-31.
30. Jensen J, Riis BJ, Hummer L, Christiansen C. The effects of age and body composition on circulating serum estrogen and androstenedione after the menopause. Br J Obstet Gynaecol. 1985;92(3):260-5.
31. Reyes FI, Winter JS, Faiman C. Pituitary ovarian relationships preceding the menopause. A cross sectional study of serum FSH, LH, prolactin, estradiol and progesterone levels. Am J Obstet Gynaecol. 1977;129(5):557-64.

32. Baglietto L, English DR, Hopper JL, MacInnis RJ, Morris HA, Tilley WD, et al. Circulating steroid hormone concentration in post-menopausal women in relation to body size and composition. Breast Cancer Res Treat. 2009;115(1):171-9.
33. Klinga K, von Holst T, Runnebaum B. Serum concentration of FSH, estradiol, oestrone and androstenedione in normal and obese women. Mauritas. 1982;4(1):9-17.

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