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The effect of maternal ABO blood groups and rhesus status on first trimester biochemical markers

İlk trimester biyokimyasal belirteçleri üzerine maternal ABO ve Rh kan gruplarının etkisi

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Abstract

Aim. To explore whether first-trimester levels of pregnancy-associated plasma protein-A (PAPP-A) and serum free ß-human chorionic gonadotrophin (free ß-hCG) vary with maternal blood group and rhesus status and to determine their implications for Down syndrome. **Methods.** Blood samples were collected from all 539 singleton pregnancies undergoing first-trimester screening. Values of maternal serum PAPP-A and ß-hCG were compared among women with different ABO and Rh groups. **Results.** Although ß-hCG MoM values were increased in Rh negative women compared with Rh positive controls, PAPP-A and ß-hCG MoM values did not differ significantly. Compared to other groups, the combined risk was higher in B Rh negative group (25%). **Conclusions.** A larger study is required to establish the validity of this correlation between groups. Corrections in the MoM values of serum analytes used in the first-trimester screening depending on the rhesus and ABO status of the pregnant women may be necessary.

Keywords: Prenatal screening,blood group,rhesus status

Özet

Amaç. İlk trimesterde pregnancy-associated plasma protein-A (PAPP-A) ve serum serbest ß-human chorionic gonadotropin (ß-HCG) düzeylerinin anne kan grubu ve rh durumuyla olan değişimlerinin incelenmesi ve bunların Down sendromuna etkilerinin araştırılması. **Yöntem.** Birinci trimester tarama yapılan 539 tekiz gebeliği olan kadından kan örnekleri toplandıktan sonra maternal serumdaki PAPP-A ve ß-HCG seviyeleri,değişik ABO ve Rh grupları arasında karşılaştırılmıştır. **Bulgular.** Her ne kadar ß-HCG MoM değerleri Rh negatif kadınlarda Rh pozitif kontrol grubuna göre artmışsa da PAPP-A ve ß-HCG MoM değerlerinde anlamlı bir değişim olmamıştır.B Rh negatif grupta diğer gruplara göre kombine risk yüksek bulunmuştur. **Sonuçlar.** Gruplar arası bu bağlantının değerinin kanıtlanması için geniş serili çalışmalara gerek vardır.İlk trimester tarama testlerindeki serum MoM değerlerinin gebe kadının ABO ve Rh durumuna göre düzeltilmesi gereklidir.

Anahtar sözcükler: Prenatal tarama, kan grupları, rh durumu

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Introduction

In the first trimester of pregnancy, the influential screening for trisomi 21 is achieved by a

combination of maternal age, fetal nuchal translucency(NT) thickness and maternal serum free ß-human chorionic gonadotropin (ß-HCG) and pregnancy-associated plasma protein-A (PAPP-A) at 11 to 13+6 weeks of gestation [1]. The detection rate of trisomy 21 by this method is about 90% with a false positive rate of 5%. [2]A range of other factors are known to impact the first-trimester markers,including gravidity,parity,fetal gender,maternal body weight,diabetes mellitus,smoking and assisted reproduction [3,4,5]. Correction for such agents is necessary to prevent indirect individual risk calculations.The first trimester biochemical markers determines the correct risk measurement for Down syndrome. The screening is adjusted with decreased levels of PAPP-A and incresed levels of ß-HCG.

In the literature, there are two studies regarding the variability of second trimester serum biomarkers.Sancken et al. compared these markers in 606 Rh-negative women with 18960 controls and found no significant differences in the distribution of hCG and AFP, but a significant decreased unconjugated estriol values in Rh-negative women [6]. In another recent study Muhcu et al. also found decreased uE3 multiple of median values in Rh-negative women [7].

The aim of this study was to examine whether the level of first trimester maternal serum biochemical markers were related to the mothers ABO and Rh status.

Material and methods

This retrospective cohort study was performed in our institution between October 2006 to August 2008.The information about the patiens and their laboratory findings were collected from their folder records. We followed up 1239 pregnancies and performed first trimester screening routinly. Blood samples were collected from all of pregnant women for ABO and Rh status and first trimester screening. Pregnant women with systemic diseases, *in vitro* fertilization, gestational hypertension, gestational diabetes, or chromosomal and structural abnormalities were excluded. Some of them lost to follow-up and we did not complete recording of their data. Maternal ABO group and Rh status were recorded. No information on the paternal and fetal Rhesus type was available for our groups.

Serum analysis of both PAPP-A and hCG were performed by radio-immunoassay (using the CIS,Medipro,Teufen,Switzerland). The concentration of biochemical markers was determined by trading kits using the DELFİA fluorescent assay system. Information on maternal body weight, maternal gravidity and parity, ethnic origin, smoking habits and diabetes mellitus status was sought at the time of blood sample collection using a standardized questionnaire and the risk was calculated using the Prisca 4.0 software (Typolog Software, GmbH, Munich, Germany).

All pregnant women were examined by ultrasound scan in order to confirm the pregnancy and assess fetal age. Fetal NT and crown-rump length (CRL) were measured using standardized techniques. [6]Ultrasound examinations were performed transabdominally using a curvilinear 5.0 mHz transducer. (Shimadzu 1200,Tokyo, Japan) A first-trimester risk for Down syndrome greater than or equal to 1:270 was used to define the population of women that were screen positive.

Statistical analysis was accomplished on a personal computer by using statistical program for social sciences version 12.0 (SPSS 12.0, demo, SPSS Inc. Chicago, Illinois). Kolmogorov-Smirnov test with Lillefor's correction was used to test whether the variables used in the study were normally distributed. It was found that MoM values of fβ-hCG and PAPP-A were not normally distributed. Log10 transformation was applied to MoM values of fβ-hCG and PAPP-A and it was shown that both the transformed markers had normal distribution using Kolmogorov-Smirnov test. Independent samples t test, chi-square tests and one way ANOVA tests were used where appropriate. Statistical significance level was set at 5%.

Results

After exclusion, the study population comprised 539 singleton pregnancies at 11+0 to 13+6 weeks of gestation of which we followed up until the end of pregnancy. The demographic characteristics and NT,free ß-h CG and PAPP-A MoM values adjusted for maternal weight, cigarette smoking and diabetes mellitus condition of study groups according to their Rh status were determined.

Pregnancies with a maternal Rh-negative blood-group status were identified in 84 patients.The overall prevalance of pregnancies with a maternal Rh-negative blood-group status were 15.58%(84 of 539 cases) A comparison of the first-trimester screening test results between pregnancies with a maternal Rh status and ABO blood group are shown in Table 1.

Table 1. Comparison of the screening test results in the first trimester of pregnancy.

	0(+)	0(-)	A(+)	A(-)	B(+)	B(-)	AB(+)	AB(-)	Total
Risk (+)	11 (8.3%)	6 (24%)	15 (7.2%)	6 (15%)	10 (11%)	4 (25%)	1 (3%)	0	53 (10%)
Risk(-)	121 (91.7%)	19 (76%)	191 (92.8%)	33 (85%)	75 (89%)	12 (75%)	31 (97%)	4 (100%)	486 (90%)
Total	132	25	206	39	85	16	32	4	539

Screen positive rate after maternal serum biochemistry were 16/68 (23%) and 37/418 (9%) for Rh-negative blood group and Rh-positive blood group,respectively. Table 2 summarizes the median MoMs for PAPP-A and free ß-hCG for each blood group as well as the log10 MoM , standart deviations and p statistics.

Table 2. The median MoMs for PAPP-A and β-hCG for each blood group as well as the log10 MoM,standart deviations and p statistics.

		Free β-hCG		PAPP-A	
	n	Median	Mean ± SD*	Median	Mean ± SD**
		MoM	Log 10 MoM	MoM	Log 10 MoM
0	157	-0.061	-0.071 ± 0,290	-0.081	-0.077 ± 0.259
0 positive	131	-0.071	-0.083 ± 0.303	-0.081	-0.069 ± 0.245
0 negative	25	-0.032	-0.021 ± 0.217	-0.137	-0.119 ± 0.329
A	246	-0.071	-0.051 ± 0.269	-0.027	-0.035 ± 0.234
A positive	207	-0.076	-0.056 ± 0.263	-0.036	-0.043 ± 0.235
A negative	39	-0.056	-0.017 ± 0.302	-0.004	-0.011 ± 0.227
B	101	-0.097	-0.054 ± 0.286	-0.022	-0.037 ± 0.241
B positive	85	-0.102	-0.073 ± 0.281	-0.022	-0.039 ± 0.244
B negative	16	-0.076	0.04 ± 0.297	-0.092	-0.026 ± 0.230
AB	36	-0.108	-0.103 ± 0.303	0.008	0.038 ± 0.269
AB positive	32	-0.108	-0.083 ± 0.303	0.008	0.032 ± 0.269
AB negative	4	-0.155	-0.264 ± 0.298	0.048	0.089 ± 0.323

*P=0.785; one way ANOVA test. **P=0.348; one way ANOVA test.

There were no statistically significant differences between groups (p>0.05). ß-hCG and PAPP-A MoMs in the different blood type groups analysed and the medians, inter-quartile range and maximum and minimum after the removal of extreme and outlier values are depicted graphically in figure 1 and 2.

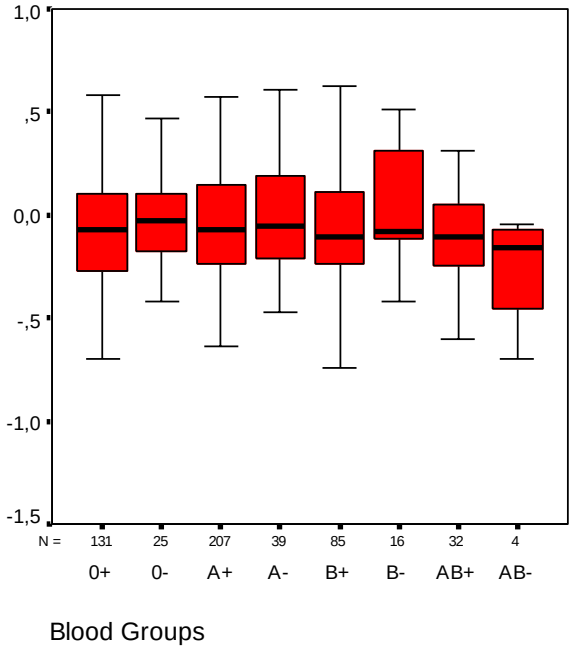

Figure 1. Median, interquartile range and minimum-maximum values of free βhCG MoMs in different blood groups are depicted.

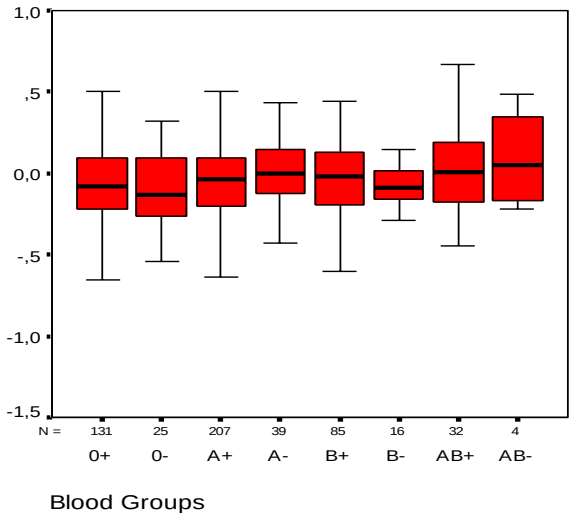

Figure 2. Median, interquartile range and minimum-maximum values of PAPP-A MoMs in different blood groups are depicted.

Discussion

The measurement of fetal NT and maternal serum levels of PAPP-A and free ß-hCG is an accepted screening system for chromosomal abnormalities, which has an 80-90% detection rate with a 5% false positive rate [2, 7]. On the basis of maternal age, nuchal-translucency and biochemical values, the patient-specific risks must to be reported for clinical decision making.

In our study, we concentrated on measurements of ß-hCG and PAPP-A in the serum of pregnants with ABO blood group and Rh status and compared the combined screening results according to them. Although ß-hCG MoM values were increased in Rh-negative women compared with Rh-positive controls. PAPP-A and ß-hCG MoM values did not

differ significantly. Rhesus opposition might be the cause for the increased maternal serum levels of ß-hCG. And also the experimental data allows us to suppose that PAPP-A serves to prevent the recognition of the fetus by the maternal immune system and to suppress locally the host's immune response. The placenta is essentially a fetal organ and it secretes hCG . Because of the aim of our study and to establish the value of maternal blood groups to the screening results, we checked the blood groups of babies but did not take these values into consideration. Cowans et al. [8] found that B Rh-positive blood group had a significantly higher level of PAPP-A. In our series the combined risk was higher in B Rh-negative group (25%) according to the other groups.

There are only a few studies in the literature, comparing Rh status and biochemical screening tests for Down syndrome. But there is only one study about ABO groups and screening test results [8]. One group found that rhesus negative mothers had a decreased uE3 in the second trimester [7]. In another study PAPP-A was significantly higher at 34 weeks in women who were rhesus negative [9]. Our results generally show little difference. The results of our study suggest that corrections in the MoM values of serum analytes used in the first-trimester screening depending on the rhesus and ABO status of the pregnant women may be necessary. An increased maternal serum free beta hCG MoM value leads to a falsely increased risk value in first trimester screening test [10]. In our study, false positive screening rates were 16/68(23%), 37/418(8.8%), 21/245(8.5%), 14/101(13%), 1/36(2.7%) and 17/157(10%) in Rh-negative, Rh-positive, A, B, AB and O blood groups respectively. There were no statistically significant differences between two groups($p>0.05$).Using a level of significance of 5%,the B rhesus negative blood group had a higher level of PAPP-A and O rhesus negative blood group had a higher level of beta hCG.It is interesting to note that the entire B and O group is also approaching a significant increase in PAPP-A and beta hCG, although all others tested ,did not have significantly different marker levels compared to the whole control group. Despite the fact that significantly higher proportion of Rh negative women were screen positive, the MOM values for the serum markers were not different among women with different blood types. There was no age distribution difference between Rh negative and Rh positive women and no other disease or situation to explain this dilemma.

In conclusion, further studies on larger populations are required to determine if adjustment for rhesus and ABO groups should be recommended and corrections would be appropriate when screening for chromosomal anomalies in the first trimester.

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