Mid-trimester maternal serum hCG levels in predicting adverse pregnancy outcome

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Summary

Objective: In this prospective study, we investigated the association between mid-trimester maternal serum human chorionic gonadotropin (ms-hCG) levels and adverse pregnancy outcome in a South-Western Greek population. *Materials and Methods:* 130 healthy Greek women with spontaneous pregnancies were investigated for ms-hCG levels between the 13th and 24th weeks of gestation and followed for adverse pregnancy outcome. hCG levels > 2.0 multiples of the median value for gestation were considered abnormal. Statistical analysis was performed by Pearson's chi-square test. *Results:* Gestational complications developed in a total of 12 of the 130 women studied (9.23%). Elevated ms-hCG levels were detected in a total of 14 of the 130 women studied (10.77%). *Conclusion:* Multiparameter testing of placental function in the mid-trimester (uterine artery Doppler, placental morphology and ms-hCG screening) may allow us to identify women with increased risk of developing severe placental insufficiency and pregnancy complications.

Key words: Maternal serum hCG levels; Adverse pregnancy outcome.

Introduction

Maternal serum human chorionic gonadotropin (ms-hCG) was originally introduced into the screening assay to derive risks for trisomy 21. However, the introduction of high-resolution first trimester ultrasound (US) screening for aneuploidy at 11-13 weeks of gestation has greatly reduced the need for ms-hCG screening in mid-trimester [1].

Pregnancies with unexplained mid-trimester elevation in ms-hCG are at increased risk of pregnancy complications [intrauterine growth restriction (IUGR), intrauterine foetal death (IUFD), preeclampsia (PE)] resulting from placental insufficiency [2-5].

In our prospective study, we investigated the association between mid-trimester ms-hCG levels and adverse pregnancy outcome in a South-Western Greek population.

Material and Methods

Between February 2005 and February 2008, about 130 women with spontaneous pregnancies were referred to the Outpatient Clinic of the Obstetrics and Gynaecology Department of the University of Patras Medical School. All women were investigated for ms-hCG between the 13th and 24th weeks of gestation and followed for adverse pregnancy outcome.

Gestational age was estimated from the last menstrual period for women with regular (21-35 days) menstrual cycles or confirmed from US scan in the first trimester for women with irregular menstrual cycles. Women with multiple pregnancies, diabetes mellitus, pregnancy with chromosomal or structural abnormality, hypertension diagnosed before the 20th week of gestation and history of PE in previous pregnancy were excluded from the study.

All women had a dating US examination at their first visit, followed by a detailed examination at the 18th-22nd week of gestation. The study was approved by the Ethical Committee of the Hospital. Informed consent was obtained from each woman.

Serum samples were collected from all women between the 13th-24th weeks of gestation. All serum samples had been stored at -20°C. hCG levels were measured with immunoradiometric assay using two highly specific monoclonal antibodies for coating of the solid phase and the tracer. The tracer antibody and the coated antibody react simultaneously with the b-hCG present in patient samples or standards. Excess tracer is removed by a washing step and the radioactivity bound to the tube wall is measured in a gamma counter (b-hCG IRMA CT, Radim S.p.A.). Levels of ms-hCG > 2.0 multiples of the median value for gestation (MoM) were considered as abnormal.

As adverse pregnancy outcomes all gestational complications with fetomaternal circulatory disturbances [placental abruption (PA), IUGR, IUFD, PE] were considered.

PA was defined as the separation of the placenta from its site of implantation before delivery of the foetus [6].

IUGR was defined as a birth weight below the 5th percentile for gestational age [7].

IUFD was defined as foetal loss after 24 weeks' gestation.

PE was defined by a blood pressure above 140/90 mmHg after 20 weeks' gestation, proteinuria > 300 mg/24 hours or persistent 30 mg/dl (1+ dipstick) in random urine samples. The term severe preeclampsia is used when blood pressure above 160/110 mmHg is recorded at least six hours apart, and proteinuria of more than 5 g during 24 h occurs [8].

Statistical analyses were performed using the SPSS-12 for Windows. The chi-square test was used to assess the association between categoric variables.

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Results

Serum samples were collected at a median gestation of 19 weeks (range 13-24). The median weight of the women at the time of serum sampling was 71 kg (range 50-105). The median age at estimated delivery date was 30 years (range 17-50).

From the 130 women included in the study, 12 (9.23%) developed gestational complications during the follow-up of their current pregnancy. The demographics of women with gestational complications compared to those without are shown in Table 1.

Table 1. — *Women's demographics (n = 130).*

		Women with complications (n = 12)	Women without complications (n = 118)
Number of pregnancies	1 pregnancy	12 (100%)	100 (84.75%)
	≥ 2 pregnancies	0 (0%)	18 (15.25%)
Age of women	< 25	1 (8.33%)	23 (19.49%)
	25-35	7 (58.33%)	70 (59.32%)
	> 35	4 (33.33%)	25 (21.18%)
Complications in previous pregnancies	No	8 (66.67%)	106 (89.83%)
	Yes	4 (33.33%)	12 (10.17%)
Smoking	No	10 (83.33%)	106 (89.83%)
	Yes	2 (16.67%)	12 (10.17%)

Abnormal ms-hCG levels were detected in a total of 14 of the 130 women studied (10.77%). None of them developed gestational complications in the current pregnancy (Tables 2 and 3).

Table 2. — *Women's demographics (n = 130).*

ms-hCG levels	Women with complications (n = 12)	Women without complications (n = 118)	*p* value
ms-hCG > 2 MoM (n: 14)	0	14	ns
ms-hCG ≤ 2 MoM (n: 116)	12	104	

p value was calculated by the chi-square test.

Table 3. — *ms-hCG levels in women with specific gestational complications in current pregnancy (n = 12).*

ms-hCG levels	PA	IUGR	PE	IUFD
ms-hCG > 2 MoM (n = 14)	0	0	0	0
ms-hCG ≤ 2 MoM (n = 116)	4	6	0	2
Total	4	6	0	2

PA = placental abruption; IUGR = intrauterine growth restriction; PE = preeclampsia; IUFD = intrauterine foetal death.

Discussion

Serum hCG appears early during pregnancy [9]. Its concentration increases gradually by reaching a peak at the end of the first trimester, after which it progressively decreases until delivery [10].

During pregnancy hCG is produced almost exclusively in the placenta, but also is synthesised in the fetal kidney and foetal liver [11]. Most of the hCG in circulation is metabolized by the liver, whereas about 20% is excreted by the kidneys [12].

The aetiology of the increased hCG production by the placenta is not clear. Experimental evidence from trophoblastic cells cultured in vitro showed that hypoxia increases hCG production [13]. Many mechanisms leading to elevations of ms-hCG have been proposed.

Increased ms-hCG concentrations have been related to the presence of placental pathology, such as infarction, ischemic changes, villitis and intervillus thrombosis [3, 14]. Velamentous cord insertion has been described to be associated with elevated mid-trimester ms-hCG concentration [15]. The presence of chromosomally abnormal areas in the placenta known as confined placental mosaicism, has been found to be associated with high mid-trimester ms-hCG levels [16]. All these placental pathologies may be associated with overproduction of hCG [3, 14, 16-18].

Another possible explanation may be inadequate trophoblastic remodelling of the maternal uterine vasculature, with an absence of normal physiologic changes in the spiral arteries leading to placental hypoxia and hCG overproduction [3, 17, 18].

Pregnancies complicated by an unexplained mid-trimester elevation in ms-hCG are at increased risk of perinatal complications resulting from placental insufficiency, including combinations of IUGR, IUFD and PE [2-5, 19, 20]. In our study mid-trimester elevated ms-hCG levels were detected in a total of 14 from the 130 women studied (10.77%). None of them developed pregnancy complications.

In our study the main limitation was the small number of cases with gestational complications. It is possible that ms-hCG would perform better in a high-risk population.

According to the results shown in Table 2, elevated mid-trimester ms-hCG levels alone can not detect pregnant women with increased risk of developing pregnancy complications. However, uterine artery Doppler screening alone is superior to ms-hCG screening for the identification of significant placental pathology leading to PE and IUGR [21-23]. Multiparameter testing of placental function in the mid-trimester (uterine artery Doppler, placental morphology and ms-hCG screening) may allow us to identify women with increased risk of developing severe placental insufficiency and pregnancy complications [23].

Conclusion

Multiparameter testing of placental function in the mid-trimester (uterine artery Doppler, placental morphology and ms-hCG screening) may be useful in identifying women with increased risk of developing severe placental insufficiency and pregnancy complications.

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