Serum AMH (Anti-Müllerian Hormone) as a predictor of Polycystic Ovarian Syndrome among the Women of Reproductive Age – a study in a tertiary care hospital

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Abstract

Background: Anti-Müllerian Hormone (AMH) is multiple fold increased in PCOS women compared to normal women. The increase in AMH is due to an increase in the number of antral follicles which increases in response to gonadotropin hormone. This study aims to determine the specificity and sensitivity of AMH in the diagnosis of polycystic ovarian syndrome.

Method: A cross-sectional study was carried out. 100 women diagnosed with PCOS participated in the study. They were examined for their reproductive characteristics and demographic characteristics. The AMH levels were assessed in these women with an immunoassay. The correlation between the levels of AMH and reproductive characteristics was determined statistically.

Results: It was found that the number of days in the menstrual cycle, volume of the left ovary, and level of luteinizing hormone were significantly different in both types of women. Hence, the p-value for the menstrual cycle, volume of the left ovary, and level of luteinizing hormone were 0.03, 0.05 and 0.01, respectively, when correlated with the levels of anti-Müllerian hormone.

Conclusion: Assessment of AMH levels can aid in the diagnosis of PCOS. Increased levels of AMH indicate hormonal imbalance, irregularities in the menstrual cycle and polycystic morphology of the ovary. These three characteristics are often associated with polycystic ovarian syndrome.

Keywords: *Anti-Müllerian hormone, PCOS, hormonal imbalance*

Introduction

Metabolic disorders related to the endocrine system are common due to lifestyle changes. However, polycystic ovarian syndrome was defined back in 1935 [1]. Polycystic ovarian syndrome is the most prevalent disorder among women of reproductive age. The symptoms of this disorder vary significantly. The phenotype of the disorder determines the characteristics of this disorder in a patient. Rotterdam stated that any two of the hyperandrogenism, the release of more than one or no ovum from the ovary, and ovaries with multiple cysts in a patient confirm the presence of PCOS [2].

PCOS can be a combination of any two of the above characteristics. Previously, biochemical tests were performed to determine the morphology of the ovaries [3]. Since enlarged and polycystic ovaries are peculiar characteristics of PCOS, determining the morphology of the ovary is of utmost importance. With the advent of ultrasound sonography, the morphology of the ovaries can be viewed by the interpersonal differences in the observation, which can lead to false positive results. PCOS has multiple hormonal imbalances associated but the diagnosis of PCOS does not have a proper hallmark. However, in the literature and from the clinical studies conducted on different populations, it is found that PCOS has a 3:1 ratio of follicle-stimulating hormone and luteinizing hormone [4, 5]. There are several other hormonal imbalances such as imbalance in calcitonin, gonadotropin hormone, vitamin D deficiency and Anti-Müllerian Hormone.

Recently 'AMH' has been studied for its sensitivity and specificity in diagnosis of PCOS [6]. A study reports that assay of 'AMH' along with morphology of the ovary can help in accurate diagnosis of PCOS in women [7]. 'AMH' is multiple fold increased in PCOS women compared

to normal women. The increase in 'AMH' is due to an increase in the number of antral follicles which increases in response to gonadotropin hormone. This study aims to determine the specificity and sensitivity of the 'AMH' in the diagnosis of polycystic ovarian syndrome.

Methods

Study design: A cross-sectional study was carried out at the Regional Institute of Medical Sciences (RIMS) in Imphal, Manipur, India in 2019.

Participants: Women visiting the outpatient Gynaecology Department of the Regional Institute of Medical Sciences (RIMS) in Imphal, Manipur, India and diagnosed with polycystic ovarian syndrome were included in the study. The age of women selected for the study ranged from 15 to 45 years. Women who had a history of endocrine disorders were on medication that could affect the hormones, and had undergone major surgical procedures were not included in the study.

Data collection: Women who participated in the study and were diagnosed with polycystic ovary syndrome underwent an ultrasound sonography; their ovary volume and the number of antral follicles were determined. The participants were interviewed regarding the history of the menstrual cycle. Women who had a menstrual cycle of 20-33 days were considered to have a normal cycle. The women who had cycles of more than or equal to 35 days were considered to have amenorrhea.

The demographic characteristics of the women were determined. Hyperandrogenism in the women was determined based on the level of hirsutism. The scale of hirsutism that is modified Ferriman Gallwey scale was used. The scores were assigned to the hirsutism of each participant. Less than 8 was considered as no hyperandrogenism, women with an 8-15 score had mild symptoms of hyperandrogenism, women with a 16-25 score had moderate hyperandrogenism, and those with greater than 25 had serious hyperandrogenism. Biochemical immunoassays were

performed to determine the levels of luteinizing hormone, follicle-stimulating hormone, thyroid-stimulating hormone, and prolactin. These tests were performed when the women were in the follicular phase of the menstrual cycle. The 'AMH' was determined using immunoassay by enzyme binding.

Ethical consideration: All the participants consented to the study and the approval for this study was obtained from the institutional ethics committee.

Statistical analysis: The data obtained from both groups was compared statistically using a t-test. The significance of the correlation between variables was determined and the correlation was considered significant if the p-value was less than 0.05.

Results

In total 100 women participated in this study. The mean age of the women participating in the study was 29 years. 20 among the 100 showed severe hirsutism indicating hyperandrogenism. 43 had milder symptoms of hyperandrogenism and 27 had moderate symptoms of hyperandrogenism. Table no. 1 illustrates the reproductive characteristics of the participating women and its correlation n with anti-Müllerian hormone.

Table no.1: Correlation of the reproductive parameters with levels of anti-Müllerian hormone

Parameters	Criteria	Frequency	Correlation with levels of Anti-Müllerian hormone
Age	Less than 20	31	Not significant
	20 to 35	63	
	More than 35	06	

Hirsutism score	Score between 8 to 15	43	Not significant
	Score between 16-25	37	
	Score more than 25	20	
Menstrual cycle	20 to 33 days	35	Significant
	More than 33 days	35	
	No cycle	30	
Volume of left ovary	Less than 10ml	10	Significant
	More than 10 ml	90	
Volume of right ovary	Less than 10ml	16	Not significant
	More than 10 ml	84	
Thyroid stimulating hormone	Normal	98	Not significant
	High	2	
Prolactin	Normal	88	Not significant
	High	12	
Follicle stimulating hormone	Normal	96	Not significant
	High	04	
Luteinizing hormone	Normal	84	Not significant
	High	16	

The cut-off value of the hormones was preset, more than that was considered to be higher than normal. The cut-off value for follicle-stimulating hormone was 9 IU/ml, the cut-off value for

luteinizing hormone was 12.5 IU/L, the cut-off value for prolactin was 29 ng/ml, and the cut-off value for thyroid stimulating hormone was 4.0 IU/ml.

The cut-off value for 'AMH' was 3.9 ng/ml. 70 women among the 100 had raised levels of anti-Müllerian hormone. When reproductive characteristics were compared within the women having higher 'AMH' and normal 'AMH' it was found that the number of days in the menstrual cycle, volume of the left ovary, and level of luteinizing hormone were significantly different in both the types of women. Hence the p-value for the menstrual cycle, volume of left ovary and level of luteinizing hormone were 0.03, 0.05 and 0.01 respectively, when correlated with the levels of anti-Müllerian hormone.

The women who had 'AMH' higher than 3.9 ng had an average menstrual cycle of 41 days compared to women with 'AMH' less than 3.9 ng and had an average menstrual cycle of 30 days on an average. Similarly, women with higher 'AMH' had a left ovary volume of 18 cm3 compared to the women with lower 'AMH' who had a volume of 14 cm3. Also, women with high 'AMH' had a 9.2 IU/ml average of follicle-stimulating hormone compared to women with lower 'AMH' had an average follicle-stimulating hormone of 5.6 IU/ml.

Discussion

It was found in this study that women with increased 'AMH' have longer duration of menstrual cycle. According to Rotterdam criteria longer duration of the menstrual cycle is related to either oligoamenorrhea or amenorrhea [8]. A study conducted on 'AMH' in PCOS women had similar findings [9].

In PCOS the hormonal imbalance causes an increase in the number of antral follicles which leads to an increase in the anti-Müllerian hormone. The increase in the antral follicles increases the ovary volume. An increase in the ovary volume is a significant characteristic of polycystic ovary

morphology. This finding is consistent with studies conducted previously to determine the level of 'AMH' in women with polycystic ovaries [10, 11].

The increase in the level of luteinizing hormone is due to an increase in the hormonal imbalance in women with polycystic ovary syndrome. Luteinizing hormone and follicle-stimulating hormone maintain the regular menstrual cycle. The women participating in the study showed a substantial increase in the ratio of luteinizing hormone and follicle-stimulating hormone during their follicular stage causing irregularities in the menstrual cycle.

Hirsutism and 'AMH' levels were not found to be significant but according to Rotterdam criteria, hyperandrogenism is an important characteristic of PCOS women. In a study, it was found that women with PCOS and higher BMI had severe hyperandrogenism [12]. In our study majority of the women had mild hirsutism. As PCOS is a syndrome which is associated with several biochemical and physiological changes the diagnosis of PCOS cannot be dependent on a single factor [13]. In a review of the literature, authors reported that PCOS can be diagnosed with a combination of biochemical tests such as 'AMH' assay, TSH level, sex hormone levels and physical examination to determine hyperandrogenism [14]. Rotterdam criteria should be applied while diagnosing PCOS [15].

Conclusion

Assessment of Anti-Müllerian Hormone level can aid in the diagnosis of PCOS. Increased levels of it indicates hormonal imbalance, irregularities in the menstrual cycle and polycystic morphology of the ovary. These three characteristics are often associated with polycystic ovarian syndrome.

Acknowledgement

References

1. Michelmore KF, Balen AH, Dunger DB, Vessey MP. Polycystic ovaries and associated clinical and biochemical features in young women. Clin Endocrinol. 1999;51(6):779–86. doi: 10.1046/j.1365- 2265.1999.00886.x

2. Koivunen R, Laatikainen T, Tomas C, Huhtaniemi I, Tapanainen J, Martikainen H. The prevalence of polycystic ovaries in healthy women. Acta Obstet Gynecol Scand. 1999;78(2):13741.

3. Farquhar CM, Birdsall M, Manning P, Mitchell JM, France JT. The Prevalence of Polycystic Ovaries on Ultrasound Scanning in a Population of Randomly Selected Women. Aust New Zeal J Obstet Gynaecol. 1994;34(1):67–72. doi: 10.1111/j.1479-828x.1994.tb01041.x

4. Lowe P, Kovacs G, Howlett D. Incidence of polycystic ovaries and polycystic ovary syndrome amongst women in Melbourne, Australia. Aust New Zeal J Obstet Gynaecol. 2005;45(1):17–9. doi:10.1111/j.1479-828X.2005.00334.x

5. Akram M, Roohi N. Endocrine correlates of polycystic ovary syndrome in Pakistani women. J Coll Physicians Surg Pakistan. 2015;25(1):22–6.

6. Stein IF, Leventhal ML. Amenorrhea is associated with bilateral polycystic ovaries. Am J Obstet Gynecol. 1935;29(2):181–91. doi: 10.1016/j.ajog.2015.12.013

7. Fauser BCJM. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril. 2004;81(1):19–25. doi: 10.1016/j.fertnstert.2003.10.004

8. Sobti S, Dewan R, Ranga S. Metabolic syndrome and insulin resistance in PCOS phenotypes. Int J Reprod Contraception Obstet Gynecol. 2017;6(11):5067. doi: 10.18203/2320-1770.ijrcog20175027 Page 13/16

9. Kar S. Anthropometric, clinical, and metabolic comparisons of the four Rotterdam PCOS phenotypes: A prospective study of PCOS women. J Hum Reprod Sci. 2013;6(3):194–200. doi: 10.4103/0974- 1208.121422

10. Legro RS, Arslanian SA, Ehrmann DA, Hoeger KM, Murad MH, Pasquali R et al. Diagnosis and treatment of polycystic ovary syndrome: An endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2013;98(12):4565–92. doi: 10.1210/jc.2013-2350

11. Tsilchorozidou T, Overton C, Conway GS. The pathophysiology of polycystic ovary syndrome. Clinical Endocrinology. 2004;60:1–17. doi: 10.1046/j.1365-2265.2003.01842.x

12. Sahmay S, Aydin Y, Oncul M, Senturk LM. Diagnosis of polycystic ovary syndrome: AMH in combination with clinical symptoms. J Assist Reprod Genet. 2014;31(2):213–20. doi:10.1007/s10815-013-0149-0

13. Dewailly D, Gronier H, Poncelet E, Robin G, Leroy M, Pigny P et al. Diagnosis of polycystic ovary syndrome (PCOS): Revisiting the threshold values of follicle count on ultrasound and of the serum AMH level for the definition of polycystic ovaries. Hum Reprod. 201;26(11):3123–29. doi: 10.1093/humrep/der297

14. Mohammad MB, Seghinsara AM. Polycystic ovary syndrome (PCOS), diagnostic criteria, and AMH. Asian Pacific J Cancer Prev. 2017;18(1):17–21. doi: 10.22034/APJCP.2017.18.1.17

15. Balen AH, Laven JSE, Tan SL, Dewailly D. Ultrasound assessment of the polycystic ovary: International consensus definitions. Hum Reprod Update. 2003;9(6):505–14. doi: 10.1093/humupd/dmg044