

Correlation of Anti-Müllerian Hormone Levels with Ovarian Reserve Patterns in Women Evaluated for Infertility

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Abstract

Background: Anti-Mullerian hormone (AMH) is an established biomarker of ovarian reserve that is now being brought into the situations involving infertile women. AMH is an indicator of the number of the remaining primordial follicle pool and is very useful in counseling, prognosis, and plans of fertility treatment. But these differences in the levels of AMH among various ovarian reserve patterns and age groups represent a reason that requires the use of region-specific data in the clinical decision-making. The objective is to determine how much serum AMH is correlated with the patterns of ovarian reserves in women undergoing infertility assessment in a tertiary care centre in North Gujarat.

Material and Methods: It was an observational study that was conducted at one year in a tertiary care centre in North Gujarat. Women with a history of infertility were subjected to comprehensive clinical examination, transvaginal ultrasound on the number of antral follicles (AFC), and estrogen AMH levels. Ovarian reserve was divided into normal cystic reserve, diminished reserve and polycystic ovarian morphology. The comparative analysis of the AMH with both age groups and ovarian reserve patterns was applied with the help of the appropriate statistical tests. **Results:** The level of AMH was highly found to be inversely related to age with the highest mean values obtained in women who were below 25 years and the subsequent low levels in older age. Women with low ovarian reserve depicted a considerably lower level of AMH than those with normal ovarian reserve, whereas women with a polycystic ovarian morphology showed considerably high levels of AMH. The correlation between AMH and ovarian reserve pattern was found to be statistically significant meaning that AMH is the reliable marker of underlying ovarian reserve status. **Conclusion:** The serum AMH levels are strongly correlated to the patterns of ovarian reserve and reduce with advanced age among infertile women assessed. AMH is an unaffected and handy clinical tool in the determination of ovarian reserve, which assists in the early detection of low reserve and adequate fertility-related counseling. The integration of AMH estimation in the normal practice of infertility assessment can enhance customized treatment planning and prediction.

Keywords: Anti-Mullerian hormone, ovarian reserve, infertility, antral follicle count and polycystic ovarian morphology and diminished ovarian reserve.

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INTRODUCTION

Infertility is an important reproductive health issue that concerns an estimated 1015 per cent of couples in the world with a woman being a causative agent in almost half of the instances.^[1] The patterns of infertility in India have been gradually rising with the delays in marriage, delays in bearing children, changes in lifestyle, obesity, stress, and metabolic conditions.^[2] This has led to the evaluation of female reproductive potential taking a core role in the work-up of infertile women especially those presenting in tertiary care centres.

Ovarian reserve as a factor of determination of reproductive potential and is a reflection of the number of remaining primordial ovaries follicles in the ovaries and its quality. Though physiologically, age-related loss of ovarian reserve takes place with age, interference or early loss can happen because of genetic predispositions, auto immune, endometriosis, pelvic modulations, chemotherapy, or environmental influences.^[3] Due to poor reaction to ovarian stimulation, increased cycle abolition, and diminished pregnancy rate during assisted reproduction methods

(ART), reduced ovarian reserve is linked to bad outcome.^[4]

Anti-Mullerian Hormone (AMH) is a glycoprotein which is part of family of transforming growth factors-b, and is secreted by the granulosa cells of pre-antral and small antral follicles. The serum AMH levels are positively correlated with the count of growing follicles and are now an acceptable biochemical predictor of ovarian reserve.^[5] In contrast to follicle-stimulating hormone (FSH) AMH, has little inter and intra cycle variability and can be determined at any stage within the menstrual cycle, a feature that makes it convenient and reliable in clinical practice.^[6]

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Ultrasonographic examination of ovarian reserve, especially antral follicle count (AFC) and ovarian volume is a valuable adjuvant test. According to the hormonal and sonographic parameters, the patterns of ovarian reserve are regularly divided into normal ovarian reserve, diminished ovarian reserve, and polycystic ovarian morphology.^[7] A number of studies have shown that the levels of serum AMH are strongly associated with AFC, and ovarian response to controlled ovarian stimulation.^[8]

AMH levels are affected by ethnic and regional differences to a great extent. There is also evidence that Indian women will experience a lower AMH level at younger age than the population of the west which shows that there is the earlier loss of ovarian reserve.^[9] Even though the application of AMH in infertility assessment is increasing, there is little data at North Gujarat that will match AMH levels with ovarian reserve trends in women undertaking infertility assessment. Evidence based on the region is the key to proper counseling, treatment planning as well as the best reproductive outcomes. Hence this study was conducted at a tertiary care centre within North Gujarat within one-year time to determine the relationship between the level of serum Anti-Mullerian hormone and the ovarian reserve patterns in infertile women who were assessed.

MATERIALS AND METHODS

It was an observational study at a one-year period in a tertiary care centre within Gujarat at a hospital. It involved women who brought up their primary or secondary infertility cases to the outpatient unit of Obstetrics and Gynaecology. With an informed written consent, qualified participants were recruited according to the set inclusion and exclusion criteria. The age range of women who were to be evaluated in the infertility area was between 20-40 years, with a general exclusion of a history of ovarian surgery, a history of chemotherapy or radiotherapy, certain endocrine disorders to the functioning of the ovary, and current hormonal therapy treatment. Each participant was given a was obtained with literature-based clinical history which includes age, infertility period and type, menstrual cycle, obstetric history, and medical or surgical history. General chat and systemic checkup were done and detailed gynaecology checkup was conducted. Sample of blood was taken to estimate serum Anti-Mullerian Hormone; it was done by using the enzyme-linked immunosorbent assay (ELISA) method. In AMH sampling, the sampling was not conditioned on the phases of the menstrual cycle since it had very low levels of intra-cycle variation.

The ultrasonography of the transvagina was conducted

during the early follicular phase (day 25) of the menstrual period with a high-frequency transducer. Antral follicle count was determined by the total number of follicles that had a size of 2-10mm in both of the ovaries and the volume of the ovaries determined. The patterns of ovarian reserve have been divided into normal ovarian reserve, diminished ovarian reserve, and polycystic ovarian morphology basing on the standard cut-off values based on serum AMH levels and ultrasonographic results. All the data were then keyed in a predetermined pro forma and analyzed using Statistical Package for Social Sciences (SPSS) software. Also, continuous variables were converted into a form of mean and standard deviation, and categorical variables were shown in the form of frequencies and percentages. Serum AMH levels were correlated with the appropriate statistical tests to ovarian reserve parameters in order to establish the correlation. The p-value of less than 0.05 was taken to be statistically significant. The study was initiated after the study received an ethical approval of the Institutional Ethics Committee.

RESULTS

In the paper assessing the relationship of serum Anti-Mullerian Hormone (AMH) levels with ovarian reserve patterns among women with infertility assessment on a tertiary care unit in North Gujarat, 120 subjects were studied. Most of the women were of the 26 years to 30 years age group with the age range of 3135 years coming in second, which is the general age at which infertility is presented. Primary infertility was more common than secondary and the majority of the subjects had regular cycles with occasional cases (almost 1/3rd) having irregular menstrual cycles. The serum AMH level analysis revealed that nearly 50-percent of the study group displayed more normal AMH levels and a significant percentage displayed AMH levels that indicated low ovarian reserve. A lesser but important group had high AMH levels which is usually linked to polycystic ovarian reserve patterns. In line with this, the most common occurrence was normal ovarian reserve, secondly, diminished ovarian reserve and thirdly, polycystic ovarian morphology. Correlation analysis showed significant negative correlation between serum AMH and age that were found to be statistically significant thereby showing a decrease in ovarian reserve with age. Conversely, AMH and antral follicles count were highly and statistically significantly correlated, which indicates that AMH is a valid surrogate endpoint of follicles in quantity. A significant positive relationship was also found between Ovarian volume and AMH levels. On balance, the findings add to the clinical relevance of AMH as a strong biomarker to determine ovarian reserve and infertility management in a woman assessed at a tertiary care facility.

Table 1: Demographic and Clinical Profile of Study Participants (n = 120)

Variable	Frequency	Percentage (%)
Age Group (years)		
20-25	24	20.0
26-30	46	38.3
31-35	32	26.7
36-40	18	15.0
Type of Infertility		
Primary infertility	78	65.0

Secondary infertility	42	35.0
Menstrual Pattern		
Regular cycles	82	68.3
Irregular cycles	38	31.7

Table 2: Distribution of Serum Anti-Müllerian Hormone (AMH) Levels

AMH Category (ng/mL)	Interpretation	Frequency	Percentage (%)
< 1.0	Low AMH	34	28.3
1.0 – 3.5	Normal AMH	56	46.7
> 3.5	High AMH	30	25.0
Total		120	100

Table 3: Ovarian Reserve Pattern Based on AMH and AFC

Ovarian Reserve Pattern	Frequency	Percentage (%)
Normal ovarian reserve	54	45.0
Diminished ovarian reserve	38	31.7
Polycystic ovarian reserve	28	23.3
Total	120	100

Table 4: Correlation of Serum AMH with Ovarian Reserve Parameters (Test of Significance)

Parameter	Correlation Coefficient (r)	p-value	Interpretation
AMH vs Age	-0.61	<0.001	Significant negative correlation
AMH vs Antral Follicle Count	+0.74	<0.001	Significant positive correlation
AMH vs Ovarian Volume	+0.52	<0.001	Significant positive correlation

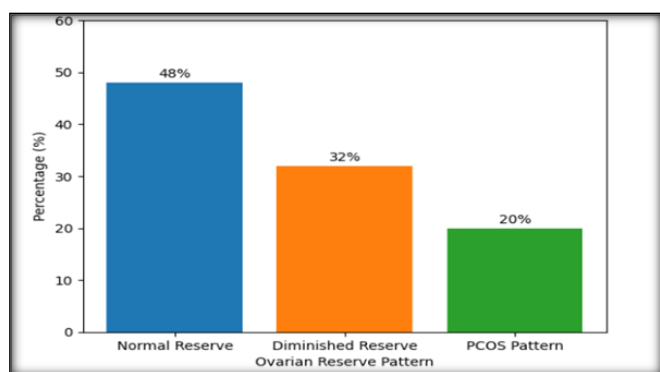


Figure 1: Distribution of Ovarian Reserve Patterns

DISCUSSION

The current paper tested the correlation between serum Anti-Mullerian hormone (AMH) concentration and ovarian reserve phenotype in women who were being tested on the grounds of infertility in a tertiary care centre in North Gujarat. These results indicate that AMH is valid as a biochemical parameter representative of ovarian reserve and has a consistent correlation with age, antral follicle count (AFC) and ovarian morphology. A gradual aging effect of a gradual decrease of AMH levels with age was also realized in this study, the older age group of women over the age of 35 had a significantly lower AMH reading when compared to the younger age groups. The literature is very specific in presenting this inverse relationship between age and AMH. The study by Seifer et al. (2011) indicated that the AMH levels were on a steady downward trend because the study was conducted to identify whether AMH is a marker of reproductive aging or not.^[10] On the same note, La Marca et al. (2010) proved that AMH levels decline earlier and are more predictable compared with traditional markers like FSH, and as a result made AMH be a sensitive marker of early aging in the ovaries,^[11] of an individual. The

observations of the current study are in tandem with these observations and they support the age dependent depletion of ovarian reserve.

In terms of ovarian reserve patterns, close to fifty percent of the women that were studied in this research found themselves with a normal level of AMH in that, a good proportion of the women had low levels of AMH that indicated a reduced ovarian reserve (DOR). This is similar to the results of Broer et al. (2014), who also found that about one-third of the women tested on their infertility were found to have a low ovarian reserve due to the assessment of AMH and AFC.^[12] An Indian study that was hospital based and was reported by Joshi et al. (2019) also confirmed reduced ovarian reserve in an approximate of 35-40% of the women who were found to be infertile, especially when they brought in the matter at the age of above 30 years.^[13] These resemblances underscore the increased excess of diminished ovarian reserve in women who pursue infertility treatment both in India and other global locations. This study found a strong positive relationship between AMH and antral follicle count to support the use of AMH as a surrogate of follicular pool size. This result supports the findings of Anderson et al. (2015), who showed a high level of correlation between AMH and AFC and various age groups and states of reproductive opportunities.^[14] Dewailly et al. (2014) further indicated that AMH is also more precise than AFC because it is based on the number of the small antral and pre-antral follicles in ordinary clinical practice.^[15] The agreements of the current research with these reports prove the clinical validity of the AMH measurement in evaluating the ovarian reserve. In this study, high AMH levels among women were typically characterized with the pattern of polycystic ovarian reserves. The same observation has been reported in the case of Pigny et al. (2006) who found a strongly increased level of AMH in women with polycystic ovary syndrome (PCOS) owing to the increase of follicular mass and activity of granulosa cells.^[16] Iliodromiti et al. (2020) in a more recent study also

substantiated that AMH is always high in PCOS and could help to distinguish polycystic ovarian morphology among other infertility etiologies.^[17]

On the whole, this study provides results that are parallel to the existing new national and international literature and prove the fact that serum AMH is strongly correlated with ovarian reserve patterns, AFC, and ovarian morphology. As a highly predictive and stable measure throughout the menstrual cycle, AMH can be useful in personal infertility counseling and treatment planning in resource-base tertiary care units.

CONCLUSION

This paper has shown that there is a strong correlation between the levels of serum Anti-Müllerian Hormone (AMH) and the patterns of ovarian reserve among women who are tested by a tertiary care infertility assessment centre in North Gujarat. The levels of AMH were observed to have an age-dependent drop and had a positive strong relationship between AMH and the number of antral follicles, which validated that AMH is a reliable measure of ovarian reserve. Women having low ovarian reserve had far less AMH values whereas high levels of AMH were usually related to polycystic ovarian reserve pattern. Such results highlight the use of AMH in clinical practice by early detection of diminished ovarian reserves, customized infertility counseling, and choice of supportive reproductive methods.

Limitations

In spite of the strengths, the research is limited in several ways. As a single-centre study, the duration of the study can only be one year in length and therefore the results might not be entirely applicable to the general population. No assessment was done regarding long term reproductive outcome, including response to ovarian stimulation, pregnancy rate, and live birth rate. Other endocrine parameters that might affect ovarian reserve like the inhibin-B were also not evaluated. Cross-sectional study design also fails to provide causality between AMH levels and infertility outcomes.

Recommendations

To determine reproductive outcomes of AMH with respect to the AMH level, future research should involve multicentric and larger-sample, prospective designs with a long-term follow-up. Predictability may be enhanced through the incorporation of AMH with other ovarian reserve variables and ultrasound variables. Regular AMH testing (particularly in women older than 30 years or with risk factors of reduced ovarian reserve) as a regular procedure during infertility assessment, should be considered. Prenatal counseling, basing on AMH levels, this will help in planning fertility and optimization of assisted reproductive procedures in time especially in resource constrained areas.

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Conflicts of interest

There are no conflicts of interest.

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