International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2024; 8(3): 168-170
Received: 25-03-2024
Accepted: 27-04-2024

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Role of serum AMH in PCOS patients: Mini review

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DOI: https://doi.org/10.33545/gynae.2024.v8.i3c.1465

Abstract
Polycystic ovary syndrome (PCOS) is a common endocrinological disorder in women with significant reproductive, metabolic, and psychological health implications. The lack of a specific diagnostic test poses challenges in making the diagnosis of PCOS, resulting in underdiagnosis and undertreatment. Anti-Mullerian hormone (AMH) synthesized by the pre-antral and small antral ovarian follicles appears to play an important role in the pathophysiology of PCOS, and serum AMH levels are often elevated in women with PCOS. The aim of this review is to inform the possibility of utilizing anti-Mullerian hormone either as a diagnostic test for PCOS or as an alternative diagnostic criterion in place of polycystic ovarian morphology, hyperandrogenism, and oligo-anovulation. Increased levels of serum AMH correlate highly with PCOS, polycystic ovarian morphology, hyperandrogenism, and oligo/amenorrhea. Additionally, serum AMH has high diagnostic accuracy as an isolated marker for PCOS or as a replacement for polycystic ovarian morphology.

Keywords: Anti-mullerian hormone, diagnosis, hyperandrogenism, oligomenorrhea, polycystic ovary syndrome

Introduction
Definition
Resistant Polycystic ovary syndrome (PCOS) is a category of women who diagnosed as polycystic ovary syndrome and have resistance to ovulation induction drugs and failed to give response in the form of ovulation and to get pregnant.

Originally clomiphene citrate resistance defined as failure of ovulation response after at least 3months up to six months by (150-200mg per day for five days in the follicular phase of cycle (Homburg., 2005) [1].

It is estimated that approximately 10% polycystic ovary syndrome women show Letrozole resistance and about 20% of PCOS patients show clomophine citrate resistance (Polycystic Ovary Syndrome. Available online., 2021).

Research indicates the impact of a variety of internal and external elements, such as epigenetics, genetics, environmental factors, hyperandrogenism (HA), and insulin resistance (IR). Furthermore, it is important to note that resistant PCOS raises the possibility of developing other problems, such as cardiovascular illnesses (Damone *et al*., 2019) [2].

AMH is produced by small antral (less than 2 mm) and pre-antral ovarian follicles, and it is a fundamental component for folliculogenesis and PCOS diagnostic indicators. Because it reveals the tiny antral and pre-antral ovarian follicles, the serum AMH has a better sensitivity compared to the antral follicle count (Weerakiet *et al*., 2007) [3].

The present PCOS diagnosis criteria may be modified to take into account the predictive value of AMH for the PCOM components. We looked at research investigations that assessed blood AMH as a replacement for PCOM in accordance with the Rotterdam criteria, as reported by Anand *et al*. in 2022. Therefore, the presence of two of the three characteristics of either hyperandrogenism, oligo/amenorrhea, or AMH over a threshold was sufficient to diagnose PCOS. These investigations showed that the existence of PCOS may be reliably predicted by substituting blood AMH levels for PCOM in the Rotterdam criteria (Pellat *et al*., 2007) [4].

Research has shown a robust correlation between antral follicle reserves and hyperandrogenism in the body, indicating that AMH is a potent diagnostic tool for PCOS (Begawy *et al*., 2010) [5]. According to some research, Rotterdam criteria and AMH levels should be utilized in conjunction for an early and precise diagnosis of PCOS.

An AMH level more than 3.8–5 ng/mL may be utilized as a diagnostic indicator (Dewailly *et al*., 2010) [6].

Application in clinical practice

- About 60% of women with PCOS exhibited poor pregnancy outcomes throughout controlled intrauterine insemination cycles and a high blood AMH levels (Median 5.62 ng/mL) (Skałba *et al*., 2011) [7].
- Based on the Rotterdam criteria, individuals who had previously been diagnosed with PCOS showed 100% specificity and 96% sensitivity when two of the three clinical characteristics (OA, HA, and AMH) were present (La Marca *et al*., 2006) [8].
- The antral follicle count, a biomarker for ovarian responses, has a strong correlation with serum AMH. Serum AMH values in PCOS women may be used as a predictor for oligo- or amenorrhea with increased preantral secretion (Singer *et al*., 2009).
- Prognostic role as it is considered one of the factors that indicates high ovarian response and risk of OHSS and modification of ovulation induction protocol, doses and strategy of freeze all (Rani and Chandna., 2023) [9].
- There was a notable correlation between serum AHM levels and LH levels. Additionally, greater levels of AHM were associated with a rise in LH production. The primary release of LH in women with PCOS was shown to have a strong correlation with menstrual irregularities (Amner *et al*., 2009) [10].

The presence of LH dominance during the follicular phase, comparable to that induced by GnRH, is associated with elevated levels of AMH and disruptions in the menstrual cycle (Rani and Chandna., 2023) [9].

- Elevated LH secretion abnormalities have been seen in women with PCOS due to faster GnRH/LH pulsatility. The levels of FSH were seen to be within the normal range, leading to an elevated LH/FSH ratio throughout the follicular phase of the menstrual cycle in women with PCOS.
- (Skałba *et al*., 2011) [7].

AMH as an alternative to oligo/amenorrhea (OA)

Serum AMH can additionally act as an indicator of ovulatory dysfunction, which includes both oligomenorrhea and amenorrhea. There have been few research investigating the potential of employing AMH as a substitute for the oligo/amenorrhea criteria in PCOS. There have been studies indicating a correlation with oligo/amenorrhea and elevated blood AMH levels.

AMH instead of hyperandrogenism

Previous research has shown a direct relationship between the levels of AMH in the blood and androgen. Hyperandrogenism is a known inherent abnormality of theca cells in women with PCOS. It is directly linked to higher amounts of testosterone and larger ovarian volume. (Pellatt *et al*., 2011) [16].

Uses of AMH in PCOS diagnosis

Recommendations from the 2023 International Evidence-based Guidelines for assessment and Management of PCOS

- Serum AMH may be utilized to identify PCOM in adults.
- Serum AMH ought to be utilized only following the diagnostic protocol. It is important to note that in individuals with irregular menstrual cycles and HA, an AMH level isn't required for the diagnosis of PCOS (Jiang *et al*., 2021) [11].
- It is advised against using serum AMH as the only diagnostic test for PCOS.
- Serum AMH shouldn't be utilized in adolescents (Lamba *et al*., 2022) [12].
- Either serum anti-Müllerian hormone AMH or ultrasound might be utilized to determine the presence of PCOM. However, it isn't necessary to do both tests in order to avoid over diagnosis (Teede *et al*., 2023) [2].

Factors affecting AMH

Laboratories and healthcare practitioners should possess knowledge about the variables that have an impact on AMH levels in the general population, which include:

- **Age:** Serum AMH typically reaches its highest levels between the ages of 20 and 25 in the general public.
- **Body mass index (BMI):** Serum AMH levels are inversely correlated with BMI in humans in general.
- **Hormonal contraception with ovarian surgery:** The usage of current or recent COCP may lower the levels of serum AMH.
- Serum AMH levels may fluctuate during the menstrual cycle.
- It is recommended that laboratories measuring AMH levels in females ought to employ cut-off values that are unique to the population being tested and the assay being used (Zhang *et al*., 2023) [13].
- A significant elevation of AMH, particularly over 7.5 ng/ml, in individuals with anovulatory PCOS may be responsible for an amplified inhibitory impact on the development of ovarian follicles. AMH also suppresses the expression of P450scc and CYP19A genes, which are activated by gonadotropins, in cultures of human granulosa lutein cells. This suggests that AMH may play a regulatory function in the production of ovarian steroids (Mumford *et al*., 2016) [14].
- **Serum AMH assay benefits:** has many advantages over AFC or other ultrasound features, this is a point and also may replace the detection of biochemical hyperandrogenism.
- The plasma level of AMH remains consistent between cycles and during the same cycle due to the absence of AMH secretion by the dominant follicle and corpus luteum.

Mechanism of its inhibitory effect on ovulation in PCOS

Research has shown that AMH has a significant impact on reducing both the expression of the FSH receptor and the expression of ovarian aromatase (Pellatt *et al*., 2011) [16]. This enables the safeguarding of the diminutive follicles from premature aromatase expression. Nevertheless, if the protective impact of AMH becomes too strong or lasts longer than necessary in bigger follicles, it might disrupt the selection of the dominant follicle, leading to a condition known as "follicular arrest." In women with PCOS, it has been shown that LH stimulates the generation of AMH by the granulosa cells (Pellatt *et al*., 2007) [16]. The granulosa cells in individuals with PCOS acquire LH receptors at an earlier stage.

AMH & resistance to ovulation induction in PCOS

The increased AMH level was an additional factor that significantly influenced the response to LET and shown a correlation with fertility in PCOS. Excessive production of AMH in granulosa cells might hinder the formation of follicles

by suppressing FSH and, to some degree, can impact the functioning of aromatase (Broekmans *et al*., 2008) [16].

A study conducted by Mumford *et al*. in 2016 [14] found that blood levels of AMH were substantially reduced in cycles where clomiphene had a positive effect compared to cycles where it had no effect (Mumford *et al*., 2016) [14].

A further research shown that individuals with PCOS who had elevated levels of AMH in their blood are less likely to have a favorable reaction to clomiphene or letrozole. In addition, elevated levels of AMH in the bloodstream are linked to a notably reduced likelihood of responding to stimulation with human menopausal gonadotrophin (Kamel *et al*., 2018) [17].

•Elevated AMH levels are linked to decreased chances of successful live births in women with PCOS who are undergoing ART.

An idea that has been suggested is that hyperandrogenism in PCOS makes granulosa cells more sensitive to FSH, leading to excessive proliferation of pre-antral follicles and increased production of AMH. This, in turn, inhibits the expression of aromatase triggered by FSH (see Figure 2). This leads to modified development of antral follicles, resulting in the absence of ovulation. (Menon *et al*., 2021) [18].

Conflict of Interest
Not available

Financial Support
Not available

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How to Cite This Article
Rania Alkhalili. Role of serum AMH in PCOS patients: Mini review. International Journal of Clinical Obstetrics and Gynaecology 2024; 8(3): 168-170.