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Original Article

Biochemistry Section

Utility of Ovarian Tumour Marker Cancer Antigen-125 and Endocrine Hormonal Status in Polycystic Ovary Syndrome

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ABSTRACT

Introduction: Polycystic Ovary Syndrome (PCOS) is the most common endocrinopathy in women of reproductive age. Women with PCOS are at increased risk of reproductive abnormalities with a prevalence of up to 10%.

Aim: To assess the concentrations of ovarian tumour marker Cancer Antigen-125 (CA125), Luteinizing Hormone (LH), Follicle Stimulating Hormone (FSH) And Prolactin (PRL) among women with PCOS in order to get insight of how these biochemical parameters play a crucial role in the pathogenesis of PCOS and to evaluate their diagnostic utility.

Materials and Methods: A total of 60 subjects were enrolled for the prospective comparative case-control study. Out of these 60 subjects, a healthy control group of 30 subjects with non-hirsute, non-obese women with regular menstrual cycles were included as control. PCOS group of 30 women were selected as a study group who were already diagnosed by clinician. Their height (meters) and weight (kg) were measured and recorded. This measurement was used for calculating Body Mass Index (BMI) in kg/m^2. Serum CA-125, LH, FSH and PRL were estimated by the chemiluminescent method on Immulite 1000. Data were presented as number, percentage, mean and standard deviation. Statistical analysis was done by normal distribution z-test.

Results: The statistical significant alterations were observed in the levels of CA125, LH and PRL between PCOS group and control group. FSH level was insignificantly different in PCOS as compared with that of controls.

Conclusion: An ovarian tumour marker CA125 and endocrine hormones such as LH, FSH and PRL are of paramount importance for the correct diagnosis with degree of severity in patients with PCOS. The present study confirms the elevated levels of LH as a regular feature of PCOS. Also, the possible correlation of CA125 and PRL in women having PCOS suggests that the combination of the ovarian tumour marker and this hormonal status can be used in biochemical screening of ovarian cancer. However, further prospective and controlled studies are needed to investigate their utility in prediction of ovarian cancer in women having PCOS.

Keywords: Follicle stimulating hormone, Luteinizing hormone, Prolactin

INTRODUCTION

Polycystic ovarian syndrome is most commonly encountered endocrinopathy in women of reproductive age having significant reproductive and non-reproductive consequences, still there is lack of consensus on its definition [1]. Women with PCOS may develop a wide range of clinical and biochemical symptoms, however usually present for three primary reasons-menstruation irregularities, infertility and symptoms associated with hyperandrogenism [2,3]. Obesity is present in patients with PCOS and can aggravate PCOS because fatty tissues are hormonally active and they produce estrogen which disrupts ovulation and thus thought to be one of the leading causes of female infertility [4-6].

PCOS is simply not easy to manage. However, to some extent, it can be easy to diagnose patients presenting symptoms such as amenorrhoea, hirsutism, obesity, etc., in addition to this laparoscopic examination can reveal thick, smooth, pearl white surface of the ovary to analyse the presence of polycystic ovaries. Blood tests are also useful for analysing altered serum levels of hormones associated with the normal functioning of female reproductive system in order to confirm the diagnosis of PCOS [7,8].

The aim was to study the concentrations of ovarian Tumour Marker Cancer Antigen (CA-125, expected reference values were 1.9-16.3U/mL in healthy females), Luteinizing Hormone (LH, expected reference values were 0-77 mIU/mL in healthy females), Follicle Stimulating Hormone (FSH, expected reference values were 1.2-21 mIU/mL in healthy females) and Prolactin (PRL, expected reference values were 1.9-25 ng/mL in healthy females) among women with polycystic ovarian syndrome in order to get insight of how these biochemical parameters plays crucial role in pathogenesis of PCOS and to evaluate their diagnostic value [9].

MATERIALS AND METHODS

A prospective comparative case-control study carried out at Department of Biochemistry, Grant Government Medical College and Sir JJ Group of Government Hospitals, Mumbai, India. All participants completed a medical history form and provided informed consent. A total of 30 study cases of PCOS with mean age was 29.7±5.51 years, who attended to the gynaecology OPD were studied for estimation of serum CA-125, LH, FSH and PRL over a period of eight months from July 2010 to March 2011. Age-matched 30 subjects were taken as controls. The Institutional Ethical Committee (vide approval letter No. GMC/Pharm/610/2010, dated-15/07/2010) at the Grant Medical College and Sir J. J. Group of Government Hospitals, Mumbai, approved the study.

A necessary criterion for recruitment amongst all the women was complete absence of any form of pituitary, thyroid, or adrenal disorder, as well as any form of hormonal treatment before the study. Study cases who were already diagnosed with PCOS by clinician-the criteria were the recruitment of women in the reproductive age group, with varying degrees of oligomenorrhoea and chronic anovulation. Presence of polycystic ovaries as a common underlying feature in these women with infertility was confirmed through detection by transvaginal ultrasonography by the clinician. The healthy subjects of non-hirsute, non-obese women with regular menstrual cycles came for the general checkup in the Sir JJ Hospital, Mumbai were included as control.

Laboratory Workup

Five millilitres fasting venous blood samples were drawn from an antecubital vein of the included women in red coloured coded plain vacutainers. Blood samples were allowed to be clotted for 30 minutes then centrifuged for 15 minutes at 3000 rpm and sera used for the biochemical analysis. We used fully automated enzyme amplified chemiluminescent immunoassay analyser model Immulite 1000 for measurement of CA-125, LH, FSH and PRL. The principle of method is based on a solid-phase, two-site chemiluminescent immunometric assay [10,11]. Measurement of these blood parameters was done by using commercial kits from Siemens Medical Solutions Diagnostics, Los Angeles, CA, USA.

STATISTICAL ANALYSIS

The date entry and data analysis were done using the Statistical Package for the Social Sciences (SPSS) version 19.0. Data were presented as number, percentage, mean and standard deviation. Statistical analysis was done by normal distribution 'z' test. The p-values were considered statistically significant and highly significant when $p<0.05$ and $p<0.001$ respectively.

RESULTS

In the present study, 30 patients with PCOS, mean age 29.7 years (±5.51) and 30 controls, mean age 30.8 years (±4.65) were included.

There were insignificant differences in the mean levels of age of the study cases however, significant difference found in mean levels of haemoglobin (Hb) and BMI among patients versus controls ($p<0.05$ and $p<0.001$ respectively), which were all within the normal range to confirm the inclusion criteria as presented in [Table/Fig-1].

Demographic parameters	Control group (n=30)	PCOS group (n=30)
Age (years)	30.8±4.65	29.7±5.51^{NS}
Hb (gm/dL)	11.8±1.10	10.3±1.08*
BMI (Kg/m^2)	21.6±1.96	27.9±3.18**

[Table/Fig-1]: Comparison of demographic data controls and subjects with PCOS.
*p<0.05; **p<0.001; NS: Not Significant
Statistical analysis was done by normal distribution 'z' test.

Comparison of the mean±SD of CA-125, LH, FSH and PRL among patients versus controls is presented in [Table/Fig-2], which showed significantly higher ($p<0.001$) serum CA-125 levels with insignificantly lower serum levels of FSH among patients versus controls. Serum levels of LH and PRL were significantly elevated in the PCOS cases with controls.

Biochemical parameters	Control group (n=30)	PCOS group (n=30)
CA-125 (U/mL)	3.38±1.48	23.8±37.5**
LH (mIU/mL)	4.85±1.85	6.95±4.91*
FSH (mIU/mL)	7.78±2.11	7.05±2.81^{NS}
PRL (ng/dL)	10.9±5.02	14.3±6.82*

[Table/Fig-2]: Serum CA-125, LH, FSH and PRL in controls and subjects with PCOS.
*p<0.05;**p<0.001; NS: Not significant
Statistical analysis was done by normal distribution 'z' test.

DISCUSSION

Polycystic ovarian syndrome is a herald of lifelong conditions that can lead to serious sequelae such as endometrial or ovarian cancer, diabetes mellitus and cardiovascular disease [12]. Demographic data of study subjects such as age was statistically insignificant, mean Hb level significantly change ($p<0.05$) whereas BMI was highly significant as compared with those of control group in patients.

The present study showed highly significant ($p<0.001$) i.e., seven times increase in serum CA-125 levels in subjects with PCOS as compared to that of control group. In the present study, it is not possible to understand the meaning of an abnormally high CA-125 without supplementary information about the particular patient being evaluated. The cause is that blood levels of this tumour marker can be elevated in many different benign and malignant conditions. Even though CA-125 is a helpful investigation in examining patients who are being treated for ovarian cancer [13], however, a single CA-125 test is not considered to be a useful screening test for cancer reported by Magrina JF and Cornella JL [14].

Serum levels of LH were elevated significantly ($p<0.05$) in the group of patients with PCOS. Similar to present results Lobo RA et al., also observed increased serum LH levels [15]. On the contrary, serum FSH levels were reduced insignificantly as compared to those of controls. Serum FSH concentration usually normal or low found in PCOS patients [16]. One probable clarification for this observation may be a speed up Gonadotropin Releasing Hormone (GnRH) pulse generator activity and heightened pituitary response to GnRH. Because the synthesis and secretion of LH and FSH are highly dependent on the pattern of GnRH stimulation [15,16].

Authors observed statistically significant increase ($p<0.05$) in serum PRL levels in PCOS subjects as compared to that of the control group which might be a result of a defect in hypothalamic dopaminergic activity [17]. Kyritsi EM et al., identified a serum PRL cut-off value indicative of a PRL producing adenoma in women with PCOS and hyperprolactinemia and characterised such patients. They found, in women with PCOS, PRL levels exceeding 85.2 ng/mL are highly suggestive of a prolactinoma justified pituitary imaging [18]. No single subject with prolactinemia found in present study.

Patients with PCOS have a 2.7-fold increased risk for developing endometrial cancer. A major factor for this increased malignancy risk is prolonged exposure of the endometrium to unopposed estrogen that results from anovulation. Additionally, secretory endometrium of some women with PCOS undergoing ovulation induction or receiving exogenous progestin exhibits progesterone resistance accompanied by dysregulation of gene expression controlling steroid action and cell proliferation, reported by Dumesic DA and Lobo RA [19]. Fearnley EJ et al., suggested PCOS is a risk factor for endometrial cancer [20].

Barry JA et al., examined gynaecological malignancies in women with PCOS and their systemic review and meta-analysis data suggested that women of all ages with PCOS are at higher risk of endometrial cancer but the risk of ovarian and breast cancer was not significantly increased overall [21]. The precise possibility of ovarian malignancy in patients with PCOS is difficult to conclude.

LIMITATION

The present study was a short-term project, has been limited to a comparatively small number of cases of ovarian cancer identified specifically in PCOS. However, the limitation of present study was small sample size; so, more studies with good sample size are required to corroborate these results.

CONCLUSION

The present findings suggest that increased levels of CA-125, LH, PRL and low levels of FSH may be an indicator of ovarian abnormalities in PCOS. Authors therefore, suggest that these investigations should be performed routinely in women having PCOS. This will definitely aid in the management of PCOS which would otherwise lead to life-threatening conditions such as ovarian cancer or endometrial cancer. Further prospective and controlled studies are required to investigate the power and reliability of tumour markers and endocrine hormones in the early diagnosis of ovarian or endometrial tumours.

REFERENCES

[1] Franks S. Polycystic ovary syndrome. N Engl J Med. 1995;333:853-61.
[2] Stein IF, Leventhal ML. Amenorrhea associated with bilateral polycystic ovaries. Am J Obstet Gynaecol. 1935;29:181-91.

[3] Goldenberg N, Glueck C. Medical therapy in women with polycystic ovarian syndrome before and during pregnancy and lactation. Minerva Ginecol. 2008;60(1):63-75.
[4] Boomsma CM, Fauser BC, Macklon NS. Pregnancy complications in women with polycystic ovary syndrome. Semin Reprod Med. 2008;26(1):72-84.
[5] Palacio JR, Iborra A, Ulcova-Gallova Z, Badia R, Martínez P. The presence of antibodies to oxidative modified proteins in serum from polycystic ovary syndrome patients. Clin Exp Immunol. 2006;144(2):217-22.
[6] Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The prevalence and features of the polycystic ovary syndrome in an unselected population. J Clin Endocrinol Metab. 2004;89(6):2745-49.
[7] Somani N, Harrison S, Bergfeld WF. The clinical evaluation of hirsutism. Dermatologic Therapy. 2008;21(5):376-91.
[8] Banaszewska B, Spaczyński RZ, Pelesz M, Pawelczyk L. Incidence of elevated LH/FSH ratio in polycystic ovary syndrome women with normo- and hyperinsulinemia. Rocz Akad Med. Bialymst. 2003;48:131-34.
[9] Immulite Reference ranges. Siemens Medical Solution Diagnostics, Los Angeles, CA, USA ; 2006
[10] Sibley PEC, Vankrieken L, Durham AP, El Shami AS. Impact of the menstrual cycle on BR-MA (CA15-3) and OM-MA (CA125) values, as determined by automated chemiluminescent assays on the IMMULITE Analyser [abstract]. Clin Chem. 1999;45 Suppl 6:A109.
[11] Babson AL. The IMMULITE automated immunoassay system. J Clin Immunoassay. 1991;14:83-88.
[12] The Rotterdam ESHRE/ASRM- sponsored PCOS consensus workshop group. Revised 2003 consensus on diagnostic criteria and long term health risks related to Polycystic Ovary Syndrome (PCOS). Hum Reprod. 2004;19(1):41-47.
[13] Anastasi E, Marchei GG, Viggiani V, Gennarini G, Frati L, Reale MG. HE4: a new potential early biomarker for the recurrence of ovarian cancer. Tumour Biol. 2010;31:113-19.
[14] Magrina JF, Cornella JL. Office management of ovarian cysts. Mayo Clin Proc. 1997;72(7):653-56.
[15] Lobo RA, Kletzky OA, Campeau JD, diZerega GS. Elevated bioactive luteinizing hormone in women with polycystic ovary syndrome. Fertil Steril. 1983;39(5):674-78.
[16] Pastor CL, Griffin-Korf ML, Aloi JA, Evans WS, Marshall JC. Polycystic ovary syndrome: evidence for reduced sensitivity of the gonadotropin-releasing hormone pulse generator to inhibition by estradiol and progesterone. J Clin Endocrinol Metab. 1998;83(2):582-90.
[17] Luciano AA, Chapler FK, Sherman BM. Hyperprolactinemia in polycystic ovary syndrome. Fertil Steril. 1984;41(4):719-25.
[18] Kyritsi EM, Dimitriadis GK, Angelousi A, Mehta H, Shad A, Mytilinaiou M, et al. The value of prolactin in predicting prolactinoma in hyperprolactinaemic polycystic ovarian syndrome. Eur J Clin Invest. 2018;48(7):e12961.
[19] Dumesic DA, Lobo RA. Cancer risk and PCOS. Steroids. 2013;78(8):782-85.
[20] Fearnley EJ, Marquart L, Spurdle AB, Weinstein P, Webb PM. Polycystic ovary syndrome increases the risk of endometrial cancer in women aged less than 50 years: an Australian case-control study. Cancer Causes Control. 2010;21(12):2303-08.
[21] Barry JA, Azizia MM, Hardiman PJ. Risk of endometrial, ovarian and breast cancer in women with polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod Update. 2014;(5):748-58.

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