VOL. 7 NO. 1, JANUARY 2012 ISSN 1990-6145
ARPN Journal of Agricultural and Biological Science


www.arpnjournals.com

EFFECT OF FEMALE HORMONES IN DIFFERENT OVARIAN CONDITIONS

Rabail Javed[1], Saima Younas[2], Farkhanda Ghafoor[1] and Muhammad Asim Jajja[1]
[1]Pakistan Medical Research Council Centre NHRC, PGMI Building, Sheikh Zayed Medical Complex, Lahore, Pakistan
[2]Department of Zoology, University of the Punjab, Lahore, Pakistan
E-Mail: rabailjaveed@hotmail.com

ABSTRACT

This study measures the levels of estrogen, progesterone, follicle stimulating hormone in females suffering from ovarian cancer (OCA) and polycystic ovarian syndrome (PCO). Thirty one (31) OCA, twenty nine (29) PCO cases and 35 controls were matched by age ($p>0.05$), and hormonal levels in different phases of their menstrual cycle. Blood samples were collected from each person. Sera were separated and stored at -20°C. Enzyme linked immunosorbent assay (ELISA) for the estrogen, progesterone, FSH was performed using commercially available kits from Biocheck, USA. Follicle stimulating hormone (FSH) levels in follicular and leuteal phase or menopause were found in normal range (8.5±2.4 mIU/ml, 7.4±2.3 mIU/ml and 95±1.3 mIU/ml) among controls and was significantly lower in the OCA group (3.4±1.3 mIU/ml, 3.8±0.2 mIU/ml and 71.8±2.3 mIU/ml) and in PCO group (2.9±0.6 mIU/ml and 3.2±1.4 mIU/ml), respectively. Progesterone levels in follicular, leuteal phase and menopause were found in the normal range among control group (0.6 ± 0.03 ng/ml, 8.1±5.4 ng/ml and 1.2±1.3 ng/ml) whereas in OCA group progesterone levels were significantly higher in follicular phase (2±0.4 ng/ml) and lower in leuteal phase (0.6±4.7 ng/ml). In PCO group progesterone levels were found significantly lower in follicular phase (0.1±0.6 ng/ml) and normal in leuteal phase (2.5±0.8 ng/ml). Estrogen levels were seen significantly higher in OCA group (119 ±2.9 pg/ml) and PCOS (109 ±1.9 pg/ml) group in follicular phase and normal in control group (63.7±2.3 pg/ml). However, in the leuteal phase estrogen levels were in normal range among controls (76.7±3.4 pg/ml), OCA (140.3±2.5 pg/ml) and PCO group (82.5±1.9 pg//ml) whereas in menopause estrogen levels increased in OCA group (21.3±1.2 pg/ml) and remained within normal range among normal controls (13.5±2.3 pg/ml). Level of FSH and progesterone almost remained normal in ovarian cancer and showed a decreasing trend in polycystic ovarian syndrome. Estrogen was increased in ovarian cancer while it slightly decreased in polycystic ovarian syndrome.

Keywords: female hormones, ovarian cancer, polycystic ovarian syndrome, follicle stimulating hormone, progesterone, estrogen.

INTRODUCTION

The ovaries have two main functions: Ovulation (release of an egg each month) and production of estrogen and progesterone (female hormones). Hormones from the hypothalamus and anterior pituitary control the ovarian hormone secretion. Estrogen and progesterone are steroid hormones. Synthesis of these hormones requires series of enzymes that modify the basic cholesterol molecule [1].

Estrogens function as the primary female sex hormone. There are three types of estrogens which are estradiol, estriol, and estrone. Estradiol is the most important ovarian estrogen[2]. Progesterone with estrogen plays a vital role in stimulating growth of the breasts and in regulating the uterine cycle. Progesterone plays a role in promoting diuresis, and increasing the body temperature [2].

In normal conditions the hypothalamus secretes gonadotropin releasing hormone (GnRH), which induces the secretion of follicle stimulating hormone (FSH) from anterior pituitary [3]. The increase in FSH stimulates several follicles during follicular phase, which is the first phase of mentural cycle. With the development of follicle, estradiol is secreted slowly in the beginning of menstrual cycle and is maximisesd on the day 12 or 13 of the cycle. The estrogens secreted by follicle initate the formation of a new layer of endometrium in the uterus, which is identified as the proliferative endometrium. This phase is also called proliferative phase. Progesterone acts on estrogen primed endometrium to convert it into a hospitable and nutritious lining suitable for implantation of fetus. Under the influence, progesterone endometrial tissue becomes loose and edematous, facilitates implantation [1,4]. If fertilization does not occur corpus luteum degenerates, with this endometrium also degenerates resulting into menstrual flow [1].

Complete cessation of menstrual cycle occurs between the age of 45 and 55 years leading into menopause which is result of limited supply of the ovarian follicles which are present at birth. In postmenopausal female ovarian estrogen and progesterone production is decreased [1]. The decrease in ovarian estrogen is responsible for physical postmenopausal changes that occur in the reproductive tract such as vaginal dryness and gradual atrophy of genital organs.

In abnormal conditions ovarian activity is changed and the amount of female hormones produce by ovaries is also changed. There are several different abnormal ovarian conditions. The conditions which are discussed in this article are ovarian cancer and poly cystic ovarian syndrome. In Ovarian cancer estrogen is considered as etiologic factor [5]. Ovarian cancer develops as a consequence of excessive stimulation of ovarian tissue by pituitary gonadotropins (LH and/or FSH) [6] whereas progesterone appears to offer protection against ovarian carcinogenesis [7].

Another important abnormal ovarian condition is polycystic ovarian syndrome (PCO) which is one of the most common female hormonal disorders. Women with PCO have consistent abnormalities in gonadotropin secretion. They have elevated LH levels [8,9]. Whereas plasma FSH levels are relatively low [10]. Low FSH levels lead to impaired follicular development [11].

In this study female hormones (estrogen, progesterone, follicle stimulating hormone) were measured among females with ovarian cancer and polycystic ovarian syndrome (PCO). The levels of hormones in diseased participants were compared with the levels of normal controls. This study could help in initial diagnosis of ovarian cancer and polycystic ovarian syndrome cases by measuring estrogen, progesterone and FSH levels.

PATIENTS AND METHOD

A cross-sectional, analytical study was performed at Department of Gynecology and Immunoassay lab NHRC Sheikh Zayed Medical complex Lahore. Conveniently selected groups of total 95 (31 ovarian cancer, 29 PCO cases and 35 control) participants in the range of 15-65 years were studied.

The study was approved by the Institutional Review Board of Sheikh Zayed Medical Complex. After explaining the objectives of the study informed consent was obtained from voluntary participants. Blood samples were collected up to 5.c.c from each participant. Sera were separated and stored at -20°C until analyzed. Enzyme Linked Immunosorbent Assay (ELISA) for the female hormones profile (estrogen, progesterone, FSH) was performed using commercially available kits from Biocheck USA. All assays were run in duplicates, which included 5-7 standards, 3 quality control pools and samples. Absorbance of these assays was read at 450 nm verses 630 nm reference on Anthox 2010 plate reader. Data analysis was carried out using stingray package for statistical analysis.

RESULTS

The mean age of control group was 47.3±7.1 years, ovarian cancer cases was 50.2±7.8 years and that of PCO cases was 45.2±6.3 years, respectively (Table-1).

Table-1. Distribution of study cases by age.

Study groups	No. of cases		Mean Age	
	N*	%	**Age** (yr)	±SD
Controls	35	36.8	47.3	7.1
Ovarian cancer	31	32.6	50.2	7.8
PCO	29	30.6	45.2	6.3
Total	95	100	47.2	7.06

N* is the total number of participants in the particular study group

Mean age of the control group was not found significantly different from that of ovarian cancer and PCOS group, whereas mean age of ovarian cancer patients was significantly different from that of PCOS group ($p<0.02$) (Table-2).

Age of Menarche has been reported factor for PCOS. In this study no association was found between the age of menarche and ovarian cancer and PCOS (Table-2).

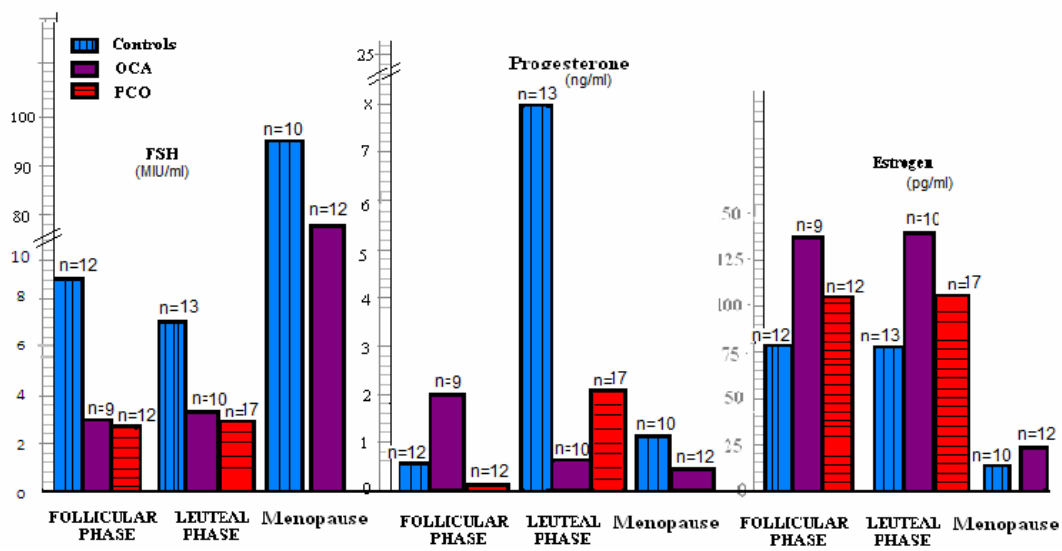
Table-2. Distribution of study groups by age of menarche.

Study groups	Age of menarche				Total
	>12 yr*		<12 yr*		
	N	%	N	%	
Controls	5	14.2	30	85.7	35
OCA	4	12.9	27	87	31
PCO	9	31	20	68.9	29
Total	18	19.9	77	81.0	95

chi square: 3.978 p value : 0.21

Considering the menstrual cycle, in the diseased group 64.5% of cases had regular cycles in OCA group and 13.7% in PCOS group, respectively where as females of control group had normal menstrual cycle.

Regular menstrual cycle is very much dependent on levels of FSH, progesterone and estrogen in different phases of the cycle it was seen at the time of registration that out of 35 normal controls, 13 participants were in luteal phase while 12 were in follicular phase of their menstrual cycle, and 10 participants were menopausal. Of the 31 ovarian cancer cases, 10 were in luteal phase, 9 cases were in follicular phase and 12 cases were menopausal. PCO included 17 cases in luteal phase, 12 in follicular phase, respectively.



Normal Ranges:

FSH	follicular phase 2-10MIU/ml	Luteal phase	3-8 MIU/ml	Menopause	94 MIU/ml
Progesterone	follicular phase 0.15-0.70 ng/ml	Luteal phase	2-25 ng/ml	Menopause	0.06-1.6 ng/ml
Estrogen	follicular phase 30-100 pg/ml	Luteal phase	60-150pg/ml	Menopause	18 pg/ml

It was seen among control study group FSH levels in the normal range either in follicular phase, leuteal phase or at menopause. However the levels of FSH were significantly lower in OCA and PCOS groups, respectively than that of control group (Figure-1).

In study groups progesterone levels were found in the normal range among control group regardless of the phase of menstrual cycle. Whereas in OCA group progesterone levels were significantly higher in follicular phase and lower in leuteal phase. In PCOS group progesterone levels were significantly lower in follicular phase and normal in leuteal phase. Progesterone levels in OCA group were also seen normal in menopausal females (Figure-1).

Estrogen levels were seen significantly higher in OCA group and PCOS group in follicular phase and normal range in control group however in the leuteal phase estrogen levels were in normal range in all three study groups whereas in menopause estrogen levels increased in OCA group and remained within normal range in normal controls (Figure-1).

DISCUSSIONS

The present study was designed to compare the levels of estrogen, progesterone and FSH (female hormones) in ovarian cancer and PCO and normal controls and also age of menarche if it has any influence in OCA and PCO.

In our study it was found that age of menarche has no association with progression of disease This highlights that hormone of the diseased patients work in a normal pattern in prehistory of a patient. A study conducted by Lukanova and Kaaks has also reported that ovarian cancer risk is not clearly related to age at menarche [6].

Ovarian cancer being the sixth most common cancer and the fifth leading cause of cancer-related death among women in developed countries [13, 14]. Among OCA cases present study has shown, FSH levels were found either within normal range or decrease depending upon their menstrual phase and menopause, respectively. This decrease in FSH may be because of increase production of other female hormones such as estrogen. Lower levels of FSH (gonadotropins) in malignant ovarian cancer were also reported elsewhere [15].

In the current study it was seen that among ovarian cancer cases the progesterone remained within normal range in follicular phase and menopause while it decreased in luteal phase. The decrease in progesterone levels may be because of loss of heterozygosity at 11q23.3-24.3 that harbors progesterone receptor (PR) gene locus[7]. This genetic alteration has been observed in number of ovarian cancer specimens[7]. Decreased levels of progesterone in ovarian cancer were also reported by Lukanova and Kaaks [6].

Measurement of estrogen showed an increase levels in follicular phase and menopause while in luteal phase estrogen remained within normal range. This infers that ovarian cancer could produce estrogen by itself. The high level of estrogen can be caused by intratumoral production of estrogen. Similar observation was reported in another study which emphasized that stromal ovarian tumors and malignant epithelial ovarian tumors are capable of producing estrogen [16]. Studies have also demonstrated elevated levels of estrogen in patients with malignant or benign ovarian tumors, as compared to controls [17]. Most ovarian cancer patients had increased

serum concentrations of estrogen [15]. Increased levels of estrogen in follicular phase of menstrual cycle of women with ovarian cancer were also reported elsewhere [18].

Polycystic ovarian syndrome (PCO) is one of the common female hormonal disorders [19, 20]. In this study it was found that FSH, estrogen and progesterone remained within normal range with a decreasing trend in cases with PCO. These results incorporate with other studies as well [9]. Neuroendocrine hallmark of PCO is persistently rapid LH (GnRH) pulsatility, which favors pituitary synthesis of LH over that of FSH, leading to decreased FSH levels [11, 20].

A defining feature of PCO is chronic oligoovulation or anovulation. Therefore, women with PCO do not regularly experience the post-ovulatory rise in progesterone seen in normally mensturating women [11]. same results were seen in current study.

Comparison of values of estrogen controls to that of PCO cases showed slight increase in levels of PCO cases against normal controls. High levels of androgens in PCO peripherally converted to estrogens may lead to their increased concentration. High levels of estrogen in PCO patients have also been reported in other studies [20].

This study clearly explained effect of female hormones (estrogen, progesterone, FSH) in normal and abnormal conditions such as OCA and PCOS. It was also observed that these hormones have rise and fall at different stages of menstrual cycle and at menopause.

CONCLUSIONS

From this study it was concluded that in ovarian cancer FSH and progesterone are decreased as compared to controls, and estrogen is increased. In PCO, FSH and progesterone are lowered and estrogen is elevated as compared to normal controls. Thus changes in the hormonal parameters may help in identifying these disorders.

ACKNOWLEDGEMENTS

The Authors are greatly thankful for the funding provided by the Department of Zoology, University of the Punjab for this study. Further they also acknowledge support of staff of National Health Research Complex. Without their kind help it would have been difficult to complete this study within time.

REFERENCES

[1] Sherwood L. Human Physiology from cells to systems. 4th Ed. ©2001.Brooks/cole.

[2] Marieb EN. Human Anatomy and Physiology. 2nd Ed. ©1992. Benjamin Cummings publishing company.

[3] Knobil E. 1980. The neuroendocrine control of the menstrual cycle. Rec. Program. Hormones. Research. 36: 52-88.

[4] Musarrat Jabeen Babar and Mir Hassan Khan. 2003. A two way action of Progesterone in fertility management. J. Postgrad Med. Inst. 17(2): 231-234.

[5] Lindgren P, Bäckström T, Mählck CG, Ridderheim M and Cajander S. 2001. Steroid receptors and hormones in relation to cell proliferation and apoptosis in poorly differentiated epithelial ovarian tumors. International Journal of Oncology. 19: 31-38.

[6] Lukanova A and Kaaks R. 2005. Endogenous hormones and ovarian cancer: epidemiology and current hypotheses. Cancer Epidemiology, Biomarkers and Prevention. 14: 98-107.

[7] Syed V, Ulinski G, Mok SC, Yiu GK and Ho SM. 2001. Expression of gonadotropin receptor and growth responses to key reproductive hormones in normal and malignant human ovarian surface epithelial cells. Cancer Res. Sep. 15. 61(18): 6768-6776.

[8] Stener-Victorin E, Holm G, Labrie F, Nilsson L, Janson PO and Ohlsson C. 2002. Are there any sensitive and specific sex steroid markers for polycystic ovary syndrome? J Clin Endocrinol Metab. 2010 Feb. 95(2): 810-9. Epub 2009 Dec 16. Cheung AP, Pride SM, Yuen BH and Sy LIn-vivo. Ovarian androgen responses to recombinant FSH with and without recombinant LH in polycystic ovarian syndrome. Hum Reprod. 17(10): 2540-2547.

[9] Haq F, Aftab O. and Rizvi J. 2007. Clinical, biochemical and ultrasonographic features of infertile women with polycystic ovarian syndrome. J Coll Physicians Surg Pak. 17(2): 76-80.

[10] http://labtestsonline.org/understanding/conditions/PCO?start=2. Date accessed 07/07/2011.

[11] Blank SK, McCartney CR and Marshall JC. 2006. The origins and sequelae of abnormal neuroendocrine function in polycystic ovary syndrome. Human Reproduction Update. 12: 351-361.

[12] Gadducci A, Cosio S, Gargini A and Genazzani AR. 2004. Sex-steroid hormones, gonadotropin and ovarian carcinogenesis: A review of epidemiological and experimental data. Gynecological Endocrinology. 19: 216-228.

[13] McSorley MA, Alberg AJ, Allen DS, Allen NE, Brinton LA, Dorgan JF, Kaaks R, Rinaldi S and Helzlsouer KJ. 2009. Prediagnostic circulating follicle stimulating hormone concentrations and ovarian cancer risk. Int. J Cancer. Aug 1. 125(3): 674-679.

[14] Mehboob S, Ghafoor F, Yunus S and Sajjad R. 2009. Role of CA125 as an ovarian tumor marker. Pak J Med Res. 48(3).

[15] Tokunaga H, Akahira J, Suzuki T, Moriya T, Sasano H, Ito K, Yaegashi N. 2007. Ovarian epithelial carcinoma with estrogen-producing stroma. Pathology International. 57: 285-290.

[16] Jale Metindir, Sabahattin Aslan and Gülay Bilir. Ovarian Cyst Formation in Patients Using Tamoxifen for Breast Cancer 2005 Japanese Journal of Clinical Oncology. 35(10): 607-611.

[17] http://www.sensiblehealth.com/Journey-04.xhtml. Date accessed 07/07/2011.

[18] http://www.hormonehelpny.com/column/PCO.htm. Date accessed 07/07/2011.

[19] http://PCOinfo.com/elevated-estrogen/ Date accessed 07/07/2011.

[20] Raja A, Hashmi SN, Sultana N, Rashid H. 2005. Presentation of polycystic ovary syndrome and its management with clomiphene alone and in combination with metformin. J. Ayub Med Coll Abbott bad, Pakistan. 17(2): 50-53.