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STUDY OF SERUM ANTI-MÜLLERIAN HORMONE LEVEL IN POLYCYSTIC OVARY SYNDROME

Biochemistry

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a heterogeneous disorder characterized by hormonal imbalance, which in turn results in infertility in young women. Traditionally, along with ultrasound reports, changes in luteinizing hormone (LH), follicle stimulating hormone (FSH), and the LH/FSH ratio are employed for the diagnosis of PCOS. In the present study, we report the usefulness of the serum Anti-Müllerian hormone (AMH) levels in PCOS diagnosis. The study group had 125 PCOS cases and an equal number of healthy controls. Their serum status of Estradiol (E2), LH, FSH, AMH, and prolactin (PRL) were estimated by Electro-Chemiluminescence immunoassay (ECLIA). We observed a significant rise in LH, FSH, LH/FSH ratio and AMH in PCOS cases when compared to control subjects, whereas no significant variation was observed in estradiol and PRL. The LH/FSH ratio was inconclusive in 11 of the 125 PCOS cases (8.8%), where AMH was found to be elevated in all of them. Hence, we recommend the elevated AMH as a potential indicator for the diagnosis of PCOS.

KEYWORDS

PCOS, Infertility, FSH/LH ratio, AMH

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a group of disorders that affect the functioning of ovaries in young women during their reproductive age. It is featured by multiple cysts in ovaries, irregular menstrual cycle, hirsutism, and hormonal imbalance which in turn results in infertility in affected women[1]. As per WHO reports, around 116 million young women (3.4%) are affected worldwide with PCOS[2]. Prevalence of PCOS in Indian population is estimated to be 6-9% with higher prevalence in urban area[3,4]. The gonadotropic hormones – LH and FSH are essential for maintaining the normal ovarian physiology. The LH triggers ovulation and development of corpus luteum in ovaries. It is also important for the production of androgens and estradiol from theca cells. The hormone FSH helps in the growth and development of immature ovarian follicles. The LH/FSH ratio in normal subjects is found to be 1:1 and it is found to be increased in the majority of the PCOS cases[5]. The AMH, a glycoprotein which is structurally related to transforming growth factor β family, inhibits the effect of FSH on primordial and growing follicles. Expression of AMH in growing follicles is affected in PCOS rendering it an ideal marker for ovarian physiology[5,6]. The traditional trend in clinical diagnosis is an evaluation of clinical history in combination with ultrasound scan ovaries and biochemical changes in estradiol, LH, FSH and LH/FSH ratio. Here we report the usefulness and advantage of serum status of AMH in the PCOS diagnosis.

MATERIALS AND METHODS

The study was conducted from IVF wing of Department of Obstetrics and Gynaecology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan. The study group was constituted by 125 newly diagnosed cases of women with PCOS as confirmed by clinical history and ultrasound reports. The case group (27.5 ± 5.9 years) was compared with age-matched healthy controls (29.2 ± 5.6 years) were included. The study was conducted during their mid-cycle period and cases like pregnant women and subjects with severe diseases like malignant tumor were excluded from the study. About 5 mL of blood was collected by venipuncture in the plain vial as per the standard protocols. The serum was used for the estimation of estradiol, LH, FSH, PRL, and AMH, and the method employed was Electrochemiluminescence immunoassay (ECLIA) on Cobas e411 autoanalyzer (Roche Holding AG, Switzerland). Patient recruitment and study design were according to the institutional ethical committee (IEC) recommendations. Samples were run in triplicates and the mean results obtained are represented as mean ± SD. We have used a nonparametric statistical tool, the student *t*-test for comparing one variable between two independent samples (or groups). Correlation analysis was done by Spearman rank correlation method. A *p*-value <0.05 was considered to be significant and a *p*-value of <0.01 was considered to be highly significant for a given hypothesis testing. All the statistical analysis were performed using GraphPad Prism Ver.6.0 (GraphPad Software, Inc., CA, USA) and Microsoft Excel, MS office 2013 (Redmond, WA, USA).

RESULTS

In the present study, 51 cases (40.8%) of PCOS got an LH/FSH ratio <2.0 and the rest 74 cases (59.2%) got an LH/FSH ratio 2.0 or above (Fig. 1: A). Among the PCOS subjects, 67% had complications of primary infertility and 33% had secondary infertility complications (Fig 1: B). The serum AMH level (Fig. 1: C) in PCOS (11.33 ± 4.85 ng/mL) was significantly high (*p*-value <0.01) when compared to that of control group (3.15 ± 1.38 ng/mL). The serum LH level (Fig. 1: D) in PCOS (16.09 ± 9.91 IU/L) was also significantly high (*p*-value <0.01) when compared to that of the control group (7.1 ± 5.33 IU/L). The serum FSH level (Fig. 2: A) in PCOS (8.17 ± 4.95 IU/L) was significantly elevated (*p*-value <0.05) when compared to that of the control group (6.86 ± 3.45 IU/L). The serum LH/FSH ratio (Fig. 2: B) in PCOS (1.97 ± 0.95) was found to be elevated (*p*-value <0.01) significantly when compared to that of the control group (1.11 ± 0.21).

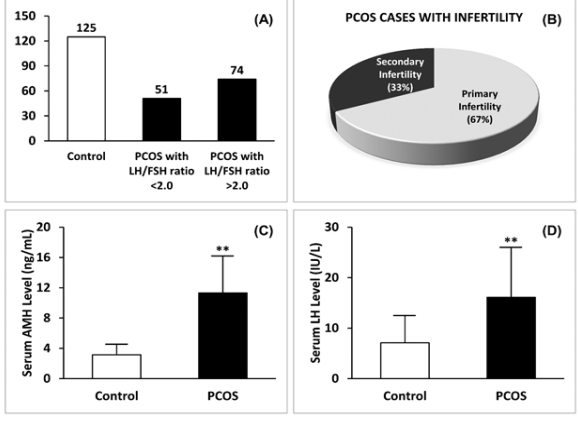

Fig. 1: (A) Study group with 125 controls and 125 cases (total $n = 250$). **(B)** Percentage of infertility in PCOS cases. **(C)** Comparison of serum AMH level. **(D)** Comparison of serum LH level. ***p*-value <0.01.

The serum estradiol level (Fig. 2: C) in PCOS (41.69 ± 17.13 pg/mL) did not show any significant variation when compared to that of the control group (42.14 ± 11.11 pg/mL). The serum PRL level (Fig. 2: D) in PCOS (11.79 ± 5.99 µg/L) also did not show any significant variation when compared to that of the control group (10.85 ± 5.54 µg/L).

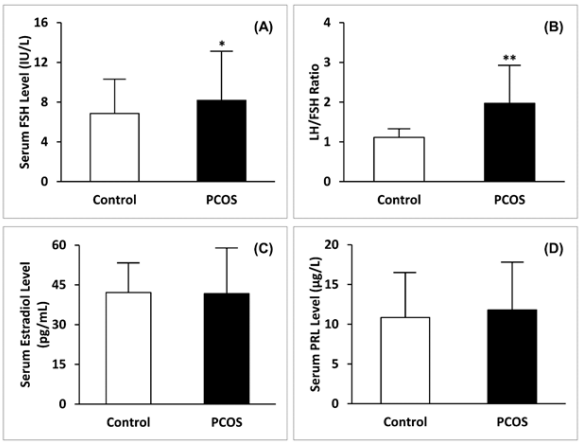

Fig. 2: (A) Comparison of serum FSH level. **(B)** Comparison of serum LH/FSH ratio. **(C)** Comparison of serum Estradiol level. **(D)** Comparison of serum PRL level. ***p*-value <0.01, **p*-value <0.05.

DISCUSSION

The reference range for serum AMH is 1.5-5 ng/mL and our test population showed a significant increase when compared to control group. Serum AMH usually falls with the advance in age, but, an impaired ovarian physiology stimulates AMH production to an abnormal level[7]. Recent studies show that elevated serum AMH could be treated as a potential tool for the clinical diagnosis of PCOS[8]. Studies have also shown that elevated AMH may be found in the pre-pubertal or adolescent period and even in daughters of PCOS mothers[9,10].

In our study, the LH/FSH ratio was found to be elevated in PCOS (1.97 ± 0.95) when compared to that of the control group (1.11 ± 0.21). In the test group, among 125 PCOS cases, 74 cases (59.2%) had an elevated LH/FSH ratio above 2.0. However, 11 women with PCOS (8.8%) had normal or near-normal or inconclusive LH/FSH ratio. Interestingly, all these 11 cases had elevated AMH level, pointing out the relevance of AMH in such situations. There was a positive correlation between elevated serum AMH and an elevated LH/FSH ratio 2.0 or above. Moreover, both the elevated AMH and LH/FSH ratio were positively correlated with the infertility complications. The elevation of serum AMH in some of the cases was 3 to 4 times normal, indicative of the extent of ovarian pathology and comparable with the recent studies[11,12,13].

Serum LH/FSH ratio is a routinely employed tool in the PCOS diagnosis[5], and our results also showed a positive correlation between PCOS with primary infertility and elevated LH/FSH ratio. However, the elevated serum AMH clearly ruled out the PCOS and associated infertility complications in those 11 cases where LH/FSH ratio was inconclusive. The serum estradiol and PRL may or may not be affected in the PCOS pathogenesis[14,15]. Our results did not show any significant variation in serum estradiol and PRL in PCOS subjects.

CONCLUSION

From our study, it is clear that elevated serum AMH levels can be used as a potential marker for the clinical diagnosis of PCOS, especially when LH/FSH ratio is inconclusive. By applying a combination of serum AMH, LH, FSH, LH/FSH ratio we can rule out PCOS without any ambiguity. An extended study on a larger population would definitely add more validity to the current topic of study.

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