Diagnostic Role of Anti-Mullerian hormone in Polycystic Ovarian Syndrome

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Abstract

Objective: To evaluate if the elevated levels of Anti-Mullerian hormone (AMH) could serve as an indicator of polycystic ovarian syndrome (PCOS) in patients presenting with infertility.

Method: The present study was conducted at Institute of Molecular Biology and Biotechnology, The University of Lahore and Australian Concept Infertility Medical Center (ACIMC), Lahore. It was a case control study. A total of 101 females aged between 20-40 years presenting with infertility were included in this study. Among study participants, 51 infertile females had PCOS and 50 were non-PCOS infertile subjects. After taking informed consent, medical history and anthropometric indices were recorded on standardized proforma. Transvaginal ultrasound was done to assess ovarian morphology. Serum AMH, follicle stimulating hormone (FSH), luteinizing hormone (LH), thyroid stimulating hormone (TSH) and prolactin levels were measured by commercially available ELISA kits. Serum AMH levels were measured in 10 healthy, fertile females having normal menstrual cycle as normal reference values in our population.

Results: Mean AMH levels were significantly higher (9.9±1.1ng/ml) in females with polycystic ovarian syndrome as compared to subjects without this syndrome (1.0± 0.3ng/ml). Mean FSH levels were significantly lower in females with PCOS (p value 0.001) but LH: FSH ratio, serum luteinizing hormone and prolactin level were not significantly different in two groups.

Conclusion: The study provides evidence that raised serum levels of AMH are associated with the presence of PCOS and therefore can serve as useful marker in diagnosis of PCOS.

Keywords: PCOS, AMH, infertility

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Introduction

Polycystic ovarian syndrome (PCOS), one of the common diseases effecting females of reproductive age, was for the first time, described by Stein and Leventhal in 1935.[1] It is a multisystem disease which is characterized by increased levels of androgens, irregular menstrual periods, hirsutism and cyst formation in the ovaries.[2] The delayed sequels of this condition include diabetes mellitus, obesity and cardiovascular disease.[3] Over the years, a number of screening procedures, imaging techniques and biochemical markers have been used for diagnosis of polycystic ovarian disease. The gold standard for diagnosing the PCOS is Rotterdam criteria (2003). According to this criterion, the diagnosis of PCOS is made if any two of the following three are present: Oligo/anovulation, clinical or biochemical hyperandrogenism, polycystic ovaries on ultrasound (≥12 follicles with a diameter of 2-9mm or/and ovarian volume >10ml).[4] The Rotterdam criteria relies on findings of ultrasound as cornerstone for diagnosis of PCOS.[5] Although high resolution sonographic techniques are developed, yet there is still a deal of observer variability regarding ovarian morphology and technical difficulties in performing ultrasound.[5] Another reason for avoiding ultrasound for diagnosis of PCOS is that majority of ultrasounds are made trans-abdominally not trans-

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vaginally affecting the accuracy of findings.[6] Abnormal FSH and LH secretion has also been observed in patients having PCOS resulting in altered FSH/LH ratio but studies have shown that these values do not significantly differ between PCOS and non-effected group.[7]

Anti-Mullerian hormone which is produced by granulosa cell correlates with number of antral follicles which are 2-9mm in size.[4] Studies have shown that anti-mullerian hormone levels show a significant increase in females having PCOS due to excessive accumulation of preantral and small antral follicles as result of impaired folliculogenesis.[5,8] It has also been suggested that increased levels of AMH may also be associated with ovarian hyperandrogenism.[5] It is a less invasive and stable parameter during menstrual cycle.[9] The present study was conducted to find out whether serum AMH can be used as biomarker to diagnose PCOS in females of reproductive age group in our population presenting with infertility.

Material and Methods

The present study was conducted at Institute of Molecular Biology and Biotechnology and The University of Lahore and Australian Concept Infertility Medical Center (ACIMC), Lahore. The present study was conducted at Institute of Molecular Biology and Biotechnology, The University of Lahore and Australian Concept Infertility Medical Center (ACIMC), Lahore. Study population and sample size, consisted of 111 females between age of 20-40 years. The females diagnosed for PCOS according to Rotterdam criteria were included as study subjects.[4] An equal number of age-matched non-PCOS infertility subjects were included as control group in the present study. Exclusion criteria was the patients with other systemic or chronic diseases, congenital adrenal hyperplasia, Cushing syndrome and androgen secreting tumors. The subjects who used hormonal drugs within three months before beginning of the study were also excluded. It was a case control study. The subjects were divided into two age-matched groups as Group-1 (cases), consisted of infertile patients diagnosed to have PCOS on the basis of Rotterdam criteria. (n=51) Group-2 (controls) consisted of patients without PCOS but presenting with infertility due to other factors. (n= 50). In addition, a group of 10 healthy fertile women were included for reference level of AMH. Physical characteristics and history of the subjects were recorded on Preforma. Body weight and height were recorded using Camry weight scale. Body mass index (BMI) was calculated according to following equation: BMI= Body Weight (kg)/Height (m^2). BMI of 18.5-24.9 kg/m^2 was taken as normal. Physical examination for evaluation of hirsutism was based on modified Ferriman-Gallwey Score. To determine the biochemical markers, 5 ml of blood sample was collected from each participant under aseptic techniques on third day of menstrual cycle. Blood sample was transferred to evacuated serum tubes. Serum was separated by allowing the blood to clot and centrifuged at 3000 rmp for 10 minutes. Serum AMH, FSH, LH, Prolactin and TSH were determined by enzyme-linked immune-sorbent assay using commercially available kits, AMH (Beckman Coulter, Inc. Brea, USA), FSH (Cloud-Clone Corp, Housten, TX, USA), LH and TSH (Cayman Chemical, Ann Arbor, MI, USA), Prolactin (Abcam, Cambridge, MA, USA). All determinations were made in duplicate. Data was analyzed using SPSS version 20. Quantitative variables were described using means and standard deviations. Qualitative variables were described using percentages. The significance of differences between two groups were determined by student's t-test. The p value of <0.05 was considered significant.

Results

The general characteristics of the subjects are given in table I. The medical history of the subjects and controls is given in table II. Table 3 shows mean ± SEM of the FSH, LH, Prolactin, AMH and TSH. The p value shows significantly increased levels of AMH in subjects with PCO as compared to control group.

Discussion

Table 1: *Physical characteristics of subjects (n=111)*

Characteristics	Subjects with PCOS n=51 mean ± SEM	Subjects without PCOS n=50 mean ± SEM
Age (Years)	33.3±0.4	33±0.4
BMI	26.6±0.6	27.0±0.6

Table 2: *Medical history of subjects (n= 111)*

Medical History	Subjects with PCOS (n= 51)	Subjects without PCOS (n=50)
Age at menarche (mean± SEM)	13.4± 0.1	13.1±0.2
Primary infertility (%)	78	68
Irregular menstrual cycle (%)	24	12
Dysmenorrhea (%)	20	4
Heavy bleeding (%)	26	6

Table 3: *Levels of biochemical markers*

Biochemical marker	Subjects with PCOS n=51	Subjects without PCOS n= 50	p-value
AMH[a] (ng/ml)	9.9±1.1	2.1±0.4	0.001*
FSH (m IU/ml)	6.4±0.3	10.1±0.9	0.001*
LH (m IU/ml)	6.9±0.6	7.8±1.2	0.18
Prolactin	15.6±0.9	17.1±1.0	0.6
TSH (µIU/ml)	3.5±1.5	1.4±0.1	0.095

a-Mean AMH level in healthy fertile women (n=10);1.8± 1.0ng/ml
p-value less than 0.05 is considered significant

The current study was carried out to find out the association between PCOS and AMH levels in infertile patients in our settings. In this study, significantly high levels of AMH were seen in patients diagnosed with PCOS as compared to those without PCOS. Previous studies have shown that secretion of AMH by granulosa cells in polycystic ovaries increases several folds as compared to normal ovaries. Christina et al conducted a study to determine the effectiveness of AMH in detection and diagnosis of polycystic ovaries. On the basis of the results, he concluded that AMH levels were significantly high in patients with PCOS and that serum AMH levels have a sensitivity and specificity as in screening of PCOS[10]. In another study conducted by Nada et all, high serum AMH levels were correlated with PCOS. They found that AMH can be a promising marker in diagnosis of PCOS especially if evaluation of ovarian morphology was complicated[11]. Similar results were also found in a study conducted for hormonal profiling for diagnosis of polycystic ovarian syndrome by Henri et al[12]. Muhammad Salman et al also recommended that elevated AMH serum levels can be used as a strong predictor to reflect the certainty of PCOS diagnosis among women of reproductive age13. Studies have demonstrated that AMH level do not change with menstrual cycle as FSH, LH and inhibin do. In present study, FSH level were significantly lower in patients with PCOS but LH/FSH ratio was normal in majority of the patients. Similar results were also reported in a study conducted by Li Wei Cho et al. They found that LH /FSH ratio was not significantly different between PCOS and normal subjects.[7] The stability in levels of AMH regard-less of menstrual cycle further favors the use of AMH as biomarker for diagnosis of AMH.[14]

Conclusion

Raised AMH level have significant association with PCOS.

Conflict of Interest *None*

Funding Source *None*

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Authors Contribution

MUQ: Conceptualization of Project
SK: Data Collection
FS: Literature Search
SQA: Statistical Analysis
YA: Drafting, Revision
SK: Writing of Manuscript