EXPERT VIEW/REVIEW PAPER

Low Anti-Müllerian Hormone as Predictor of Preeclampsia: A Scoping Review

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Abstract

Objective: Low levels of serum anti-Müllerian hormone (AMH) have been linked to heart disease. It's been suggested that it can help forecast the risk of preeclampsia. The goal of this scoping review is to present the most recent evidence on the function of AMH in preeclampsia prediction.

Materials and methods: We looked through web-based databases and key terms like AMH, preeclampsia, predictor, and inclusion and exclusion criteria. Eight research papers were evaluated; however, two studies with retrospective cohorts and follow-up were removed, resulting in a final analysis of six investigations. There were 558 subjects examined in all. There were 243 with preeclampsia and 315 with normal blood pressure.

Results: Three of the six studies found a statistically significant link between low AMH levels and preeclampsia ($p = 0.05$), while the other two studies were near to the level of statistical significance ($p = 0.06$). The current literature implies that low-blood AMH levels may have a prognostic value in women developing preeclampsia.

Conclusion: Higher levels of serum AMH are associated with a decreased risk of preeclampsia, according to current research.

Keywords: Anti-Müllerian hormone, Preeclampsia, Preeclampsia, Predictor.

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Introduction

Preeclampsia affects 2–8% of all pregnancies worldwide, and it is a leading cause of maternal morbidity and mortality.[1] Preeclampsia is the leading cause of maternal death, accounting for 10–15% of all cases.[2] A multitude of risk factors in the mother, such as autoimmune diseases (systemic lupus erythematosus, antiphospholipid syndrome) and a family history of hypertension, diabetes, or preeclampsia, can induce preeclampsia.[3] Preeclampsia's ethology is unknown, however, it has been suggested that the placenta has a role in the disease. Incorrect placentation is caused by faulty trophoblastic invasion of the uterine spiral arteries, which results in hypoperfusion, hypoxia, the release of inflammatory agents, and endothelial dysfunction, leading to thrombosis and preeclampsia.[4,5] Placental hormones (hCG, activin, and inhibin) and placental factors (PlGF) have all been identified as biomarkers. Anti-Müllerian hormone is a glycosylated glycoprotein that is used to assess ovarian reserve and even provides information on the antral follicles, which decrease in number as women become older.[6,7] Anti-Müllerian hormone is a hormone that has an impact on the cardiovascular system, according to Dennis et al.[8] Ovarian suppression, according to Koninger et al., is the cause of lower AMH levels during pregnancy.[9] According to La Marca, maternal serum AMH is dynamic, decreases as pregnancy continues, and poor placentation is associated with increased AMH levels.[10] Several observational studies have revealed that decreased blood AMH levels are associated with the development of preeclampsia.

The goal of this study is to look at how serum AMH levels change in women who are at risk of developing preeclampsia.

Materials and Methods

Study Design

The current study followed the preferred reporting items for systematic reviews and meta-analyses (PRISMA) standards.[11]

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Eligibility Criteria

The current review includes all (prospective and retrospective) studies that assessed anti-Mullerian hormone levels in preeclampsia and normotensive women.

Case studies, review papers, and animal studies were all eliminated.

Literature Search and Data Collection

We examined web-based databases for key terms like AMH, preeclampsia, and predictor, as well as inclusion and exclusion criteria. Full-text papers were discovered by searching the Medline, Scopus, Clinicaltrials.gov, and Cochrane Central Register of Controlled Trials CENTRAL databases. In all, 8 studies were reviewed,[12–19] but two studies with retrospective cohorts with follow-up were excluded,[16,17] resulting in a final analysis of 6 studies. The total number of subjects investigated is 558. There were 243 preeclampsia cases and 315 normotensive cases.

Table 1: Study characteristics

Study	*Mean age*	*Type of study*	*Exclusion criteria*	*Sample size*	*AMH levels*
Zebra Jamil et al., 2019	29.7 ± 9.1 vs 25.9 ± 5.3	Cross-sectional	Chronic systemic disease, such as cardiovascular, urogenital, immunological, endocrinological, and renal	20/30	0.85 ± 1.07 vs 1.62 ± 2.29
Begum Mathyk et al., 2018	28.56 ± 6.8 vs 26.31 ± 4.04	Case-control	BMI more than 35	32/30	0.79 ± 0.40 ng/mL vs 1.45 ± 0.93 ng/mL ($p = 0.01$)
Agabain et al., 2017	27.7 ± 6.9 vs 29.5 ± 6.7	Case-control	Thyroid, hypertension, diabetes, liver, renal disorders	40/40	0.700 (0.225–1.500) vs 0.700 (0.400–1.275) ng/mL
Birdie et al., 2014	32.6 (29.4–37.1) vs 31.9 (26.9–35.9)	Case-control	Gestational age less tax 11 weeks and more than 13 weeks	50/150	2.140 (1.968–2.273) vs 2.062 (1.938–2.181) ng/L
Tokmak et al., 2014	28.7 ± 6.2 vs 27.0 ± 4.2	Case-control	Early onset preeclampsia, gestational age less than 20 weeks	45/42	0.62 ± 0.51 vs 0.93 ± 0.83 ng/mL
Shand et al., 2014	NA	Retrospective cohort	Multiple pregnancies, pregnancy more than 1st trimester, Birth less than 20 weeks	11/23	4.7 (1.8–13.2) vs 5.5 (1.4–16.1) pmol/L

Definitions

Preeclampsia was defined as hypertension (systolic blood pressure 140 mm Hg or diastolic blood pressure 90 mm Hg found on at least two consecutive occasions 6 hours apart) plus proteinuria (1+ in urine dipstick or 300 mg per 24-h urine excretion) that appeared after 20 weeks of gestation in previously normotensive women. Preeclampsia was classified as early or late onset based on whether it appeared before or after 34 weeks of pregnancy.

Results

Included Studies

Finally, 6 papers with a total of 558 women were included in our evaluation.[12–17] In total, 243 of them had preeclampsia, whereas 315 were recruited as normotensive controls. Table 1 shows the research design, patient eligibility criteria, patient characteristics, including the number of patients, mother age, gestational age, and AMH levels.

Excluded Studies

After reviewing the complete text, we eliminated two studies because they did not match our inclusion criteria.

Outcomes

Table 1 shows the research results as well as the maternal AMH levels in preeclamptic and normotensive women. Three of the six studies indicated a statistically significant association between low AMH levels and preeclampsia ($p = 0.05$),[12–14] while the other two were close to the level of statistical significance ($p = 0.06$).[15,16]

In their studies, Tokmak et al. and Shand et al. discovered larger levels of maternal AMH in normotensive women than in preeclamptic women. Birdir et al. discovered that AMH levels were higher in preeclamptic women and that AMH is not an effective early predictor of preeclampsia. They compared the case and control groups using multiples of the median (MoM) methodology, and no significant difference was seen (1.040, IQR 0.941–1.081 vs 0.995, IQR 0.939–1.065, $p = 0.147$).[14] He also said that AMH has a sensitivity of 67.4% and a specificity of 47.1%.

Shand et al. who conducted on research on pregnant women with lower AMH levels (tenth centile) in the first trimester had a 3.3-fold greater risk of gestational hypertension (OR 3.3, 95% CI, 1.2–8.7, $p = 0.01$).[15] To examine the usefulness of maternal AMH levels in the prediction of preeclampsia, Tokamak et al. developed a receiver operator characteristics curve (ROC).

Biomarkers, according to Zebra Jamil et al., play a role in detecting hypertension and later ovarian rage with decreased levels of AMH.[16]

Begum Mathyk et al. discovered a relationship between reduced AMH levels and preeclampsia vascular factors in their study.[17]

Discussion

The review thus concentrates on the assumption that higher AMH levels are seen in normotensive women. It is still uncertain if AMH has a protective impact on the endothelium. Despite the fact that studies support the low AMH value for predicting preeclampsia because low AMH levels signal poor ovarian reserve status, preeclampsia is the cause of low AMH values.[17,20]

Anti-Müllerian hormone testing is used to assess ovarian reserve. It contributes in assessing the antral follicle count[8,7] and is thus associated with fertility.[21] Over the next decade, researchers will look at the cardioprotective and endothelial-beneficial properties of AMH.

Women with greater blood AMH levels had a decreased risk of atherosclerosis.[22] According to Dennis et al., there is a negative connection between AMH and infrarenal aortic diameter.[8]

Pregnancy-associated plasma protein A (PAPP-A) demonstrates impaired placental function, which boosts AMH levels during the first trimester of pregnancy.[23] A vascular component contributes to early menopause.

Preeclampsia changes cardiovascular parameters, leading to premature vascular aging, which causes ovarian flaring and a

decrease in AMH levels.[17] In preeclamptic pregnant women, low AMH levels are produced by vascular factors that limit ovarian AMH production.

Limitations of our Study

Due to a lack of data, only six publications were chosen for examination. Only two of the six studies examined AMH levels in the first trimester of pregnancy and recommended for it as an early predictor of preeclampsia. However, just one paper discusses the biomarker's sensitivity and specificity.[13]

Implications for Further Research

Current research suggests a relationship between serum AMH and vascular disease. However, its application as a screening marker for preeclampsia is currently understudied, and further study is needed to establish definite conclusions. Outcomes in patients should be examined based on prepregnancy AMH levels, spontaneous conception or conception with ART, and the degree of preeclampsia development. More study is needed to find the appropriate cutoff values for varied groups using ROC plots, as well as the specificity and sensitivity of an understudied biomarker during the first trimester of pregnancy.

Conclusion

According to current studies, higher levels of serum AMH are related with a lower risk of developing preeclampsia. The negative connection is based on pathophysiological and clinical research that reveals a relationship between low AMH and cardiovascular disease. Because present evidence in the field of preeclampsia has minimal validity, more study is needed to validate the role of AMH in preeclampsia prediction.

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