Reference ranges of AMH in early pregnancy: the Generation R Study, a population-based prospective cohort study

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Abstract

Objective: The objective of this study is to establish maternal reference values of AMH in a fertile multi-ethnic urban pregnant population and to evaluate the effect of gestational age. Design: The Generation R Study is an ongoing population-based prospective cohort study from early pregnancy onwards. Setting: Rotterdam, the Netherlands, out of hospital setting. Population: In 5806 women serum AMH levels were determined in early pregnancy (median 13.5 weeks; 95% range 10.5-17.2). Methods: The model-based AMH reference ranges for maternal age and gestational age were created using GAMLSS. Associations between AMH and several first trimester biomarkers were analyzed using multivariate linear regression analyses. Main outcome measures: AMH levels in early pregnancy and the association with placental biomarkers, hCG, sFLT, and PLGF. Results: A nomogram of AMH in early pregnancy was developed. Serum AMH levels showed a decline with advancing gestational age. Higher AMH levels were associated with a higher level of hCG and sFLT. This last association was predominantly mediated by hCG. AMH levels were negatively associated with PLGF levels. Conclusion: In this large study we show that AMH levels in the first trimester decrease with advancing gestational age. The association between AMH and the placental biomarkers hCG, sFLT and PLGF suggests a better placental development with a lower vascular resistance in mothers with higher AMH levels. AMH might be useful in predicting adverse pregnancy outcome due to impaired placental development. Keywords: Ovarian reserve, placental biomarker, nomogram, first trimester, human Choriogonadotrophin (hCG), soluble FMS-Like Tyrosine kinase-1 (sFLT), Placental Growth Factor (PLGF).

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8976	women included during the prenatal phase in the Generation R study

2793	Excluded: women without available blood samples

6183	women with AMH measurement

377	Excluded: Multiple AMH measurements due to participation within Generation R with more than one pregnancy

5806	Population for analysis: pregnant women with a known AMH measurement

P < 0.001

P = 0.002

4

P = 0.01

hCG

a=1368,33 *

b=9,90E-6 *

sFLT

C=0,015 *

AMH

C'=0,002

hCG

a=-167,46 *

b=9,90E-6 *

PLGF

C=-0,003 *

AMH

C'=-0,002*