**Review article**

# 'Anti Mullerian Hormone and its role in Gynecological Endocrinology: A review'

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**Abstract**:

Anti Mullerian Hormone (AMH) is a glycoprotein belonging to the family of transforming growth factor-beta. The molecule has evolved in the last few decades for the assessment of ovarian reserve in females. Additionally this hormone has been found to be useful in predicting the success of in-vitro fertilization, marker of polycystic ovarian syndrome, granulosa cell tumor of ovary and prediction of premature ovarian failure. This article will help the consultant gynecologist to use this novel hormone in these clinical situations.

**Key Words**: Anti Mullerian Hormone, premature ovarian failure, ovarian reserve

**Introduction:**

Anti Mullerian Hormone (AMH) was first mentioned in literature as a reference to a protein formed in the testes of mammals including man and was different from testosterone. This protein was causing regression of the Mullerian ducts and hence was named 'Mullerian Inhibiting substance'.[1] This novel molecule has undergone large amount of research and number of uses in gynecology have been evolved in the recent years. It was initially used as a marker of ovarian reserve and subsequently has found to be useful in prediction of fertility, polycystic ovarian syndrome, marker for granulosa cell tumors and other uses.

**AMH Characteristics**:

It is a peptide belonging to the family of transforming growth factor- beta and is a homodimer of weight 140 kDa. The gene for human AMH is present on the short arm of chromosome 19. It has a unique effect in males causing regression of Mullerian ducts during embryonal period leading to development of male phenotype. In the males it is synthesized by the Sertoli cells of the testes since the 5$^{th}$ week of embryonal life. It is secreted by the granulosa cells of small growing follicles especially the primary and preantral follicles. It is not formed by the antral FSH dependent follicles. AMH is the biological regulator of folliculogenesis and of primordial follicle rupture. AMH inhibits the recruitment of primordial follicles and diminishes the response of the selectable follicles to FSH, hence impairing the selection of the dominant follicle.

AMH levels can be detected in the females from perinatal stage till menopause. The levels of the hormone as lower in values as compared with the males. AMH inhibits the initial selection of the follicles for further developmental stages and hence plays an important role in selection of the dominant follicle.



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Normal values of AMH in the females are: 1-8 µg/l in the fertile phase. Values below 1 µg/l suggest reduce fertility and values below 0.025 µg/l suggest infertile phase.

**AMH as a marker of ovarian reserve:**

AMH is an ideal marker for ovarian reserve as it is formed only by the primary follicles, which are potentially capable of maturation. [2]

The level of AMH reflects the number of preantral follicles and hence is a very good and reliable marker of the oocyte pool. Plasma levels of AMH highly correlate with the number of mature follicles. Assay of the plasma AMH in fertile women enables to assess the extent of her ovarian reserve. AMH measurement is more specific for the ovarian reserve as compared to assays involving FSH and inhibin as AMH is not involved in the feed-back mechanism of the hypothalamo-pituitary-ovarian axis. Hence the AMH levels are independent of the phase of menstrual cycle.[3] Single measurement of AMH serves this purpose. [2]

AMH can be used as a screening test of assess the fertility status of women wishing to have children beyond 35 years of age.[4]

**AMH in assisted reproduction:**

As mentioned AMH values reflect the ovarian reserve potential with great accuracy. Hence AMH measurement can be the prognostic marker of the response of the ovary during controlled ovarian stimulation during IVF cycles. The values have a prognostic values both for the number of oocytes retrieved during aspiration and the number of arrested cycles. [5]

As compared to antral follicular count, AMH concentrations could predict poor response to ovarian stimulation during IVF cycles.[6] AMH levels could also predict ovarian hyper-stimulation syndrome (OHSS) during multiple ovulation induction with gonadotropins.[7] Studies have revealed that live birth rate, following IVF, was increased when AMH levels were high prior to ovulation induction with human gonadotropins. [8]

Patients with low AMH values require much higher doses of FSH for stimulation than women with normal or high levels. Hence, AMH values are advisable before every IVF cycles to predict the outcome and to reduce the risk of OHSS. [9]

**AMH as a marker of menopause:**

AMH is found to be a reliable marker for assessment of ovarian function cessation. The number of primary and preantral follicles decreases with age and hence a corresponding decrease in the levels of AMH also occurs. [2] The decrease of AMH levels and follicle number with age has been widely accepted and AMH values have greater sensitivity than inhibin B, FSH and estradiol.[10] A significant decrease in the values of AMH is detectable considerably earlier than a clear rise in the FSH levels. [10]

**AMH and PCOS:**

Analysis of AMH values can serve as an adjuvant marker in the diagnosis of polycystic ovarian syndrome (PCOS). Increase values of AMH correlate with the severity of the disease.[1] There is a linear correlation of the number of antral follicles and the values of AMH, the raised values reduce the sensitivity to FSH at the receptor level. Hence a large number of small antral follicles of 2-5 mm in size are formed, depriving the development of a dominant follicle and hence ovulation. Hence AMH values can



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be helpful especially when transvaginal ultrasound is not feasible.[11]

The high value of AMH in PCOS is attributed to high number of small antral follicles of 2-5 mm diameter. These high values are also probably related to follicular arrest during selection of dominant follicle. AMH also inhibits the production of aromatase which is activated by the action of FSH on granulosa cells. [12]

**AMH as a tumor marker:**

AMH is a very good marker of granulosa cell tumors of the ovary. They can be used as a tumor marker along with inhibin. It can predict early disease and can be useful in assessing the response to treatment. AMH levels are found increased in 76-93% of women with granulosa cell tumors.[13]

AMH can be used to follow up the gonadal function in reproduction in subjects who were subjected to chemotherapy, radiotherapy or and immunosuppressive therapy.[1]

**AMH and Obesity**:

Obese women of late reproductive age (35-49 years) had significantly lower AMH levels, (up to 65%), compared to normal-weight women of similar age.[14] This inverse relation between BMI and AMH might be because obesity affecting catabolism of AMH. Obesity itself could reduce and ovarian potential and may lead to ovarian dysfunction.[15]

**AMH in Males**:

In males, determination of AMH may be useful in investigation of gonadal function, in the differential diagnosis of intersexuality, cryptorchidism and in diagnosis of precocious or late puberty. [16]

**Conclusion:**

AMH levels in the healthy females decline gradually with age and reach non-measurable levels after attaining menopause. This review will help the practicing gynecologist to utilize this novel hormone for in an array of endocrinolgical situations. Use of this target specific hormone can be an economical advantage also.

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