Chemistry Research Journal, 2019, 4(5):76-80

Available online www.chemrj.org

Research Article

ISSN: 2455-8990
CODEN(USA): CRJHA5

Anti-Müllerian Hormone (AMH): Predictor of Follicular Function, Fertility Status and Onset of Menopause

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Abstract ***Background***: AMH regulates folliculogenesis by inhibiting recruitment of follicles from the resting pool in order to select for the dominant follicle. In clinical practice its levels are measured in peripheral blood, mainly to assess ovarian and follicle functions and/or onset of menopause. ***Aim***: Present study was undertaken to assess the viability of AMH in three age groups for the assessment of suspected infertility and onset of menopause, in selected cohorts for PCOs, non-PCOs and fertility evaluation in pregnant women. ***Materials and Methods***: One hundred and sixty individuals, all females, N = 25 in each group with known history of ploycystic ovaries (PCOs) and matching controls; N = 20 each in groups classified according to age 18-35 yrs, 36-51 yrs and > 51 yrs and N = 25 each in two groups of married-non pregnant and pregnant (1^{st} trimester) individuals were selected for this study of AMH assessment. AMH as well as FSH, LH, Estradiol and prolactin were also assessed for comparative purpose, and were analyzed on Cobas e411 integrated immunoassay system (Roche Diagnostic-Infinity Cobas-system, Basil). ***Results:*** AMH showed variable levels in 18-35 yrs, 36-51 yrs and above 51 yrs of females. Similarly AMH was also assessed during successful pregnancies in selected females with 1^{st} trimester, and exhibited suggested levels of all hormones with significant difference in values. Selected cohorts for PCOs and non-PCOs showed moderate to high significant difference in values of AMH, FSH, LH, Procaltin and Estradiol. ***Conclusion***: AMH determination in such variable groups of individuals and its related, documented outcome suggest strong predictive value for onset of menopause, PCOs and indication of pregnancies

Keywords Menopause, Anti-Müllerian hormone (AMH), Polycystic ovarian syndrome (PCOs).
Short title: Anti-Müllerian hormone (AMH) and its clinical importance.

Introduction

Women at the age of 51 starts to show signs of menopause, which is actually in most cases, last menstrual period in their life. However, it is noted that physiological menopause may occur between 40 and 60 years of age, but the decline natural fertility of women starts 10-13 years prior to menopause [1-3]. During peri-menopause the number of ovarian follicles decreases to thousands only and thus progression of menopause is characterized by a very low number of follicles. Anti-Müllerian hormone (AMH) is produced in the ovary by granulosa cells of antral follicles [4]. AMH regulates folliculogenesis by inhibiting recruitment of follicles from the resting pool in order to select for the dominant follicle. In clinical practice its levels are measured in peripheral blood, mainly to assess ovarian and follicle functions and/or onset of menopause. In an adult woman AMH levels gradually decrease until they reach

values below detectable limits in postmenopausal women. In females between the ages of 12 yrs to 45 yrs, AMH ranges from <8.8 ng/ml to 9.5 ng/ml [1,2]. However above the age of 45 yrs, its level starts to decline upto < 1.0 ng/ml. Moreover, a number of childless couples are rising due to multiple medical complications and thus couples seek to have child in later years of woman's life [5,6]. Therefore, determination of ovarian reserve is an essential component of infertility assessment. Furthermore, Polycystic ovarian syndrome (PCOs) is one of the reason of infertility in young married women and thus it was suggested in many studies to have AMH assessments of such cases [7].

Therefore we report assessment of AMH levels in selected population of females, categorized into three groups as per age, 18-35, 36-51 and above 51 for the assessment of suspected infertility and onset of menopause. In addition, selected cohorts for PCOs, non-PCOs and pregnant women were also included in the study for better understanding and diagnostic viability of AMH. AMH (Roche Diagnostics, Basil) was analyzed on Cobas e411 integrated immunoassay system (Roche Diagnostic-Infinity Cobas-system, Basil).

Materials and Methods

Study protocol and Patient's selection: One hundred and sixty individuals, all females, N = 25 in each group with known history of ploycystic ovaries (PCOs) and matching controls; N = 20 each in groups classified according to age 18-35 yrs, 36-51 yrs and > 51 yrs and N = 25 each in two groups of married-non pregnant and pregnant (1st trimester) individuals were selected for this study of AMH assessment. Study period for this prospective study was from August 2018 to June 2019. The patients who are on steroid therapy, underwent surgery, suffering from pulmonary or renal impairment were excluded from the study. Related female hormones such as FSH, LH, Estradiol and prolactin were also assessed for comparative purpose.

Analysis of Anti-Müllerian hormone (AMH), Estardiol, Luteinizing Hormone (LH), Follicle Stimulating Hormone (FSH) and Prolactin on Immunoassay analyzers

Previously described protocols were followed for standardization [8, 9]. Blood samples were collected from all 160 patients for various types of hormones, viz Anti-Müllerian hormone (AMH), Estardiol, Luteinizing Hormone (LH), Follicle Stimulating Hormone (FSH) and Prolactin. Plasma was separated and analyzed for AMH, FSH, LH, Estradiol, Prolactin on Cobas e411 using electro-chemiluminescence (ECLi) immunoassay technology (Roche Diagnostics, Basil) and Beckman Coulter Access 2 using chemiluminescence technology (Beckman, USA). Normal reference range of AMH 13-45 yrs = 0.90 -9.5 ng/ml. Ranges for LH, FSH, Estradiol and Prolactin were used as obtained from control or comparative groups. The data was compared statistically by using SPSS ver 20.0 (USA), regression correlation analysis and considered significant when $P < 0.05$.

Results

One hundred and sixty individuals, all females, were grouped, 25 in group with known history of ploycystic ovaries (PCOs) and matching controls (Table 1); 20 each in groups classified according to age 18-35 yrs, 36-51 yrs and > 51 yrs (Table 2) and 25 each in two groups of married-non pregnant and pregnant (1st trimester) (Table 3) individuals were selected for this study of AMH assessment and related fertility and female hormones. In group with confirmed cases of ploycystic ovaries (PCOs) and non-PCOs matching controls, significantly elevated levels of AMH ($P < 0.001$) was noted in patients with PCOs. Similar elevated levels were also noted for FSH, LH, Prolatin and Estradiol, suggesting ovarian stress and probability of infertility (Table 1). AMH was also assessed in various age groups of females to assess probable menopause status and fertility function. Marked significance was noted in AMH when 3 different age groups were statistically compared with each other, >51 yrs showing decline in AMH secretion and age group 36-51 in mid-range (Table 2). Similar pattern was observed for FSH, LH, Prolactin and estradiol. Although AMH mostly used for onset of menopause or dysfunctional fertilities, however we decided to have AMH assessed during successful pregnancies as well in 1st trimester (Table3). Data showed internationally known and recommended levels of all hormones including AMH, exhibiting moderate to highly significant difference in values.

Table 1: AMH, other fertility and hormones level in non-polycystic ovaries and Polycystic ovaries cohorts

Variables	Control (age matched) Non PCOs	PCOs	P< 0.05
Selected individuals	25	25	--
Age (years)	29.10 ± 6.10	28.60 ± 5.90	NS
BMI (kg/m^2)	24.35 ± 5.05	25.10 ± 4.55	NS
AMH (ng/ml)	4.10 ± 1.40	10.17 ± 3.65	0.001
FSH (IU/L)	5.80 ± 2.00	8.16 ± 3.55	0.001
LH (IU/L)	6.55 ± 3.05	11.45 ± 4.10	0.001
Estradiol (pg/ml)	60.10 ± 7.80	86.10 ± 6.75	0.001
Prolactin (ng/ml)	23.40 ± 6.85	180.30 ± 10.10	0.0001

NS = Non significant; Data is significant when P > 0.05; Results are expressed as Mean ± SD

Table 2: AMH, other fertility and hormones level in various age group cohorts

Variables	Age 18-35	Age 36-51	Age > 51	P< 0.05
Selected individuals	20	20	20	--
BMI (kg/m^2)	24.40 ± 5.60	25.45 ± 6.10	26.70 ± 5.95	NS
AMH (ng/ml)	8.70 ± 1.85	2.00 ± 1.70	0.67 ± 0.15	0.001
FSH (IU/L)	6.71 ± 2.30	8.76 ± 3.45	21.10 ± 8.90	0.001
LH (IU/L)	6.80 ± 2.60	6.55 ± 2.10	5.90 ± 1.45	0.001
Estradiol (pg/ml)	55.20 ± 10.95	28.10 ± 6.75	7.80 ± 3.20	0.0001
Prolactin (ng/ml)	18.10 ± 7.70	19.30 ± 6.75	12.55 ± 4.10	0.001

NS = Non significant; Data is significant when P > 0.05; Results are expressed as Mean ± SD

Table 3: AMH, other fertility and hormones level in non-pregnant and pregnant cohorts

Variables	Control (age matched) Non Pregnant married	Pregnant (2nd trimester)	P< 0.05
Selected individuals	25	25	--
Age (years)	29.40 ± 9.40	28.90 ± 8.65	NS
BMI (kg/m^2)	24.80 ± 6.85	26.75 ± 6.70	NS
AMH (ng/ml)	5.10 ± 2.35	2.40 ± 1.01	0.01
FSH (IU/L)	6.10 ± 1.95	3.50 ± 0.95	0.001
LH (IU/L)	6.80 ± 2.10	2.50 ± 0.85	0.001
Estradiol (pg/ml)	56.35 ± 9.60	1218.40 ± 35.60	0.0001
Prolactin (ng/ml)	19.25 ± 6.75	68.70 ± 10.15	0.0001

NS = Non significant, Data is significant when P > 0.05; Results are expressed as Mean ± SD

Discussion

In this study we report analysis of AMH levels in selected females, categorized into three groups as per age, 18-35, 36-51 and above 51 for the assessment of suspected infertility and onset of menopause. Furthermore, selected cohorts for PCOs, non-PCOs and pregnant women were also included in the study for better understanding and diagnostic viability of AMH and related fertility hormones. Patients or individuals in such a way that 25 in group with known history of ploycystic ovaries (PCOs) and matching controls (Table 1) in a separate category; 20 each in groups classified according to age 18-35 yrs, 36-51 yrs and > 51 yrs (Table 2) and 25 each in two groups of married-non pregnant and pregnant (1st trimester) (Table 3) individuals. AMH was noted to be significantly variable in 3 different age groups when compared with each other, in which >51 yrs showing decline in AMH secretion and age group 36-51 in mid-range. FSH, LH, Prolactin and estradiol were also noted to be according to age group and pre or intra-menopausal status AMH was also assessed during successful pregnancies in selected females with 1st trimester. Data exhibited suggested levels of all hormones including AMH, exhibiting moderate to highly significant difference in values.

AMH is one of the promising markers that can be useful to detect age-related infertility and fertility life-span [4]. AMH is also known to provide information regarding onset of menopause and proper functioning of primordial

follicles [10]. In addition to AMH, the existing traditional hormones, FSH, LH, Estradiol and Prolactin also provide similar status evaluation in conjunction with AMH [11, 12]. Prediction of AMH based menopausal evaluation studies done earlier also strongly suggest AMH to be considerable prediction marker [13, 14].

Dilemma of couples who wants children at a later stage faces is also rampant and induces, frustration, despair and depression. Unintentional childless couples seek to conceive for the first time in the 40 of woman's life [3]. In this regard determination of ovarian reserve is an essential component of infertility assessment and therefore AMH is one of the reliable predictor of ovarian reserve. As it is known that AMH levels decrease during pregnancy, we noted similar findings in our current study as well. Decline in AMH levels during pregnancy is natural, normal and signifies ovarian suppression [3]. Furthermore, polycystic ovarian (PCOs) syndrome is becoming a common clinical condition, even at an early of post-puberty, mostly due to obesity and menstrual dysfunctions. Since AMH can be a good predictor of ovarian reserve, it was suggestive strongly that AMH can also helpful in assessing PCOs [7]. Studies also noted that AMH value rise when hyperandrogenism is present therefore AMH determination and its assessed levels can also reveal the phenotype of PCOS [7].

Conclusion

Analysis of AMH levels in selected females, whether age categorized, or PCOs or early pregnancies; it is noted to be a good predictor of onset of menopause as well. AMH showed variable levels in 18-35 yrs, 36-51 yrs and above 51 ysr of female for assessment of suspected infertility and onset of menopause. AMH was also assessed during successful pregnancies in selected females with 1st trimester. Data exhibited suggested levels of all hormones including AMH, exhibiting moderate to highly significant difference in values. Furthermore, selected cohorts for PCOs, non-PCOs and pregnant women were also included in the study for better understanding and diagnostic viability of AMH and related fertility hormones. AMH as also assessed during successful pregnancies in selected females with 1st trimester and it exhibited suggested levels of all AMH, exhibiting moderate to highly significant difference in values. Our assessments for AMH in such variable groups of individuals and its related, documented outcome suggest strong predictive value for onset of menopause, PCOs and indication of pregnancies.

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