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INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/12365
DOI URL: http://dx.doi.org/10.21474/IJAR01/12365

ISSN NO. 2320-5407

RESEARCH ARTICLE

ANTIMÜLLERIANHORMONE: CORRELATION WITH FIRST TRIMESTER MISCARRIAGE

Mostafa Abdulla Elsayed
Assistant Professor of Obetetrics and Gynecology Benhauniversity - Qalubia - EgyptStreet no 3 ElvillalkornishElneelBenha VILA 12.

Manuscript Info

Manuscript History
Received: 25 November 2020
Final Accepted: 28 December 2020
Published: January 2021

Key words:-
Abortion, AMH, Pregnancy Beyond 22 Weeks

Abstract

Objective: The present study assessed antiMüllerian hormone (AMH) levels as a useful markerand a predictor of abortion in the first trimester among women younger than 35 years.

Methods: Prospective study of women aged 18–34 years with a spontaneous pregnancy at less than 12 gestational weeks in Benha , Egypt, between January 2019 and November 2020 samples of blood taken at the beginning of pregnancy on booking and again at 6 weeks. Cases of anembryonic abortion and assisted conception were excluded. Blood samples were collected and assayed for serum AMH levels (on booking and at 6 weeks gestation. Data were compared between women with an embryo with no cardiac activity by ultrasound (n=50) and those with a normalpulsating embryo (n=50) by using smith statistical software.

Results: Risk of pregnancy loss in the first trimester was found to be higher for low AMH (<1 ng/mL; relative risk [RR], 3.66; 95% confidence interval.

Conclusions: LowAMH concentrations found to significantly increase the risk of abortion in the first trimester of pregnancy. Serum AMH might be a valuable marker to predict the risk of early abortion when it is below 1ng/ml.

Introduction:-

Anti-Müllerian hormone (AMHis a glycoprotein hormone structurally related to inhibin and activin from the transforming growth factor beta superfamily, they participate in growth differentiation and follicle growth. [1]

The gene for AMH is AMH, on chromosome 19p13.3, while the gene AMHR2 codes for its receptor on chromosome 12[2]

AMH is activated by SOX9(SOX9 **gene** provides instructions for making a protein that plays a critical role during embryonic development.

The **SOX9** protein is important for growth and differentiation of the skeleton and plays a key role in the determination of sex). (3 **)**

Corresponding Author:- Mostafa Abdulla Elsayed
Address**:-** Assistant Professor of Obetetrics and Gynecology Benhauniversity - Qalubia - EgyptStreet no 3 elvillalkornishelneelBenha VILA 12.

AMH expression is critical to sex differentiation during fetal development, and appears to be regulated by nuclear receptor SF-1, transcription GATA factors, sex-reversal gene DAX1, and follicle-stimulating hormone (FSH).**(4.5)**

AMH secreted from the Sertoli cells of the male and inhibits the development of the female reproductivetract,so AMH arrests the development of fallopian tubes, uterus, and upper vagina.**(6,7)**

Mutations in both the AMH gene and the type II AMH receptor cause the persistence of Müllerian derivatives in masculinized males. **(9, 10)**

AMH is a product of granulosa cells of the preantral and small antral follicles in women.(**16)**
Production of AMH regulates folliculogenesis by inhibiting recruitment of follicles from the resting pool in order to select for the dominant follicle, after which the production of AMH declines. **(11-12)**

AMH can also be used as a marker for ovarian dysfunction, such as in women with polycystic ovary syndrome AMH is on the higher range.

Fetalaneuploidies are the main etiology and account for 75% of cases of first trimester abortion. Various markers of aneuploidy have been sought and evaluated but still maternal age predominantly determines and increases the risk of fetal aneuploidy.**1**3

Reproductive potential and ovarian reserve proved to be declining with a woman's age. Close correlation between maternal age and both risk of fetal aneuploidy and ovarian reserve decline, various potential markers, including follicle stimulating hormone (FSH) and anti- Müllerian hormone (AMH), have been evaluated as predictors of IVF outcomes, with a primary consideration of the risk of abortion and fetal aneuploidy.**14**

Anti- Müllerian hormone generally taken into account in assessments of ovarian reserve. According to one study, AMH levels remain constant during pregnancy.

Hamilton et al.noted insignificant serum AMH levels vary in a vast way among pregnant women with the peaks or troughs between 4 and 7 gestational weeks.

AMH levels have been shown to correlate with the number of oocytes retrieved during gonadotrophin stimulation but studies on the correlation of AMH with the number of clinically successful pregnancies are often contradictory .

Many studies showed that AMH levels do not correlate with the number of live births.(**10-14)**

The aim of the present study was therefore to study the prognostic value of AMH serum levels as a marker of first trimester miscarriage among women younger than 35 years.

Materials And Methods:-

The present prospective study was carried out among women with a spontaneous intrauterine pregnancy attending the sonolive clinic of obstetrics and gynecology Benha city Qalubia district Egypt between January 1, 2019, and january 30, 2020. The study was approved by, and informed consent was obtained from all participants.

Only women aged 18–35 years were included. All participants were in the first trimester of a spontaneous intrauterine pregnancy (<12 weeks), either with an embryo or fetus without any cardiac activity by ultrasound examination (abortion group 50) or with a normal pregnancy (control group 50).

All women recruited for the control group were in sonolive clinic a private clinic in Benha city qalubia district for observation owing to moderate pelvic pains or vaginal spotting episodes, and their pregnancy was subsequently confirmed to continue until at least 24 gestational weeks.

Samples taken from the patients on booking after cases know that they are pregnant and then samples collected again at 6 weeks gestations.Cases of anembryonic abortion were excluded.

The exclusion criteria were history of fertility treatment, endocrine disorders, PCOS, obesity (body mass index [BMI, calculated as weight in kilograms divided by the square of height in meters], >30), antiphospholipid syndrome, thrombophilia, uterine anomalies, acute infections, assisted conception, and multiple gestation.

Blood samples were collected on admission on the day of bleeding (complaining cases) and also collected on booking and again at 6 weeks if there were no complaints .

All participants undergone evaluation by ultrasound at 5 weeks 6 weeks and at 8weeks to detect viability and to exclude anemryonic sacs AKA blighted ovum

Serum was separated from whole blood, transferred to sterile polypropylene tubes.Serum AMH concentrations were assayed by using a Gen II ELISA kit.

Women in the study group had missedabortion (after confirmation of absence of fetal cardiac pulsations by ultrasound and Doppler analysis, followed by suction evacuation under ultrasound guidance this was a routine for me. Histopathology was performed in all cases.

The study data were analyzed by using Smith statistical package USA). Variables were compared by Student *t* test or by Mann–Whitney *U* test when they failed the normality test.

Relative risk (RR) of abortion was assessed by using AMH thresholds based on the 10th and 90th percentiles of the control group, and was reported with 95% confidence intervals (CI). A *P* value of less than 0.05 was considered statistically significant.

Results:-

During the study period, 100 participants were recruited, including 50 women diagnosed with spontaneous abortion and 50 control women(pregnant with confirmed viability till 24 weeks).

The mean ± SD age was 32.5 ± 3.7 years in the abortion group and 28.5 ± 4.5 years in the control group (*P*=0.06). The obstetric records showed that the abortion group and the control group had similar parity (2.1 ± 0.8 vs 1.8 ± 1.2; *P*=0.15).

On the basis of values in the control group, the 10th and 90th percentiles of serum AMH concentration were determined as 1 and 4 ng/mL, respectively. Thus, the reference range for the AMH in earlypregnancy was determined as 1–4 ng/mL.

The risk for pregnancy loss in the first trimester was found to be higher for AMH less than 1 ng/mL 7 /50 in the abortion vs 0/50 in the control *P* =0.006) and no significant difference if AMH higher than 4 ng/mL (1/ in the abortion vs 1/50 in the control group*P* =1).

Variable	Abortion group	Control group	P value
Amh<1	7	0	0.006
Amhfom (1-4)	42	49	0.09
Amh>4	1	1	1

Discussion:-

The present study shows that low serum AMH levels below the tenth percentile AKA 1ng/ml alone might increase the risk of abortion in the first trimester of pregnancy.

Recent studies have focused on the relationship between low AMH and risk of fetal aneuploidy,Rising maternal age increases the risk of fetal aneuploidy and low antral follicle counts produce smaller amounts of AMH (i.e., a general decrease in ovarian reserve is observed).**14**

Shim et al.reported that low AMH levels might be maternal age- independent markers of fetal aneuploidy; however, they noted relatively high AMH serum concentrations in the aneuploidy group as compared with the euploidy group (3.43 ± 3.18 vs 4.60 ± 3.86 ng/mL, *P*=0.022.(**15**)

Plante et al. found that AMH levels did not differ between women with an aneuploid fetus and those with aneuploid fetus.**(16)**

However, Shim et al assayed AMH levels before conception, whereas Plante et al measured them during ongoing pregnancy. Plante et al found that AMH values decreased significantly with increasing gestational age, in contrast to a previous study.(**4**)

Jiang et al. reported that fetal aneuploidy was associated with low AMH levels (<1.5 ng/mg) only among women of advanced age. Given these relatively ambiguous results, it seems that AMH serum concentrations may predict abortion but not fetal aneuploidy.(**17)**

In the present study, low AMH levels (i.e., <1 ng/mL) were found to significantly increase the risk of abortion in the first trimester of pregnancy.

Lyttle Schumacher et al reported that women with a severely diminished ovarian reserve (AMH, ≤0.4 ng/mL) were at increased risk of abortion, which in turn reversed with rising AMH concentrations.**(18)**

Zarek et al. reported that serum AMH was not associated with clinical pregnancy loss after unassisted conception among women with 1–2 previous pregnancy losses. In their study, neither low (<1.0 ng/mL) nor high (>3.5 ng/mL) AMH relative to normal values (1.0–3.5 ng/mL) was associated with clinical pregnancy loss. (1**9)**

Pils et al. evaluated AMH concentration and pregnancy loss among 76 women with recurrent abortion, found that low AMH might be a tool to predict recurrent abortion in a future pregnancy in an early gestation (≤10 weeks) abortion .**(17)**

Diminished ovarian reserve, AMH levels lower than 1 ng/mL or lower and FSH levels of 11 U/L or higher has been found to be a risk factor for abortion among women with a history of recurrent abortion.18

Tarasconi et al. showed a higher risk of abortion after IVF among women with low AMH (≤1.6 ng/mL), but only for older women (i.e., >34 years).**20**

Anti- Müllerian hormone regulates steroidogenesis of the ovary, influences folliculogenesis, and controls the growth of primary follicles, inhibiting their development. Via its paracrine action, AMH also inhibits FSH- stimulated follicular development, thereby contributing to the selection of a dominant follicle.(**21)**

The higher the concentration of AMH, the stronger the inhibition of FSH, which may result in anovulatory cycles, as in PCOS.

Women with PCOS show subfertilityand increased risk of abortion; similar pregnancy outcomes have also been noted among women with higher AMH levels (>2.5 ng/mL) who do not have PCOS.(**22-24)**

The present study found a higher risk of abortion among women with an AMH concentration lower than 0.5 ng/mL in the first trimester.

Gleicher et al. noted that the incidence of abortion was 42.9% for women younger than 36 years with AMH concentrations of 10 ng/mL, but reached 81.8% for women older than 43 years with AMH concentrations of 10 ng/mL.(**19)**

In conclusion very low AMH concentrations (less than 1 ng/mL were found to significantly increase the risk of spontaneous abortion in early pregnancy. Thus, the assessment of AMH serum concentrations might be a valuable prognostic tool to predict the risk of abortion.

Conflicts Of Interest:
The author has no conflicts of interest.

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