

ANTI-MÜLLERIAN HORMONE LEVEL AS A PREDICTIVE FACTOR IN THE DIAGNOSIS OF POLYCYSTIC OVARIAN SYNDROME IN DUHOK PROVINCE – KURDISTAN REGION, IRAQ

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ABSTRACT

Background: Polycystic ovary syndrome is one of the most common endocrine conditions upsetting fertile-aged ladies and is considered to be one of the most common causes of infertility. The study aimed at evaluating serum anti-müllerian hormone levels among patients with polycystic ovarian syndrome.

Methods: All enrolled women were subjected to clinical examination, ultrasound examination, and anti-müllerian hormone level measurement. Eighty-seven women diagnosed with clinical signs of polycystic ovary syndrome as well as 87 controls were enrolled.

Results: The current study revealed significant variation among both patients and control groups regarding parity, irregularities in menstrual cycles, ovarian sizes, and features of hyperandrogenism (abnormal hair growth; Acne). No significant difference was seen regarding age and body mass index. Using the Receiver operating characteristic curve, a serum value of anti-müllerian hormone > 3.2 ng/ml was considered specific (91.5%) and sensitive (80.5%) for diagnosis of polycystic ovary syndrome with a P value of < 0.001 .

Conclusion: Polycystic ovary syndrome can be accurately diagnosed with AMH level, being significantly associated with increased ovarian size, lower parity rate, and higher incidence of menstrual cycle disturbances.

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Keywords: Anti-mullerian Hormone (AMH); polycystic ovarian syndrome (POCS). Receiver operating characteristic (ROC).

Polycystic ovary syndrome (PCOS) is a multifactorial disorder that causes distressing fertility in aged women, with an incidence rate of 4-20%¹. PCOS is defined according to the Rotterdam consensus by the presence of more than one of the ensuing criteria: oligo/anovulation, hyperandrogenism, and polycystic ovaries (twelve follicles or more sizing 2-9 mm in diameter; and/or an ovarian volume $>$ ten milliliter in at least one ovary)². Hence polycystic ovaries syndrome manifests clinically with features of reproductive dysfunction including Amenorrhea/ oligo-amenorrhea; features of hyperandrogenism including Acne, seborrhea, increased facial

and body hair, and/or hair defeat on the scalp; and increased risk of metabolic disorders, including abnormal blood and lipid parameters, weight gain and fatty liver³.

The pathogenesis of polycystic ovaries is still not agreed upon, but one potential factor that has been suggested to play a role is anti-Müllerian hormone (AMH)⁴. Current studies regarding various aspects of PCOS have yielded novel visions for the diagnosis and management of the syndrome. The connection between PCOS and AMH gains its attention, as the last factor that shows a valuable and important regulation of the physiology of ovulation; it

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conserves the follicles in the primitive elemental phase and reflects the approximate number of ova in the ovaries, thereby giving a clue to their function⁵.

Females with the syndrome were documented to have an increased level of serum AMH, resulting from the larger number of bizarre and abnormal follicles and production of the higher level of AMH per follicle, rendering AMH feasibly a significant element in diagnosing and assessing PCOS⁶. Some previous articles have revealed the effectiveness of serum AMH as an indicative factor for the diagnosis of PCOS and in defining its best cut-off diagnostic value. A study conducted by Dewailly and his co-worker offered AMH levels higher than 5 ng/mL could be a diagnostic factor and replacement for other methods, while alternative studies proposed AMH levels higher than 3.8 ng/ml⁷.

This study aims to define the PCOS diagnostic cut-off value for AMH in women from Duhok province as well as to study the association of the serum AMH level with the noticeable clinical features in patients with PCOS. This will permit for evaluation of the diagnostic precision of utilizing AMH as an alternative in comparison to the Rotterdam criterion and may contribute to the appropriate judgment of PCOS between these women.

PATIENTS AND METHODS

A prospective case-control study was conducted at the maternity hospital in Duhok on women attending the obstetrics and gynecology clinics over six months (Dec. 2021 – June. 2022). The study was approved by the scientific and ethical committees at Duhok Medical College and Duhok Directorate of Health and followed the Helsinki Declaration for medical research on human beings.

At first, the study was explained to all enrollees, and verbal consent was taken from all enrollees. After explanation, a full history and physical examination were carried out and data was collected in specific questionnaire form. Later on, patients were sent for ultrasound examination and blood was collected in a gel tube for measurement of AMH using VIDAS®, Multiparametric Immunoassay System - (BIOMÉIEUX)

Women of similar ages, who had not shown any specific clinical signs mentioned in Rotterdam consensus, visited Duhok Hospital for obstetrics and gynecology for other complaints, recruited, and served as controls. They followed the same procedures as patients (explanation, consent, history and physical examination, blood investigation, and ultrasound examination). Pregnant women and women with chronic disorders were excluded from the current study.

Statistical analyses were performed using IBM SPSS software version 24.0 (SPSS Inc., Armonk, NY, USA). Data presented as (number, mean, median, range, and percentages), P-values calculated using a Mann-Whitney test. The ROC curve was utilized to examine the diagnostic cut-off value of AMH. The chi-squared test was used to demonstrate the correlation between AMH, PCOS, and PCOS variables. A P-value < 0.05 was considered statistically significant.

RESULTS

The current study represents a case-control study and included 87 women with clinical signs of POCS as well as other 87 women without any suspicious signs of POCS mentioned in the Rotterdam consensus². Demographic data of all enrolled women is shown in Table (1) and revealed that ages, weight, height, and BMI were

comparable among both controls and patients with PCOS (P-values of 0.89, 0.54, 0.42, 0.36 respectively). Higher levels of AMH and the existence of multiple cysts in the ovaries were significantly found among women with PCOS in comparison to a

control group. Women with PCOS tend to have significantly larger ovaries from simultaneous growth of multiple follicles at the same time in comparison to controls with single follicle growth (P-value of 0.026).

Table 1: The Demographic Data of All Enrolled Women (Cases and Controls)

| Parameters | POCS | Control | P value |
|----------------|-----------------------|-----------------------|---------|
| No. | 87 | 87 | |
| Age (Years) | 15-42 (25.59±5.83) | 15-46 (27.29±4.52) | 0.89 |
| WT (Kg) | 40-101(68.28±13.04) | 43-98 (69.49±10.35) | 0.54 |
| HT (CM) | 145-195(159.85±7.14) | 142-180 (158.42±6.42) | 0.42 |
| BMI (index) | 16.8-39.5(26.61±4.99) | 17-62.9 (28.34±6.65) | 0.36 |
| AMH (ng/ml) | 0-26 (6.22±4.77) | 0-7 (1.74±1.47) | 0.006 |
| Ovaries Volume | 1-21(8.45±3.99) | 1-11 (2.95±2.01) | 0.026 |

Using ROC analysis curve (Fig 1), higher level of AMH more than 3.2 ng/ml was considered specific (91.5%), but less

sensitive (80.5%) with a P value of < 0.001 for diagnosis of POCS.

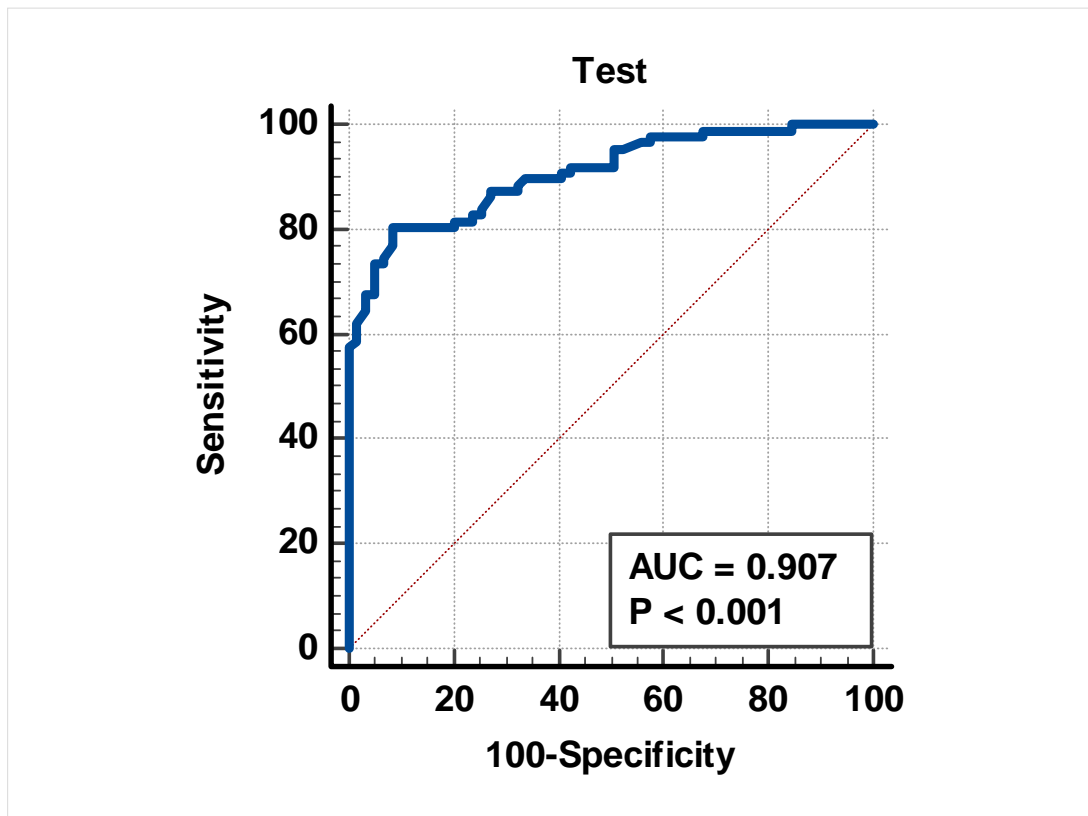


Figure 1: ROC analysis curve for estimation of reference range for AMH among studied group.

Table (2) reveals that marriage were less common among patients with POCS in comparison to control (P-value of 0.001). In

addition, women without POCS tend to have higher parity in comparison to POCS patients (P- value of 0.001).

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Table 2: The Clinical Characteristics Of All Enrolled Women (Cases And Controls).

| Parameters | | POCS | Control | P value |
|-------------------------------|----------|------------|-------------|---------|
| Marital Status | Married | 60 (69%) | 78 (89.65%) | 0.001 |
| | Single | 27 (31%) | 9 (10.35%) | |
| Parity | 0 | 56 (64.4%) | 44 (50.57%) | 0.012 |
| | 1 | 14 (16.1%) | 9(10.35%) | |
| | 2 | 7 (8%) | 13(14.94%) | |
| | 3 | 5 (5.7%) | 12(13.79%) | |
| | ≥4 | 5 (5.7%) | 9 (10.35%) | |
| Acne and abnormal hair | + | 80 (92%) | 2 (2.30 %) | < 0.005 |
| | - | 7 (8%) | 85(98.70) | |
| Menstrual cycles | A/Oligo* | 81 (93.1%) | 12 (13.79%) | <0.005 |
| | regular | 6 (6.9%) | 86.21%) | |

* A/Oligo: amenorrhea or oligo-menorrhea.

As diagnostic criteria of PCOS, patients have significantly increased incidence of acne, excess hair growth and abnormalities in the menstrual cycles (P-value of 0.001 for acne and hair growth also for abnormal menstrual cycles).

DISCUSSION:

The underlying pathogenesis of the PCOS is obscure and the talent to bring about an integrated diagnosis among gynecologists and obstetricians is problematic to some extent due to independent variations⁸. Moreover, it is well recognized that PCOS is linked to resistance of insulin that is existing in a large number of cases, with compensatory increased insulin level that yield androgen excretion through blockade of the liver sex hormone-binding globulin synthesis and stimulation of ovarian androgen secretion⁹. If the hyperinsulinemia is mixed with late or confused diagnosis of PCOS, then the scenario of type 2 diabetes and cardiac disease may be fast-tracked. Furthermore, the assessment of PCOS via abdominal ultrasound can be hard and problematic, particularly in virgins and/or fatty females. That is why, simpler, clearer, easier,

quicker, and measurable diagnostic elements are indispensable.

Serum AMH can now function within the diagnostic elements “though it is not included within the Rotterdam consensus criteria”, as serum AMH level has not merely revealed a substantial association with PCOS, but it can also imitate the strength of the condition. Furthermore, it can be simply calculated any period throughout a woman’s cycle, and as the ethnical background has been associated with variable AMH levels, and Asian women have higher AMH at a given age than Caucasians¹¹, this study was conducted to determine the AMH diagnostic cutoff value among women residing in Duhok province, Kurdistan Region – Iraq.

AMH is increased in association with various fertility and endocrine/metabolic discrepancies in PCOS¹². AMH plays a blocking role in the development and recruitment of the ovarian follicles, resulting in follicular maturation arrest. AMH blockade action on FSH-induced aromatase synthesis likely contributes to hyperandrogenism in PCOS, which additionally augments insulin resistance in these females. Raised serum AMH levels are predictive of weak response to various

treatments of PCOS including weight loss, ovulation induction and laparoscopic ovarian drilling, while improvement in various clinical parameters following treatment is associated with serum AMH decline, a point which further supports the vital role for AMH in the pathophysiology of the PCOS syndrome. In view of the above, his review emphasizes the need for understanding the exact mechanism of action of AMH in the pathophysiology of PCOS. A step may lead to the discovery and production of new treatment options aimed at targeting AMH to treat PCOS, as well as help clinicians in predicting and better adapting the existing treatments for this disease.

A study conducted by Du et al (2016) among normal Chinese population reveal that normal AMH levels consistently maintained below 2.0 and this confirm our result with a mean value of 1.74 ± 1.47 ng/ml, with occasional cases of >2.0 ng/ml particularly among women aged < 25 years¹³.

Body mass index was not different among both groups and this might reflect the higher BMI among controlled women 28.3 ± 6.65 in comparison to women from other European and Asian women with an average of 26.9¹⁴. This might reflect the nutritional, racial and economic state of the studied group.

CONCLUSION

Polycystic ovarian syndrome can be accurately diagnosed with AMH level of 3.2 ng/ml and it is significantly associated with increased ovarian size, lower parity rate and higher incidence of disturb menstrual cycle, acne and abnormal hair growth.

Conflict of interest: there are no any conflict of interest.

Abbreviation:

POCS: Polycystic ovarian syndrome;
AMH: Anti-Mullerian Hormone; ROC:
Receiver operating characteristic;

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پوخته

ناستی هۆرمۆنی دژە موللەری وەک هۆکارێکی پیشبینیکراو لە دەستنیشانکردنی نهخۆشی هیلکەدانی پۆلیسیستیک لە پارێزگای دهۆک – هەریمی کوردستان، عێراق

پیشەکی و نارمانج: نهخۆشی هیلکەدانی فرە کیسی یه‌کیکه له باوترین حالته‌کانی ناوپۆشی له‌ش که خانمانی ته‌مه‌ن به‌پیتکردن نارمحه‌ت ده‌کات و به‌یه‌کیکه له باوترین هۆکاره‌کانی نه‌زۆکی داده‌نریت. نامانجی توێژینه‌وه‌که هه‌لسه‌نگاندنی ناستی هۆرمۆنی دژە مۆلیری له‌ سیرۆمدا بووه له‌ نیوان ئەو نه‌خۆشانه‌ی که نه‌خۆشی هیلکەدانی فرە کیسیان هه‌یه.

شێوازه‌کان: هه‌موو ژنانی ناووسراو پشکنینی کلینیکی، پشکنینی سۆنەر و پێوانه‌کردنی ناستی هۆرمۆنی دژە مۆلیریان بۆ کرا. هه‌شتا و چه‌وت ژن که نیشانه‌ کلینیکیه‌کانی نیشانه‌کانی هیلکەدانی فرە کیسیان هه‌یه و هه‌روه‌ها ۸۷ کۆنترۆل ناویان تومارکرا.

ده‌ره‌نجامه‌کان: توێژینه‌وه‌که گۆرانکارییه‌کی به‌رچاوی له‌ نیوان هه‌ردوو نه‌خۆش و گروپی کۆنترۆلدا ئاشکرا کردوه سه‌باره‌ت به‌یه‌کسانی، نارێکی له‌ سوێری مانگانه، قه‌باره‌ی هیلکەدان، و تاییه‌تمه‌ندییه‌کانی زیادبوونی ئەندروۆجینیزم (گه‌شه‌ی نائاسایی قژ؛ زییکه). هه‌یج جیاوازییه‌کی به‌رچاوی سه‌باره‌ت به‌ ته‌مه‌ن و پێوه‌ره‌کانی بارسته‌ی جه‌سته‌ نه‌بینرا. به‌ به‌کاره‌ینانی کتۆی تاییه‌تمه‌ندی کارپیکردنی وه‌رگر، به‌های سیرۆمی هۆرمۆنی دژە مۆلیری < 3.2 نانوگره‌م/میلی لیتر به‌ تاییه‌ت (91.5%) و هه‌ستیار (80.5%) بۆ ده‌ستنیشانکردنی نیشانه‌کانی هیلکەدانی فرە کیسی به‌ به‌های $P < 0.001$ داده‌نرا.

ده‌ره‌نجام: نه‌خۆشی هیلکەدانی فرە کیسی ده‌توانریت به‌ وردی به‌ ناستی AMH ده‌ستنیشان بکریت، که پهیوه‌ندییه‌کی به‌رچاوی به‌ زیادبوونی قه‌باره‌ی هیلکەدان، که‌مبوونه‌وه‌ی رێژه‌ی یه‌کسانی، و به‌رزبوونه‌وه‌ی روودانی تیکچوونی سوێری مانگانه هه‌یه.

الخلاصة

مستوى الهرمون المضاد للمولر كعامل تنبئي في تشخيص متلازمة تكيس المبايض في محافظة دهوك - إقليم كردستان العراق

الخلفية والأهداف: تعد متلازمة المبيض المتعدد الكيسات من أكثر حالات الغدد الصماء شيوعا والتي تزج السيدات في سن الإنجاب وتعتبر أحد أكثر أسباب العقم شيوعا.

الهدف: هدفت الدراسة إلى تقييم مستوى الهرمون المضاد للمولر في الدم لدى مرضى متلازمة تكيس المبايض.

المرضى وطريقة عمل البحث: خضعت جميع المسجلات بالدراسة للفحص السريري والفحص بالموجات فوق الصوتية وقياس مستوى الهرمون المضاد للمولر. وقد تم تسجيل 87 امرأة تم تشخيصهن بعلامات سريرية لمتلازمة المبيض المتعدد الكيسات بالإضافة إلى 87 امرأة كعنصر تحكم.

النتائج: كشفت الدراسة الحالية عن تباين كبير بين كل من المرضى ومجموعات المراقبة فيما يتعلق بالتكافؤ، وعدم انتظام الدورة الشهرية، وأحجام المبيض، وخصائص فرط الأندروجين (نمو الشعر غير الطبيعي، حب الشباب). لم يلاحظ اختلاف كبير فيما يتعلق بمؤشر كتلة الجسم والعمر. باستخدام منحنى خاصة تشغيل جهاز الاستقبال، تم اعتبار قيمة مصل الهرمون بقيمة المضاد للمولر < 3.2 نانوغرام/مل لغرض تشخيص متلازمة تكيس المبايض حيث ترتبط بشكل كبير بزيادة حجم المبيض. $P < 0.001$ بقيمة محددة: 91.5% حساسية: 80%

الإستنتاجات: يمكن تشخيص متلازمة تكيس المبايض بدقة بمستوى الهرمون المضاد للمولر حيث ترتبط بشكل كبير بزيادة حجم المبيض، وانخفاض معدل التكافؤ وارتفاع معدل حدوث اضطرابات الدورة الشهرية.