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Review Article

A consensus on the utility of the anti-müllerian hormone assay in the assessment of ovarian reserve and gynecological conditions among Indian gynecologists

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ABSTRACT

Infertility is a global issue that causes distress. Serum anti-Müllerian hormone (AMH) and antral follicle count are reliable ovarian reserve markers. The stability of serum AMH levels throughout the menstrual cycle makes monitoring ovarian function decline convenient. This consensus aimed to develop recommendations for the application of the AMH assay in assessing ovarian reserve and broader clinical decision-making among gynecologists in India. A modified Delphi method was used, with a panel of 10 expert gynecologists and 2 lab experts from India, to establish an expert consensus. A questionnaire consisting of 29 consensus statements was administered, covering topics related to ovarian reserve, AMH markers, assay reliability, performance, and specific conditions such as ovarian tumors and endometriosis. Through two rounds of the modified Delphi method, 21 consensus statements were ultimately formulated. The consensus was determined using an 80% cutoff. The panel reached a consensus on 19 statements and a moderate consensus on two, emphasizing the significance of AMH testing in evaluating ovarian reserve and reproductive aging. The panel agreed that AMH assays were valuable in predicting ovarian response to fertility treatments, diagnosing polycystic ovary syndrome and endometriosis, and guiding fertility preservation. It was concluded that AMH testing is crucial for infertility management in India, offering insights into ovarian reserve and reproductive aging. Standardized automated assays ensure speed and precision, aiding in diagnosing fertility conditions, predicting treatment responses, and preserving fertility during therapy. International standards for accurate interpretation are imperative. Overall, AMH testing plays a pivotal role in personalized fertility care in India.

Keywords: Anti-Müllerian hormone, Infertility, Consensus

INTRODUCTION

Infertility is a prevalent global issue that gives rise to significant distress for afflicted individuals. Millions of individuals worldwide face the challenges of infertility. According to the World Health Organization (WHO), infertility is the inability to achieve pregnancy even after unprotected sexual intercourse for 12 months or more. As opposed to this, demographers state infertility as the inability of women of reproductive age (15–49 years) to conceive after ≥5 years of exposure to pregnancy.[1] Thus, varying definitions of infertility, along with variations in its etiological causes across different regions and cultures, complicate direct comparisons because of which a comprehensive understanding of this complex phenomenon is still elusive.[2]

The current global estimate for infertility stands at 17.5%, which translates to approximately one in every six adults.[3] The prevalence of infertility in India varies across different regions and ranges from 3.9% to 16.8%.[4] The reproductive lifespan of women is governed by the ovarian reserve, which represents the reservoir of primordial follicles available for follicular recruitment and maturation.[5] Serum levels of anti-Müllerian hormone (AMH) and antral follicle count (AFC) are validated markers for assessing age-related diminishing ovarian follicle pools in women of reproductive age. As both have shown good predictive values for retrieved oocyte numbers in *in vitro* fertilization (IVF) cycles, the ovarian response to stimulation can be accurately determined with the help of these biomarkers**.** A Cochrane review has illustrated the validity of these markers in deciding individually-adjusted starting doses of follicle-stimulating hormone (FSH), thus reducing the risk of ovarian hyperstimulation syndrome.[6] Growing ovarian follicles that have the potential to ovulate indicate a functional ovarian reserve that can be determined with the help of AMH levels.[7]

The stability of serum AMH levels throughout the menstrual cycle makes it a convenient and robust marker for monitoring ovarian function decline in the infertile population, benefiting both patients and clinicians.[5] Several studies have demonstrated that AMH has marginal intracycle and intercycle fluctuations that are not clinically relevant.[8,9] Thus, AMH is preferred over AFC for ovarian reserve assessments.[10,11] A reliable commercial assay is essential to demonstrate the value of AMH as a marker of ovarian reserve, and hence, various AMH assays have been developed and refined. Recently, automated AMH assays with improved standardization have gained precedence over older-generation assays.[12]

Precision and speed have become the hallmarks of the current generation of AMH assays.[13] Several studies have exhibited the superiority of newer AMH assays.[13-15] However, there is a need for standardization of the assays between the manufacturers to reduce variabilities and improve the use of AMH values in clinical interpretations. Several studies have illustrated the differences in AMH values obtained from different automated assays.[14,16] Regression equations that allow comparisons between assays have also shown variations.[16] Currently, the reasons for these inconsistencies are unclear. Storage conditions and temperatures are known to affect the results as well. An absence of uniformity in the calibration of assays and absence of internationally accepted AMH cutoff values could subsequently affect decisions made by clinicians who are unaware of these variabilities.[7,13,17,18]

The AMH levels measured in Indian women seeking infertility treatments suggest the occurrence of early ovarian senescence. As a part of routine reproductive screening or as a roadmap for fertility assessment for planned pregnancies, AMH testing needs expert validation. With scant data available on our population, this study aims to correlate serum AMH levels among Indian women with clinical, hormonal, and ultrasonographic parameters.

The objective of this consensus was to build recommendations on the utility of the AMH assay in the assessment of ovarian reserve and for other gynecological purposes to aid better clinical decision-making among gynecologists in India.

METHODS

An expert consensus was reached using the modified Delphi method with a panel of 10 expert gynecologists and 2 lab experts from India. The first round of the modified Delphi method was completed with a questionnaire containing 29 consensus statements framed under various subtopics: ovarian reserve as an indicator of reproductive aging; measures of ovarian reserve; AMH as a marker of ovarian reserve; reliability and predictability of AMH assays; performance of different AMH assays; and AMH in specific conditions. The list of these 29 statements is available in Table 1.

A cutoff of 80% agreement was used to determine if a statement reached a consensus. A second round of the modified Delphi method was conducted as a physical meeting wherein the statements that had failed to reach a consensus in the first round were reframed and revoted. Finally, eight statements were removed from the consensus list. The reasons for removal were the following: redundancy; lack of relevance to the topic; and insufficient evidence. Several statements from this list were clubbed together during the reframing process to improve clarity and conciseness.

Figure 1 outlines the modified Delphi process adopted to formulate the recommendations.

Table 1: Statements in the first round of modified Delphi.

S. no.	Statement	Consensus
1	Infertility is a serious health issue and affects 8.9% of women and has a huge detrimental impact on different aspects of life.	High
2	Poor ovarian reserve is a cause of infertility, poor response to gonadotrophin stimulation, and poor success rate after *in vitro* fertilization (IVF) cycles.	High
3	Reproductive and ovarian senescence occurs with the depletion in the number of oocytes or ovarian reserve. Ovarian reserve correlates inversely with age. However, there is considerable variation in ovarian reserve among women of the same chronological age.	High
4	Markers of the ovarian reserve include hormone levels and sonographically measured features of the ovaries.	High
5	The main goal of ovarian reserve testing is to identify those individuals who are at risk of decreased or diminished ovarian reserve.	High
6	Ovarian reserve tests include both biochemical tests and ultrasound imaging of the ovaries. Biochemical tests include early follicular phase measurements, follicle-stimulating hormone (FSH), estradiol (E2) or inhibin-B, measurement of cycle-date–independent AMH, and provocative tests such as clomiphene citrate challenge tests.	Moderate
7	Ovarian reserve testing should be performed for women older than 35 years who have not conceived after 6 months of attempting pregnancy and women at higher risk of diminished ovarian reserve.	Moderate
8	Hormone tests, such as FSH, E2, or inhibin B, and measurement of cycle-day–independent AMH are used as markers of ovarian reserve.	Removed
9	AMH level is a positive indicator of the number of mature oocytes, reproductive lifespan, and fertility rate.	High
10	AMH levels aid in understanding differences in the availability of antral ovarian follicles during the menstrual cycle to plan fertility treatment.	Removed
11	AMH might be a better test for FSH dosing compared to AFC.	Removed
12	AMH is a better indicator for the assessment of ovarian reserve compared to AFC.	High
13	AFC-based individualized FSH and standard FSH dosing are the most cost-effective when determined by AMH levels.	Removed
14	Among patients undergoing controlled ovarian stimulation, the predictive ability of AMH is better than that of estradiol.	Removed
15	AMH is the best currently available measure to predict ovarian response to controlled ovarian stimulation.	Removed
16	AMH is an indicator of PCOS-like phenotypes.	Removed
17	AMH is a reliable assay as an indicator of regaining ovarian function following chemotherapy and a predictor of ovarian tumors.	Removed
18	A decline in AMH levels is a reliable predictor of menopausal age.	High
19	Creating awareness about AMH through education programs will aid in increased AMH testing among patients.	High
20	Main limitations of the AMH test relate to assay variability and lack of standardized international assay. It is important to consider the lower limit of age-appropriate serum AMH values as a guidance for counselling while being cognizant of the effects of possible influencing factors to avoid inaccurate assessment.	High
21	Automated AMH assays offer the advantages of speed, high consolidation of the assay, efficiency, and ease of use versus manual assays.	High
22	AMH assay precision can impact diagnosis and clinical decisions, hence choosing the right assay is also important.	High
23	There is a need of standardization of assay across manufacturers, clinicians should be a part of discussion if a lab plans to switch to other platforms/assays.	High
24	Clinicians should be extremely careful in translating cutoffs from clinical studies directly into the laboratory. Reference ranges can be defined in an attempt for standardization.	High
25	The automated AMH assay predicts ovarian response in a corifollitropin alfa (CFA) antagonist protocol. The best predictors of ovarian response in CFA-treated patients were AMH and AFC.	High
26	The automated AMH assay can reliably predict hyper-response to COS in women undergoing a GnRH antagonist treatment protocol.	High

Continued.

S. no.	Statement	Consensus
27	Ovarian reserve testing should be included in the evaluation of reproductive-age women with endometriosis and considered in the decision for surgery.	High
28	Preoperative AMH is a useful marker to predict the occurrence of a natural pregnancy after endometriosis surgery. Women with low preoperative AMH levels (<1.1 ng/ml) should be counseled regarding reduced pregnancy chances and provided an assisted reproductive technology (ART) recommendation as soon as possible.	High
29	In the diagnosis of PCOS, serum AMH could be used for assessing antral follicle excess in adults and is a more accurate diagnostic tool for detecting polycystic ovarian morphology (PCOM) compared to transvaginal ultrasound (TVUS).	Removed

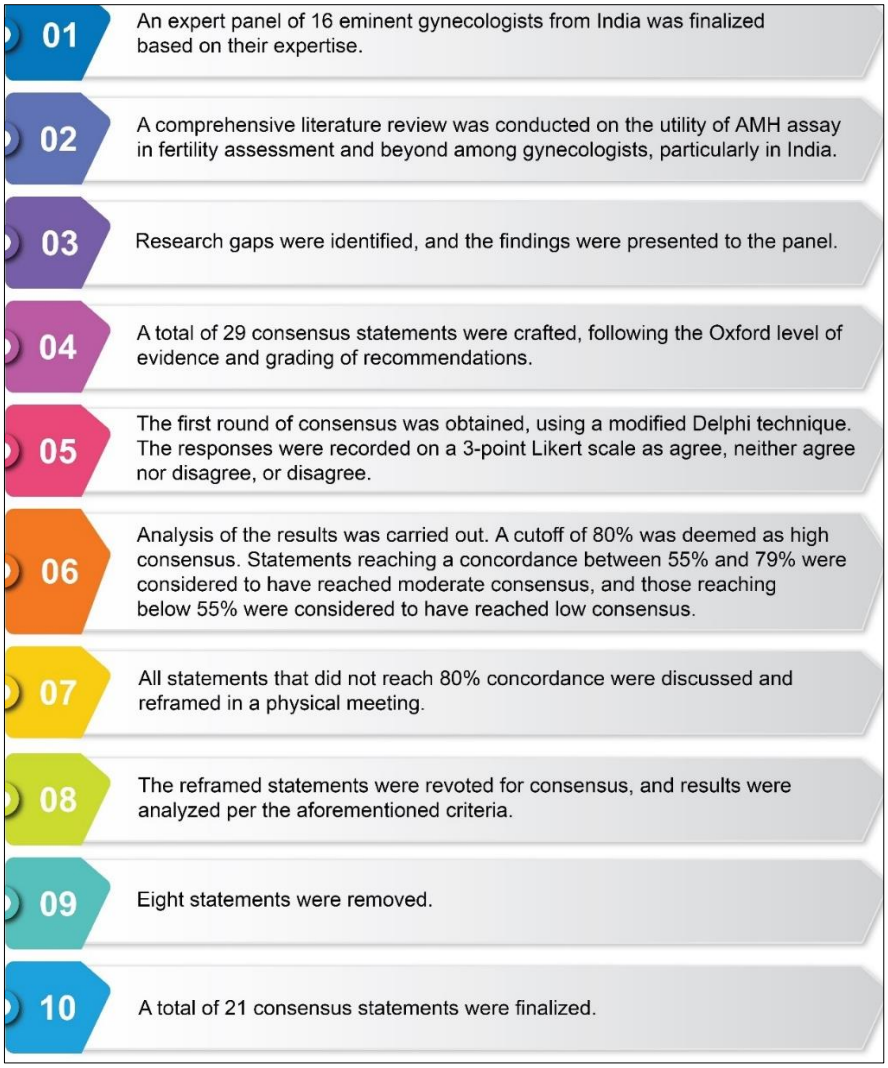

Figure 1: Steps adopted for the modified Delphi process.

AMH: anti-Müllerian hormone

RESULTS

A total of 21 final consensus statements were formulated, out of which 19 achieved a high consensus and two reached a moderate consensus. The statements are presented in Table 2. The reasons for a moderate consensus on statements 6 and 7 were the following. Most panelists agreed that provocative tests, such as the clomiphene citrate challenge test, are no longer commonly performed in clinical practice.

There were mixed opinions among panelists regarding the inclusion of specific age and waiting duration thresholds for ovarian reserve testing. While some supported the inclusion of an age limit of 35 years and a waiting duration of 6 months, others had reservations about their relevance or suggested alternative criteria.

Table 2: Finalized list of 21 consensus statements.

S. no.	Final consensus statements	Consensus
Ovarian reserve as an indicator of reproductive aging		
1	Infertility is a serious health issue that affects 17.5% of adult population and has a detrimental impact on different aspects of life. There is an urgent need of solutions for the prevention, diagnosis and treatment of infertility.	Consensus
2	Poor ovarian reserve is a cause of infertility and may be an indicator of poor success rate after in vitro fertilization (IVF) cycles.	Consensus
3	Reproductive and ovarian senescence occurs with depletion of the number of oocytes, or ovarian reserve. Ovarian reserve correlates inversely with age; however, there is considerable variation in ovarian reserve among women of the same chronologic age.	Consensus
4	Markers of ovarian reserve include hormone levels and sonographically measured features of the ovaries.	Consensus
5	The goal of ovarian reserve testing is to identify and classify individuals as having high, normal or poor ovarian reserve.	Consensus
6	Ovarian reserve tests include both biochemical tests and ultrasound imaging of the ovaries. Biochemical tests include early follicular-phase measurements of FSH, E2, or inhibin B and measurement of cycle-day–independent anti-Müllerian hormone (AMH). Sonographic measures include AFC as clinically feasible.	Moderate consensus
7	Ovarian reserve testing should be performed for women older than 35 years who have not conceived after 6 months of attempting pregnancy and women at higher risk of diminished ovarian reserve.	Moderate consensus
8	AMH level is a positive indicator of the number of antral follicles, oocytes and fertility. High AMH levels may be indicative of PCOS.	Consensus
9	AMH is a reliable measure to predict ovarian response to controlled ovarian stimulation. Assessment of AMH levels in combination with AFC is helpful in gonadotropin dosing in IVF cycles.	Consensus
10	Declining AMH levels could help in counseling women about menopause transition.	Consensus
11	Creating awareness about the importance of AMH through education programs for healthcare professionals (HCPs) and the public at large will aid in increased adoption of AMH testing among women.	Consensus
Reliability and predictability of AMH assays		
1	Main limitations of the AMH test relate to assay variability and lack of standardization. It is important to consider the cut-off of serum AMH values as a guidance for counseling.	Consensus
2	Automated AMH assays offer the advantages of speed, precision and ease of use versus manual assays. AMH assay cut-offs and precision can impact diagnosis and clinical decisions; hence, choosing the right assay is important.	Consensus
3	There is a need for standardization of assays across manufacturers. Laboratories are encouraged to keep clinicians informed if they plan to switch platforms or assays as it may impact cut-offs used for clinical decisions.	Consensus
AMH in specific conditions		
1	Evaluation of AMH levels should be an integral part of reproductive life planning and can be considered as one of the essential components of preconception care.	Consensus
2	Evaluation of AMH is an essential part of fertility preservation approaches in the context of deferred/delayed pregnancy planning.	Consensus
3	AMH testing should be done in women with cancer or other conditions requiring gonadotoxic therapy who need to be counselled for fertility preservation.	Consensus
4	AMH testing should be included in the evaluation of reproductive-age women with endometriosis/ovarian endometrioma.	Consensus
5	Preoperative AMH is a useful marker to predict the occurrence of pregnancy after endome-triosis surgery. Women with low preoperative AMH levels (<1.2 ng/ml) should be counselled regarding reduced pregnancy chances and provided an ART recommendation as soon as possible.	Consensus
6	AMH testing should be considered in benign recurrent ovarian tumors for patient counselling.	Consensus
7	In patients with genital tuberculosis, AMH testing could provide useful information for fertility counselling.	Consensus

DISCUSSION

This Indian consensus delves into the crucial role of the AMH assay in the assessment of infertility and fertility management, providing a comprehensive understanding of its significance as a diagnostic tool, and its potential implications for guiding personalized treatment approaches in the Indian context.

Ovarian reserve as an indicator of reproductive aging

The experts arrived at a consensus that ovarian and reproductive senescence occurred when the number of oocytes or the ovarian reserve was depleted. Ovarian reserve correlates inversely with age; however, there is a variance in ovarian reserve even among women of the same age. Literature corroborates these findings that reproductive aging is marked by a depleted ovarian reserve and is one of the important causes of infertility.[11] The conventional perspective on reproductive aging is centered on the notion that the abundance of human oocytes reaches its zenith during fetal development, followed by ovulation or atresia, with no subsequent replenishment. Reproductive and ovarian senescence arise from the progressive depletion of oocytes. Women at an advanced stage of reproductive aging, specifically perimenopause and menopause, characterized by irregular menstrual cycles, exhibit diminished ovarian reserve in comparison with women of earlier reproductive stages with regular menstrual cycles.[19] The experts also agreed that ovarian reserve markers include ovarian features measured sonographically (as evidenced in numerous studies) and hormone levels. The panel lacked complete consensus on the recommendation that ovarian reserve tests include both imaging of ovaries by ultrasound and biochemical tests. Biochemical tests include early follicular phase measurements of FSH, estradiol, or inhibin B and measurement of cycle-day–independent AMH. However, they agreed that sonographic measures could include AFC as clinically feasible. Serum AMH levels and AFC in the early phase of the cycle (day 2–day 4) measured sonographically serve as markers for assessing ovarian follicle reserve.[11,17,20] The study conducted by Penzias et al documented that ovarian reserve assessment can be performed indirectly by measuring hormone levels or utilizing ultrasound imaging techniques to examine the ovaries.[19]

Several studies have reported that age and AMH levels are inversely correlated.[21] A prospective observational study by Sinha et al demonstrated the reliability of AMH in flagging diminished ovarian reserve and reproductive aging.[10] However, AMH is not predictive of oocyte quality or pregnancy outcomes.[10,22] Therefore, declining AMH levels are indicative of ovarian senescence or diminished ovarian reserve, characterized by a low yield of oocytes. Hence, AMH levels can aid in infertility evaluation.[21] In a prospective study by Scheffer et al, AMH and age were independently shown to be the predictors of ovarian stimulation and ovarian reserve in women who were infertile.[23] Age considerations, along with AMH, can guide fertility counseling.[23] A systematic literature review showed that fertility preservation can be considered with the help of serum AMH assessments, as AMH levels are shown to peak in early adulthood and are indicative of functional ovarian reserve.[24] Another noteworthy point is that there is a wide variation in ovarian aging and serum AMH and AFC measures in different individuals.[7,25]

Reliability and predictability of AMH assays

There was a broad consensus among the panelists in favor of automated AMH assays vs. manual assays as automated assays offer the advantages of speed, precision, and ease of use. They also concurred that the AMH assay cutoffs and precision can impact diagnosis and clinical decisions; hence, choosing the right assay is important. However, the panelists rolled out a strong recommendation, quoting that there is a need for standardization of AMH assays across manufacturers. Additionally, laboratories must be encouraged to keep clinicians informed if they plan to switch platforms or assays, as it may impact the cutoffs used for clinical decisions. Upon its introduction in 2010, the manual AMH generation II enzyme-linked immunosorbent assay (Gen II ELISA) was extensively utilized for AMH measurements. Punchoo and Bhoora reported that AMH measurement is affected by variable assay standardization between commercial immunoassays.[26] Manufacturers utilize proprietary calibrators defined by assays with different values and derived from different sources. There is a lack of an international reference standard. The variations across AMH assays have also been traced to sample stability, antibody-related differences, and differences in calibration. Preanalytical conditions must also be standardized.[7,18] This leads to variations in standard curves among AMH assays and contributes to the variability observed in AMH measurement by immunoassays.[26] Automated assays are robust, require less trained manpower, and are more standardized, precise, and faster.[27] Novel ultrasensitive immunoassays can detect even low serum concentrations of AMH. A study on the automated Access AMH assay, which uses the electrochemiluminescence sandwich technique, showed greater sensitivity, repeatability, and reproducibility compared with the traditional ELISA method.[20] The automated assays have shown good linearity and excellent precision in interassay and intra-assay measurements. They are capable of high sensitivity and can detect even 0.1 pmol/l of AMH. They also reveal good immunoreactive stability for AMH values in both frozen and thawed samples.[15] A good correlation was seen between the AMH values of the Gen II and automated assays, with >0.9 correlation coefficients ($p<0.0001$) in pairwise comparisons.[20]

A study by Anderson et al has shown that the turnaround time for the Roche Elecsys® automated AMH assay is approximately 18 minutes.[28] It also demonstrated a functional sensitivity of 0.03 ng/ml, a coefficient of

variation for repeatability of 1–1.8%, and a coefficient of variation for reproducibility of 2.7–4.4%.[29] Several comparative studies have also shown interassay variabilities between the different commercial assays.[14] A comparative study between the newer automated assays and the existent Gen II assays showed low intra-assay coefficients of variation: Elecsys® ≤2.8%, Gen II ≤5.8%, Ansh® ≤9.0%, and Access® ≤10.7%. Although a moderate correlation was found between AFC and oocyte yield, they showed a low pregnancy prediction on the receiver operator characteristics (ROC) curve (0.62–0.63).[16] With automated assays, the AMH values were lower for frozen samples with varying freezing conditions compared with those for fresh samples.[15] Although a good concordance in calibrated values was observed for the recently automated assays, the derived values appeared to be lower.[16]

Standardization

A discordance in the reporting of AMH values due to interlaboratory and interinstrument variations has caused hesitance among clinicians about its application in practice. International standardization of AMH cutoff values and calibrations can help avoid misinterpretation of results, thereby mitigating cases of misdiagnoses.[16] The panelists reiterated that the main disadvantage of the AMH test relates to assay variability and a lack of standardization. It is important to consider serum AMH cutoff values as a reference to guide counseling. Studies cite that AMH cutoffs can vary and are assay-dependent; hence, it is necessary to report assay-specific cutoffs for the interpretation of clinical conditions, such as poor ovarian reserve.[17] An age-AMH nomogram model was developed by Kaur et al to provide reference values for various reproductive conditions using an automated AMH assay.[30] Percentile charts for AMH and AFC giving age-specific normal values can aid in individualizing fertility treatments.[25]

AMH in specific conditions

The AMH assay has numerous applications in conditions affecting the reproductive system. These assays are routinely conducted for ovarian reserve assessment, for proposing options regarding assisted reproductive technology (ART), measuring response to controlled ovarian stimulation (COS), for follow-up after gonadotoxic treatment, investigations of endocrine disorders such as polycystic ovarian disease (PCOS), and possible prediction of menopause.[30] An ROC curve analysis has shown that elevated serum levels of AMH exhibit high sensitivity and specificity in predicting PCOS.[20] Sonigo et al reported that AMH has emerged as an adjunctive diagnostic tool for identifying conditions such as premature ovarian insufficiency or PCOS.[31] As age increases, AMH levels decrease linearly, suggesting a direct correlation with the decline in the follicular pool over time. Age-stratified thresholds for AMH have been observed to enhance the predictive performance of AMH in diagnosing PCOS compared with a single nonage-adjusted threshold.[32] A prospective study aimed to establish a reference range for AMH tailored to various age groups of Indian women. Data from 1978 Indian women (N=1817; healthy controls, N=161; PCOS group) aged 12–50 years were analyzed. The normal upper 95th percentile cutoffs for AMH levels in the age groups 18–25, 26–30, 31–35, 36–40, 41–45, and >45 years were 9.69, 7.60, 6.50, 6.1, 4.80, and 4.5 ng/ml, respectively.[33] While an assay-based AMH cutoff of 6.8 ng/ml showed a sensitivity, specificity, and diagnostic accuracy of 100%, 93.23%, and 93.78%, respectively, for detecting PCOS, other research findings suggest that an AMH level exceeding 3.8–5 ng/ml can serve as a diagnostic marker for PCOS.[33,34]

Predicting menopause or early menopause based on AMH levels was not satisfactory.[35] However, with longer lead times, the decline in AMH levels demonstrated improved accuracy in predicting the onset of menopause.[20] The experts were of the view that declining AMH levels could help in counseling women about the menopause transition. A study by Finkelstein et al showed that serum AMH levels along with age and body mass index (BMI) could predict menopause in late-reproductive age women (area under the ROC curve=0.88–0.99).[36] The panelists opined that AMH testing should be done in women with cancer or other conditions requiring gonadotoxic therapy who need to be counseled for fertility preservation. Fertility assessments in cancer-treated women could be done based on AMH values, depending on the chemotherapy type and age of the patient.[20,37] According to Sonigo et al, the ability of AMH to accurately reflect ovarian reserve in women with cancer remains uncertain.[31] Their study found that some women with cancer exhibited decreased AMH levels before treatment, whereas other studies reported no significant differences compared with those in healthy individuals. Despite this uncertainty, measuring AMH at the time of cancer diagnosis can still provide valuable information for making fertility preservation decisions. However, caution should be exercised when interpreting AMH levels during and after treatment to predict ovarian function.[31]

The expert panel agreed that AMH is a reliable measure to predict ovarian response to COS. Assessment of AMH levels in combination with AFC is helpful in gonadotropin dosing in IVF cycles. Therefore, AMH and/or AFC are reliable diagnostic parameters of ovarian reserve for COS.[38] Serum AMH levels could predict ovarian response to stimulation as indicated by an ROC curve analysis that showed an AUC (95% confidence interval) of 0.85 for low response and 0.89 for high response ($p<0.001$). It also showed a strong positive correlation with the number of oocytes retrieved (Spearman's rho=0.74, $p<0.001$).[29] Several large randomized trials have shown that AMH levels were more accurate than AFC in predicting the ovarian response to gonadotropin therapy.[39] Women with endometriosis showed significantly lower AMH levels.[40] Hence, the AMH assay should be part of the preoperative

evaluation of endometriosis.[41] According to Romanski et al, infertility patients with endometriosis, irrespective of their ovarian surgery history, exhibited lower levels of ovarian reserve markers.[5] This was characterized by lower levels of AMH and higher levels of FSH compared with those in women experiencing infertility due to male factors. Moreover, a higher proportion of women with endometriosis demonstrated decreased ovarian reserve, as indicated by lower AMH levels.[5] The experts agreed that there was a need for a consensus on whether AMH testing should be included in the evaluation of women of reproductive age with endometriosis/ovarian endometrioma. They opined that preoperative AMH testing is useful for predicting the occurrence of pregnancy after endometriosis surgery. Women with low preoperative AMH levels (<1.2 ng/ml) should be counseled regarding reduced chances of pregnancy and provided an ART recommendation as soon as possible.

There may be several exogenous and endogenous factors affecting AMH levels, which could limit its use in the clinical settings.[7] Serum AMH levels showed superior sensitivity and high specificity in predicting low/high ovarian responses to fertility treatments. A meta-analysis of 5705 women receiving IVF indicated an AUC of 0.78 for AMH in predicting poor ovarian response. It also had a good predictive value for excessive ovarian responses. However, its usefulness in predicting suboptimal and optimal ovarian responses was slightly lower.[29] The expert panel opined that infertility was caused by poor ovarian reserve, and this may be an indicator of a poorer success rate following IVF cycles. The experts unanimously agreed that identifying and classifying individuals as having high, normal, or poor ovarian reserve was the goal of ovarian reserve testing. In a single-center study by Bosch et al, the AMH cutoffs using an automated assay (Elecsys® AMH) were 6.4 pmol/l for a low ovarian response, 13.4 pmol/l for a suboptimal ovarian response, and 14.2 pmol/l for a high ovarian response.[29] A study revealed that the mean AMH levels in serum were significantly higher in women with PCOS than in normal women. The serum AMH levels correlated positively ($p<0.05$) with luteinizing hormone/FSH ratio, ovarian follicle number, and ovarian volume; however, there were no significant correlations with BMI and age. A cutoff of 3.76 ng/mL showing 86.7% sensitivity and 62.7% specificity was derived from ROC analysis.[42] As this was confirmed by studies, the expert panel arrived at a consensus that serum AMH levels can be a positive indicator of fertility, the number of antral follicles, and oocytes in a woman, and that high AMH levels may be indicative of PCOS.

A retrospective cohort study demonstrated the use of AMH monitoring while offering oocyte accumulation as an option to patients with benign ovarian tumors, notwithstanding the tumor type.[43] The expert panel recommended that AMH testing be considered in benign recurrent ovarian tumors for patient counseling. According to Shrikhande et al, AMH levels can be elevated in certain ovarian tumors, specifically, adult granulosa cell tumors.[44] This makes AMH a useful tumor marker for gauging responses to therapy and monitoring recurrence in patients with ovarian tumors.[44]

The burden of infertility and the need for fertility preservation in the Indian scenario

The experts agreed with WHO statistics and recommended a statement that infertility is a serious health issue that affects 17.5% of the adult population and has a detrimental impact on different aspects of life. There is an urgent need to find solutions for preventing, diagnosing, and managing infertility. The prevalence of infertility in India, as recorded in the 1981 census, is approximately 4–6%. However, when combining both primary and secondary infertility, the total number of affected individuals amounts to an estimated 17.9 million.

Previous studies have shown that Indian women appear to have a 6-year advancement in ovarian aging compared with Spanish women.[30] Lower AMH levels were seen in healthy Indian women in comparison with those in European women of the same age.[45] A retrospective study of 5525 infertile women revealed that more than 50% of the women showing low ovarian reserve were <35 years of age, with AMH values <1.1 ng/ml. Almost 14.5% of women aged >35 years showed a low ovarian reserve. Older women (40–44 years) had an eight-fold higher probability of poor ovarian reserve compared with women <25 years of age (73% versus 8.7%, $p<0.01$).[25] A similar divergence in AMH values was observed in a study of 1600 women with infertility versus 400 healthy Indian counterparts. Higher AMH values were observed in infertile women who were <30 years of age, which is probably indicative of a high prevalence of PCOS.[45]

Results from another study showed a variation in infertility prevalence depending on socioeconomic class and demographic attributes. Several factors are responsible for infertility, and awareness programs educating people about the risk factors are crucial.[46] Backed by clinical experience, the panel members put forward a consensus recommendation stating that awareness about the importance of AMH through education programs for healthcare professionals (HCPs) and the public at large will aid in increased adoption of AMH testing among women. Recent literature shows that most women are unaware of age-related changes in fertility; therefore, fertility counseling should be offered to younger women by HCPs.[47] The experts strongly recommended that the evaluation of AMH levels should be an integral part of reproductive life planning and can be considered one of the essential components of preconception care. As serum AMH levels are a good indicator of fertility in women of late reproductive age, they can help plan delayed pregnancies.[18] Recognizing the current social trends, the panel members reached a consensus that AMH evaluation is an essential part of fertility preservation approaches in the context of deferred or delayed pregnancy planning. The

expert panel proposed that ovarian reserve testing be conducted in women >35 years of age who have not conceived following 6 months of attempting pregnancy, as well as women at a greater risk of reduced ovarian reserve. However, there was a lack of complete consensus on this statement.

India has a high burden of tuberculosis, with a prevalence of around 18%. A study by Datta et al on patients with genital tuberculosis showed reduced AMH levels and ovarian reserve.[48] Infertility evaluation in this group of patients using serum AMH levels could improve pregnancy outcomes.[48,49] The panel agreed that in patients with genital tuberculosis, AMH testing could provide useful information for fertility counseling.

The expert panel concluded that standardized AMH measurements were necessary to assess ovarian reserve and guide clinical decisions in the Indian context. They emphasized the importance of assay-specific cutoff values and assay standardization for accurate interpretation in infertility evaluation and fertility management.

Strengths

The study covers a wide range of consensus statements related to ovarian reserve, AMH assays, and specific conditions, providing a comprehensive overview of the topic. The consensus statements are based on the input and agreement of experts in the field, ensuring that the recommendations are well-informed and representative of expert consensus. The consensus statements are clearly articulated and provide specific recommendations regarding the use of AMH testing in various clinical scenarios, enhancing their practical applicability.

Limitations

While the consensus statements are based on expert opinions, they may be limited by the low availability of empirical evidence supporting certain recommendations, particularly in specific clinical conditions. In addition, the consensus statements may not fully capture the diversity of clinical contexts and patient populations in Indian settings, limiting their generalizability to different settings or populations even within India.

CONCLUSION

This Indian consensus underscores the significance of the AMH assay in evaluating and managing infertility. The measurement of AMH levels provides valuable insights into the ovarian reserve, which is closely linked to age and can vary among women of the same age group. This assessment, combined with ultrasound imaging, serves as a reliable marker for assessing ovarian follicle count and reproductive aging. Automated AMH assays offer numerous advantages in terms of speed, precision, and ease of use compared with manual assays. However, ensuring standardization of these assays across different manufacturers is crucial for minimizing variabilities in results. The utility of AMH testing extends to diagnosing conditions such as PCOS, endometriosis, and ovarian tumors, as well as predicting ovarian responses to fertility treatments. Moreover, AMH assays can also assist in making informed decisions regarding fertility preservation for women undergoing gonadotoxic therapy. It is imperative to establish international standards for AMH cutoff values and calibrations to ensure accurate interpretations of test results and prevent misdiagnoses. Overall, AMH testing plays a pivotal role in personalized fertility management within the Indian context, empowering HCPs to provide optimal care to individuals seeking to build their families.

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