Second trimester serum alpha-fetoprotein level is a significant positive predictor for intrauterine growth restriction in pregnant women with hyperemesis gravidarum

Abstract

Objective: The aim of this study was to determine the association between three parameters of second trimester serum screening and preterm labor and intrauterine growth restriction (IUGR) in patients with hyperemesis gravidarum (HG).

Material and Methods: A prospective study on 429 pregnancies with HG was designed to determine the association between alpha-fetoprotein (AFP), unconjugated estriol (uE3), human chorionic gonadotropin (HCG) and pregnancy prognosis in terms of preterm labor, IUGR and birth weight.

Results: In our study group the mean age of patients was 25.4±3.8 years. Mean birth weight was 3180±555 g. Mean AFP, uE3, hCG levels in the study group were 1.44±0.65 MoM, 0.91±0.38 MoM, 1.09±0.64 MoM, respectively. Twenty nine (6.8%) patients delivered before 37 weeks of gestation and 52 (12.1%) patients developed IUGR. Mean MoM values of AFP among patients with preterm labor, IUGR and normal delivery were 1.35±0.45, 1.97±0.81, 1.34±0.58 MoM, respectively (p<0.001). Mean MoM values of hCG among patients with preterm labor, IUGR and normal delivery were 1.46±0.90, 1.35±0.89, 1±0.5 MoM respectively (p<0.001). Mean MoM values of uE3 among patients with preterm labor, IUGR and normal delivery were 0.75±0.25, 0.80±0.30, 0.95±0.40 MoM, respectively (p=0.003). Odds ratio of AFP>1.55 was 3.73 (95% CI, 1.99-6.98, p<0.001) for IUGR after adjustment for HCG.

Conclusion: Our study suggests that AFP levels of the second trimester screening test higher than 1.55 MoM is significantly associated with IUGR in hyperemesis gravidarum. The second trimester screening test can predict poor outcome in HG.

Key words: Second trimester screening, alpha-fetoprotein, intrauterine growth restriction, preterm labor, hyperemesis gravidarum

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Bulgular: Çalışma grubunda orttalama yaş 25.4±3.8 idi. Ortalama doğum ağırlığı 3180±555 g olarak hesaplandı. Ortalama AFP, uE3, HCG düzeyleri sırası ile orttalamalı 1.44±0.65 MoM, 0.91±0.38 MoM, 1.09±0.64 MoM idi. 29 (%6.8) hastada 37 hafta öncesine доğdu ve 52 (%12.1) hastada gelişme geriliği mevcuttu. Preterm eylem, IUGR ve normal doğum yapan grupta orttalamalı AFP değerleri sırası ile 1.35±0.45, 1.97±0.81, 1.34±0.58 MoM idi (p<0.001). Preterm eylem, IUGR ve normal doğum yapan grupta orttalamalı HCG değerleri sırası ile 1.46±0.90, 1.35±0.89, 1±0.5 MoM idi (p<0.001). Preterm eylem, IUGR ve normal doğum yapan grupta orttalamalı HCG değerleri sırası ile 0.75±0.25, 0.80±0.30, 0.95±0.40 MoM idi (p=0.003). IUGR için HCG ye göre düzeltmiş AFP>1.55 için odds oranı 3.73 (%95 CI, 1.99-6.98, p<0.001) olarak saptandı.

Sonuç: Çalışmamızda göre 1.55 in üstündeki AFP düzeyleri hiperemesis gravidarum hastalarında IUGR için risk faktördür. İkinci trimester serum taraması HG de kötü prognozu öngörebilir.

Anahtar kelimeler: İkinci trimester tarama, alfa feto protein, intrauterin gelişme geriliği, preterm doğum, hyperemesis gravidarum

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Amac: Bu çalışmanın amacı hiperemesis gravidarum olan hastaların ikinci trimester taramasında kullanılan üç parametre ile preterm eylem, intrauterin gelişme geriliği arasındaki ilişkiyi belirlemek.

Gereç ve Yöntemler: Bu prospektif çalışma hiperemesis gravidarum olan 429 gebe üzerinde alfafetoprotein (AFP), unkonjuge estriol (uE3), human koryonik gonadotropin (HCG) ile preterm eylem, intrauterin gelişme geriliği arasındaki ilişkileri arastırmak amaci ile düz saydı.

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Content

Hyperemesis gravidarum is associated with high hCG levels. This study investigated the association between parameters of the second trimester screening test and pregnancy outcome in selected group of pregnancies. A high hCG level was not found to be a predictor for poor outcome of pregnancy, while the AFP level was associated with intrauterine growth restriction, with a cut off value lower than the reported value in normal pregnancies.

Introduction

A small percentage of women experience a severe form of nausea and vomiting known as hyperemesis gravidarum. Estimates of the incidence of hyperemesis vary from 0.3-1.5% of all live births. Diagnosis is subjective, but the condition is usually described as intractable vomiting leading to fluid, electrolyte and acid base imbalance, nutritional deficiency and weight loss (1). Hyperemesis gravidarum (HG) is the most common cause of hospitalization in the first half of pregnancy and the second most common cause of antenatal hospitalization during pregnancy. Extreme weight loss is common among women with HG, suggesting that HG is a form of prolonged starvation in pregnancy and that the long-term effects of this condition on women and their offspring warrant further investigation (2).

Measurement of maternal serum alpha fetoprotein (AFP), human chorionic gonadotropin (HCG), and unconjugated estradiol (uE3) at the beginning of the second trimester of pregnancy is a well-established screening test for trisomies. Association between second trimester screening test parameters and several pregnancy complications have been studied in unselected study populations. Previous studies have described the association of abnormal levels of maternal serum AFP and hCG with a variety of problems and complications of pregnancy, such as preterm delivery, fetal growth retardation, fetal death and severe hypertensive disorders in pregnancy (3-5).

Statistical analysis

Collected data was entered into SPSS version 11. For group comparisons, analysis of variance and posthoc Tukey test was used. P value smaller than 0.05 was accepted as statistically significant. Binary logistic regression was used to calculate odds ratio. Correlation analysis was used to calculate the degree of associations and ROC analysis was performed for cut off calculation. Regression analysis was used to determine associations.

Result

Means of AFP, hCG, uE3 among groups of complicated and uncomplicated pregnancies and groups divided according to birth weight percentiles:

In our study group mean age of patients was 25.4±3.8 years. Mean birth weight was 3180±555 g Mean AFP, uE3, hCG levels in the study group were 1.44±0.65 MoM, 0.91±0.38 MoM, 1.09±0.64 MoM respectively. Twenty nine (6.8%) patients delivered before 37 weeks of gestation and fifty two (12.1%) patients developed IUGR. Mean MoM values of AFP level among patients with preterm labor, IUGR and normal deliveries were 1.35±0.45, 1.97±0.81, 1.34±0.58 MoM respectively (p<0.001). Mean MoM values of hCG level among patients with preterm labor, IUGR and normal deliveries were 1.46±0.90, 1.35±0.89, 1±0.5 MoM respectively (p<0.001).
Mean MoM values of uE3 level among patients with preterm labor, IUGR and normal deliveries were 0.75±0.25, 0.80±0.30, 0.95±0.40 MoM, respectively (p=0.003). Mean ages were similar among groups (p=0.189). Mean values between pregnancy complications were shown in Table 1.

Mean MoM values of AFP levels among patients with birth weights below 3rd (n=5, 1.2%), 3-5th (n=12, 2.8%) and 5-10th (n=35, 8.1%) percentiles of that gestational age were 2.66±0.25, 1.98±0.23, 1.83±0.91 MoM, respectively (p<0.001).

Mean MoM values of hCG levels among patients with birth weights below 3rd, 3-5th and 5-10th percentiles of that gestational age were 3.0, 0.92±0.84, 1.20±0.61 MoM, respectively (p<0.001). Mean MoM values of uE3 among patients with birth weights below 3rd, 3-5th and 5-10th percentiles of that gestational age were 0.5, 0.86±0.22, 0.82±0.32 MoM, respectively (p=0.023). Highest AFP (p<0.001, p=0.012) and hCG (p<0.001) levels were seen in patients with newborn birth weights below the 3rd percentile. Mean ages were similar among different birth weight percentile groups (p=0.141).

Correlations

- AFP level was positively correlated with IUGR (r=0.351, p<0.001), negatively correlated with birth weight (r=-0.222, p<0.001). uE3 level was positively correlated with birth weight (r=0.245, p<0.001) and negatively correlated with IUGR (r=-0.123, p=0.023) and PL (r=-0.122, p=0.024). hCG level was negatively correlated with birth weight (r=-0.199, p<0.001) and positively correlated with IUGR (r=0.167, p=0.002) and PL (r=0.175, p=0.001).

Associations

Regression analysis revealed that uE3, hCG adjusted AFP; AFP, hCG adjusted uE3; uE3, AFP adjusted hCG were significantly associated with birth weight and IUGR (p<0.001, p<0.001, p<0.05, respectively, Figure 1). uE3, AFP adjusted hCG was significantly associated with PL (p<0.05).

Hyperemesis gravidarum was first diagnosed at different gestational ages in the study group: at 9th week (n=22, 5%), 10th week (n=43, 10%), 11th week (n=51, 12%), 12th week (n=61, 14%) and 13th week (n=252, 59%).

Gestational age of hyperemesis gravidarum diagnosis was positively correlated with birth weight (r=0.288, p=0.001), negatively correlated with PL (r=-0.189, p=0.001) and IUGR (r=-0.181, p=0.001).

ROC analysis

ROC analysis revealed that the AFP level is a significant predictor for IUGR (Area under curve 0.716, p<0.001, Figure 2). Cut off value was 1.55 MoM for the AFP level to predict IUGR with 66% sensitivity and 69% specificity. uE3 and hCG levels were not found to be significant predictors for either preterm labor or IUGR in ROC analysis (p>0.005). Odds ratio of AFP>1.55 was 3.73 (95% CI, 1.99-6.98, p<0.001) for IUGR after adjustment for hCG.

Discussion

In our study higher AFP levels were found to be significantly associated with increased IUGR while higher hCG levels were shown to be associated with increased preterm labor rates, higher uE3 levels were associated with both decreased preterm labor and IUGR rates. We expected to observe an association between pregnancy complications caused by hyperemesis and increased hCG levels in HG. Association between hCG and uE3 levels with preterm labor and IUGR were shown in regression analysis, however they are not found to be significant predictors for IUGR or preterm labor in ROC analysis. These results led us to hypothesize that the second trimester screening test can give more information about pregnancy outcome in HG, but only the AFP was useful as a test to predict poor outcome. Patients
and neural tube defect abnormalities but also for the detection of high-risk pregnancies (16).

Recently published data has shown that serum unconjugated estriol, AFP or hCG values in triple test results may be associated with development of oligohydramnios, gestational diabetes and macrosomia in women with healthy and normal appearing fetuses (17).

Despite the increase in prematurity and low birth weight, unexplained raised levels of AFP were not associated with an increase in perinatal mortality (18). A retrospective trial found that increased antenatal surveillance for women with unexplained elevated AFP did not provide any benefit for detection of adverse events (19). Women with elevated second-trimester hCG values have been reported to have increased risks for preeclampsia, IUGR, small for gestational age (SGA) infants, preterm delivery, spontaneous abortion, stillbirth and placental abnormalities (9, 12, 20-22). However, Ashour et al. (23) suggested that the utility of hCG level as a screening test for preeclampsia was limited. Besides, the relationship between obstetric complications and elevated hCG levels was not confirmed in two other studies (10, 24). In another study, preterm delivery, preeclampsia and large for gestational age were found to be associated with only hCG levels of 3 MoM and the authors concluded that increased fetal surveillance is not warranted with lower values (25). Consistent with our results, a low uE3 level was suggested as an independent risk factor for adverse pregnancy outcome and is particularly associated with preeclampsia, in conjunction with IUGR, SGA, oligohydramnios, preterm delivery and stillbirth (9, 12, 26). In a meta-analysis by Morris et al. Down’s serum screening analytes were found to have low predictive accuracy for pre-eclampsia and small for gestational age. The study concluded that they may be a useful means of risk assessment or of use in prediction when combined with other tests (27). This study was conducted specifically on patients with HG, and in our literature review we have not encountered a similar study. The relatively small sample size is a limitation of this study.

Our study suggests that the AFP level of the second trimester screening test of higher than 1.55 MoM is significantly associated with IUGR in HG. The highest hCG and AFP levels were found to be associated with only hCG levels of 3 MoM and the authors concluded that increased fetal surveillance is not warranted with lower values (25). Consistent with our results, a low uE3 level was suggested as an independent risk factor for adverse pregnancy outcome and is particularly associated with preeclampsia, in conjunction with IUGR, SGA, oligohydramnios, preterm delivery and stillbirth (9, 12, 26). In a meta-analysis by Morris et al. Down’s serum screening analytes were found to have low predictive accuracy for pre-eclampsia and small for gestational age. The study concluded that they may be a useful means of risk assessment or of use in prediction when combined with other tests (27). This study was conducted specifically on patients with HG, and in our literature review we have not encountered a similar study. The relatively small sample size is a limitation of this study.

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Conflict of interest
No conflict of interest was declared by the authors.

References


