Date: 20 Nov 2017
Sources: Medline, Embase.

Pregnancy Associated Plasma Protein A (PAPP-A) and Fetal Growth

Evidence Summary:

A low level of PAPP-A (defined as <0.415 MoM) is the most common first-trimester marker and is associated with an increased risk of fetal growth restriction, placental abruption and stillbirth. As a screening test however PAPP-A lacks the individual sensitivity or positive predictive value to act as a sole test.

Narayan, H.(2015). Other fetal conditions. In Compendium for the Antenatal Care of High-Risk Pregnancies. Oxford, UK: Oxford University Press. Retrieved 21 Nov. 2017, from
http://oxfordmedicine.com/view/10.1093/med/9780199673643.001.0001/med-9780199673643-chapter-28.

1. Prediction of adverse pregnancy outcomes by extreme values of first trimester screening markers.

Author(s): Gomes, Marina S; Carlos-Alves, Mariana; Trocado, Vera; Arteiro, Diana; Pinheiro, Paula

Abstract:BACKGROUND To determine the association between extreme values of first trimester markers and adverse pregnancy outcomes.METHODS A retrospective cohort study of 916 women who underwent first-trimester combined screening during 2015 was performed. Extreme values of NT, pregnancy-associated plasma protein-A (PAPP-A) and free β-hCG, and their association with adverse pregnancy outcomes were analyzed.RESULTS Low PAPP-A (<10th percentile) was associated with an increased risk for preeclampsia (adjusted odds ratio (AOR) 4.13), fetal growth restriction (AOR 3.94) and abruptio placentae (AOR 52.63). Abnormally low or high free β-hCG, high PAPP-A or increased NT was not associated with an increased risk for adverse outcomes.DISCUSSION PAPP-A <10th percentile could be associated with an increased risk for adverse outcomes. However, the majority of patients with these events do not have abnormal PAPP-A and few patients with PAPP-A <10th percentile will have an adverse outcome.

2. Pregnancy-Associated Plasma Protein A Levels in Late First Trimester Pregnancies with Small-for-Gestational Age Neonates: A Prospective Case-Control Study.

Author(s): Agarwal, Rachna; Kumari, Radhika; Mehndiratta, Mohit; Radhakrishnan, Gita; Faridi, M M A; Chandra, Nilesh

Available at The Journal of Obstetrics and Gynecology of India - from SpringerLink

Abstract:OBJECTIVEWe aimed to investigate the association of pregnancy associated plasma protein A (PAPP-A) levels in late first trimester with small for gestational age (SGA) neonates and adverse pregnancy outcomes in a low-income setting.METHODSThe inclusion criteria were late first trimester (11-13 + 6 weeks) women with singleton and non-anomalous pregnancy. Enrolled participants were sampled for PAPP-A and prospectively followed up for delivery outcome and antenatal complications. A multiple of median (MoM) was calculated and statistically compared between groups.RESULTSOut of total 284 subjects, 14.54% delivered SGA babies and formed cases (Group A), 66.5% delivered appropriate for gestational age (AGA) neonates with uneventful antenatal period (controls, Group B), and 19.3% were AGA group with adverse pregnancy complications (Group C). The late first trimester median PAPP-A MoM was significantly lower (0.61) in Group A compared to Group B (1.47). Using receiver operating characteristic (ROC) curve for PAPP-A MoM, optimal cutoff value was found at 0.45 MoM, with positive predictive value of 56.2%, specificity of 92.6% and sensitivity of 45%. The median interquartile range (IQR) of PAPP-A MoM value in Group C in comparison with Group B was significantly lower except for abruption. At PAPP-A MoM cutoff value <1, <0.8, <0.6 and <0.4, the odds ratio for adverse pregnancy outcome was 8.30, 7.29, 10.97 and 10.60, respectively, indicating an inverse relationship.CONCLUSION With 0.45 MoM cutoff of PAPP-A, the detection rate, specificity and positive predictive value for SGA were 45, 92.6 and 56.2%,

respectively. As PAPP-A MoM values decreased, the odds ratio of having adverse pregnancy outcomes increased.

Database: Medline

3. Use of prokineticin-1 (PROK1), pregnancy-associated plasma protein A (PAPP-A) and PROK1/PAPP-A ratio to predict adverse pregnancy outcomes in the first trimester: a prospective study.

Author(s): Inan, Cihan; Varol, Fusun Gulizar; Erzincan, Selen Gursoy; Uzun, Isil; Sutcu, Havva; Sayin, N Cenk

Source: The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians; Jul 2017 ; p. 1-8

Publication Date: Jul 2017

Publication Type(s): Journal Article

PubMedID: 28675948

Abstract:INTRODUCTIONTo compare the predictive effectiveness levels of prokineticin-1 (PROK1), pregnancy-associated plasma protein A (PAPP-A) and the PROK1/PAPP-A ratio in the first trimester for preeclampsia (PE), foetal growth restriction (FGR), gestational diabetes mellitus (GDM) and spontaneous preterm birth (SPB).MATERIALS AND METHODSA total of randomly selected 162 pregnant women were included. Peripheral blood samples were obtained between 110/7 and 136/7 gestational weeks (GWs). All women were followed throughout the pregnancy and classified into five groups as having PE, FGR, GDM, SPB and uncomplicated pregnancies. The cut-off levels of the markers were identified to predict adverse outcomes.RESULTSPROK1 predicted PE with 83.3% sensitivity, 85.7% specificity at a value of >293.4 pg/mL; at a value of >260.2 pg/mL, PROK1 predicted FGR with 85.7% sensitivity, 72.5% specificity in the first trimester. The area under receiver operating characteristic (ROC) curve of PAPP-A was lower than that of PROK1 and PROK1/PAPP-A in differentiating PE and FGR from the uncomplicated group (p < .001). PROK1 levels and the PROK1/PAPP-A ratios in the SPB and GDM groups were lower than in the uncomplicated group (p < .01).CONCLUSIONS Elevated PROK1 in the first trimester is a more effective marker than PAPP-A in the prediction of PE and FGR. Lower PROK1 levels are associated with the development of SPB and GDM.

Database: Medline

4. Association of maternal serum PAPP-A levels, nuchal translucency and crown-rump length in first trimester with adverse pregnancy outcomes: retrospective cohort study.

Author(s): Bilagi, Ashwini; Burke, Danielle L; Riley, Richard D; Mills, Ian; Kilby, Mark D; Katie Morris, R

Available at Prenatal diagnosis - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVEAre first trimester serum pregnancy-associated plasma protein-A (PAPP-A), nuchal translucency (NT) and crown-rump length (CRL) prognostic factors for adverse pregnancy outcomes?METHODRetrospective cohort, women, singleton pregnancies (UK 2011-2015). Unadjusted and multivariable logistic regression.OUTCOMESsmall for gestational age (SGA), pre-eclampsia (PE), preterm birth (PTB), miscarriage, stillbirth, perinatal mortality and neonatal death (NND).RESULTSA total of 12 592 pregnancies: 852 (6.8%) PTB, 352 (2.8%) PE, 1824 (14.5%) SGA, 73 (0.6%) miscarriages, 37(0.3%) stillbirths, 73 perinatal deaths (0.6%) and 38 (0.30%) NND. Multivariable analysis: lower odds of SGA [adjusted odds ratio (aOR) 0.88 (95% CI 0.85,0.91)], PTB [0.92 (95%CI 0.88,0.97)], PE [0.91 (95% CI 0.85,0.97)] and stillbirth [0.71 (95% CI 0.52,0.98)] as PAPP-A increases. Lower odds of SGA [aOR 0.79 (95% CI 0.70,0.89)] but higher odds of miscarriage [aOR 1.75 95% CI (1.12,2.72)] as NT increases, and lower odds of stillbirth as CRL increases [aOR 0.94 95% CI (0.89,0.99)]. Multivariable analysis of three factors together demonstrated strong associations: a) PAPP-A, NT, CRL and SGA, b) PAPP-A and PTB, c) PAPP-A, CRL and PE, d) NT and miscarriage.CONCLUSIONSPregnancy-associated plasma protein-A, NT and CRL are independent prognostic factors for adverse pregnancy outcomes, particularly PAPP-A and SGA with lower PAPP-A associated with increased risk. © 2017 John Wiley & Sons, Ltd.

Database: Medline

5. Maternal serum placental growth factor and pregnancy-associated plasma protein A measured in the first trimester as parameters of subsequent pre-eclampsia and small-for-gestational-age infants: A prospective observational study.

Author(s): Sung, Kyung Uk; Roh, Jeong A; Eoh, Kyung Jin; Kim, Eui Hyeok

Available at Obstetrics & Gynecology Science - from Europe PubMed Central - Open Access

Abstract:OBJECTIVETo examine the first-trimester maternal serum placental growth factor (PlGF) and pregnancy-associated plasma protein A (PAPP-A) levels in pregnancies associated with pre-eclampsia (PE) or small-for-gestational-age (SGA) infants, and determine the predictive accuracy of PlGF and of PAPP-A for either PE or SGA infants.METHODSThis prospective, observational study included 175 pregnant women, and of these women, due to participant withdrawal or loss to follow-up, delivery data were collected from the medical records of 155 women, including 4 who had twin pregnancies. The women's maternal history was recorded, and the PlGF and PAPP-A levels at 11 to 13 gestational weeks were measured. During the second trimester, the maternal uterine artery's systolic/diastolic ratio was measured. Multiples of the median (MoM) of PlGF and PAPP-A were determined, and the associations of these values with the risk factors of SGA and PE were evaluated.

Logistic regression analysis was used to determine whether PlGF and PAPP-A are useful markers for predicting SGA infants.RESULTSThe PAPP-A MoM level was significantly lower in women with advanced maternal age, multipara women, and women with gestational diabetes than in their counterparts. The PlGF and PAPP-A MoM levels were higher in women with a twin pregnancy than in those with a singleton pregnancy. There was a significant relationship between the maternal serum PAPP-A MoM level in the first trimester and the uterine artery systolic/diastolic ratio in the second trimester. Results of logistic regression analysis showed that low PlGF and PAPP-A MoM levels were predictors of SGA infants (odds ratio, 0.143; 95% confidence interval, 0.025 to 0.806; odds ratio, 0.191; 95% confidence interval, 0.051 to 0.718, respectively).CONCLUSION PlGF and PAPP-A are potentially useful as first-trimester markers for SGA infants and some hypertensive disorders of pregnancy.

Database: Medline

Abstract:OBJECTIVESTo determine association, and predictive ability, of first trimester maternal serum pregnancy associated plasma protein A (PAPP-A) with adverse pregnancy outcomes.METHODSearches of Medline, Embase and CINAHL (inception September 2015) for studies including pregnant women with first trimester PAPP-A and assessment of pregnancy outcomes. Study characteristics, quality and results extracted. Meta-analysis of odds ratios (ORs), and likelihood ratios (LRs) and 95% confidence intervals (CI).RESULTSThirty-two studies including 175 240 pregnancies. PAPP-A <5th centile had a moderate association with: birth weight <10th centile OR 2.08 (95% CI 1.89-2.29), <5th centile OR 2.83 (95% CI 2.52-3.18); pre-eclampsia OR 1.94 (95% CI 1.63-2.30), preterm birth <37 weeks OR 2.09 (95% CI 1.87-2.33), and composite adverse outcome OR 3.31 (95% CI 1.80-5.11). The predictive ability was poor: Birth weight <10th centile LR + ve 1.96 (95% CI 1.58-2.43), LR-ve 0.93 (95% CI 0.89-0.98); birth weight <5th centile LR + ve 2.65 (95% CI 2.35-2.99), LR-ve 0.85 (95% CI 0.74-0.98); PTB <37 weeks LR + ve 1.84 (95% CI 1.41-2.39), LR-ve 0.92 (95% CI 0.87-0.98).CONCLUSIONS First trimester low maternal serum PAPP-A is associated with adverse pregnancy outcome, but predictive values are poor. Further work should address PAPP-A as a continuous variable in combination with other prognostic markers as a prediction model. © 2016 John Wiley & Sons, Ltd.

Database: Medline

7. Impact of maternal serum levels of Visfatin, AFP, PAPP-A, sFlt-1 and PlGF at 11-13 weeks gestation on small for gestational age births.

Author(s): Birdir, Cahit; Fryze, Janina; Frölich, Stefanie; Schmidt, Markus; Köninger, Angela; Kimmig, Rainer; Schmidt, Börge; Gellhaus, Alexandra

Abstract:OBJECTIVEInvestigating potential value of maternal serum Visfatin, sFlt-1, PlGF, AFP, PAPP-A levels at first trimester for prediction of small for gestational age (SGA) at birth.METHODSMeasurements were performed in 20 SGA and 65 control cases. Logistic regression analysis adjusted for age and weeks of pregnancy at data collection was performed to estimate odds ratios (OR), 95% confidence intervals (95% CI) and p values separately for each potential predictor. A multiple regression model was used to assess the impact of all the promising predictors adjusted for each other. Receiver operating characteristic (ROC) analysis was used to indicate the ability to discriminate between SGA cases and controls.RESULTSThere was an association of serum PlGF levels (OR 0.53 per interquartile range [IQR] increase in PlGF; 95% CI 0.24-1.16), sFlt-1/PlGF ratio (OR 1.42 per IQR increase in sFlt-1/PlGF; 95% CI 1.03-1.96), serum Visfatin levels (OR 0.31 per IQR increase in Visfatin; 95% CI 0.10-0.95) and smoking (OR 4.24; 95% CI 1.10-16.37) with SGA at birth.CONCLUSIONS Associations between SGA and lower PlGF, Visfatin levels as well as increased sFlt-1/PlGF ratio and smoking status were detected which may contribute to predict SGA.

Database: Medline

8. Low maternal pregnancy-associated plasma protein A during the first trimester of pregnancy and pregnancy outcomes.

Author(s): Kaijomaa, Marja; Rahkonen, Leena; Ulander, Veli-Matti; Hämäläinen, Esa; Alfthan, Henrik; Markkanen, Helene; Heinonen, Seppo; Stefanovic, Vedran

Available at International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVETo assess the association between pregnancy-associated placental protein A (PAPP-A) levels in the first trimester of pregnancy and adverse pregnancy outcomes.METHODA retrospective study included data from a group of patients in the first trimester of pregnancy with PAPP-A levels below 0.3 multiples of median who attended the Helsinki University Hospital, Finland, between January 1, 2009 and December 31, 2012; an age-matched control group of patients with PAPP-A levels 0.9-1.1 multiples of median was also enrolled. The incidences of adverse pregnancy outcomes in the two groups were compared.RESULTSThere were 961 patients included in each of the groups. Significantly increased risks of aneuploidies (odds ratio [OR] 116.0; 95% confidence interval [CI] 16.2-836.6) and spontaneous abortion (OR 7.7; 95% CI 2.7-22.0) were observed among

patients with low PAPP-A (both P<0.001). Preterm delivery (OR 2.5, 95% CI 1.8-3.5), pre-eclampsia (OR 10.9, 95% CI 4.3-27.6), and small for gestational age neonates (OR 4.9, 95% CI 3.2-7.5) were also observed more frequently among patients with low PAPP-A (all P<0.001). There were 9 (0.9%) stillbirths recorded among patients with low PAPP-A and none recorded in the control group.CONCLUSIONLow PAPP-A was associated with adverse pregnancy outcomes and aneuploidy. These risks should be considered when planning follow-up for patients with low PAPP-A pregnancies.

Database: Medline

9. Low versus normal first-trimester maternal PAPP-A levels and pregnancy outcome

Author(s): Kaijomaa M.; Rahkonen L.; Ulander V.-M.; Hamalainen E.; Alfthan H.; Markkanen H.; Heinonen S.; Stefanovic V.

Abstract: Introduction: Pregnancy-associated placental protein A (PAPP-A) is a glycoprotein produced by the placental syncytiotrophoblasts, and it is detectable in the maternal circulation from early pregnancy. PAPP-A is responsible for the cleavage of insulin-like growth factor binding protein-4 (IGFBP-4) from insulin-like growth factor (IGF), and thus it contributes to the regulation of fetal growth. PAPP-A is used as part of the first-trimester combined screening (FTS) for Down's syndrome but has also been studied as an independent marker for adverse pregnancy outcome. The risks of aneuploidy, hypertensive disorders, spontaneous abortion, small for gestational age births, prematurity and stillbirths have been shown to increase with decreasing PAPP-A levels. Still, the value of PAPP-A as an individual marker is debatable, and different cut-off values for low PAPP-A have been used in previous studies. The objective of our study was to estimate the clinical significance of low PAPP-A (50.3 MoM) in our routinely screened population in the Helsinki University District area. Materials and methods: A cohort of 961 pregnant women with low PAPP-A levels (50.3 MoM) and 961 age-matched women with normal PAPP-A levels (0.9-1.1 MoM) were followed over a four year period (2009-2012).The reference group selection was based on the assumption that the exposure related to decreased PAPP-A production would be absent in women with PAPP-A level close to 1.0 MoM (0.9 - 1.1 MoM). The FTS was performed according to the guidelines of the Finnish Ministry of Social Affairs and Health and the NT measurement was performed according to the Fetal Medicine Foundation protocol. Patients were considered screen positive with NT >=3mm or a FTS risk >=1/250, and genetic counseling with chromosomal analysis was offered in these pregnancies. Pregnancyinduced hypertension (PIH) was identified as a normal blood pressure in the early pregnancy and a measurement >=145/90mmHg at least twice during pregnancy. Increased blood pressure with proteinuria 4300 mg/ 24 h was identified as preeclampsia. A spontaneous abortion was identified as a loss of the pregnancy or fetal viability before completed 22 pregnancy weeks, and preterm delivery as any delivery before completed 37 pregnancy weeks. Fetal death before delivery and after completed 22 pregnancy weeks was identified as stillbirth (SB), and small for gestational age (SGA) was identified as a gender-specific birth weight less than -2 SD. The prevalence of adverse pregnancy outcomes was determined. This included aneuploidies, fetal structural abnormalities, hypertensive disorders of pregnancy, spontaneous abortion, PTD, SB and SGA births. Clinical cases and summary results: Compared to the reference, the overall incidence of pregnancy failure (OR 17.8, p <0.001) was increased in the group with low PAPP-A. In the study group, the risk of aneuploidies (OR 116.1) and spontaneous abortion (OR7.7) was significantly higher (p<0.001), but no difference was detected in the incidence of major structural abnormalities (p=0.738). The incidences of preterm delivery (OR 2.5), PIH (OR 1.9), preeclampsia (OR 10.9) and small for gestational age births (OR 4.9) were all significantly higher in the group with low PAPP-A.

Nine cases (0.9 %) of stillbirth occurred in pregnancies with low PAPP-A whereas there were none in the reference group. Conclusion: Low PAPP-A and the associated adverse outcomes reflect poor placental function. However, due to controversial data, a low positive predictive value and a lack of follow-up consensus, PAPP-A cannot be considered suitable for routine screening of adverse pregnancy outcome. Still, low PAPP-A is clearly a warning sign and risks should to be considered in planning the follow-up scheme of pregnancies with low PAPP-A. On the contrary, normal PAPP-A appeared to be reassuring with a very low risk of adverse outcome. (Table Presented).

Database: EMBASE

10. The risk of adverse pregnancy outcome among pregnancies with extremely low maternal PAPP-A.

Author(s): Kaijomaa, Marja; Ulander, Veli-Matti; Hämäläinen, Esa; Alfthan, Henrik; Markkanen, Helene; Heinonen, Seppo; Stefanovic, Vedran

Available at Prenatal diagnosis - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVEThe aim of the study was to analyze the risk of adverse pregnancy outcome in three subgroups with extremely low maternal pregnancy-associated plasma protein-A (PAPP-A), that is, <0.3 multiples of median (MoM) at the first trimester screening.METHODA cohort of 961 pregnancies with PAPP-A levels < 0.3 MoM at the first trimester combined screening was followed up during the study period of January 2009 to December 2012. The incidences of adverse outcomes was determined in three subgroups with PAPP-A levels < 0.1 MoM, 0.1 to 0.2 MoM, and 0.2 to 0.3 MoM, respectively.RESULTSThe risks of aneuploidy and spontaneous abortion increased with decreasing PAPP-A levels (p < 0.001), but no difference was detected in the rate of structural anomalies among the three groups. Rates of preterm delivery (p < 0.001) and birth weight < 2 standard deviation below the mean (p < 0.001) increased with decreasing PAPP-A levels. The rates of preeclampsia, stillbirth, and cesarean delivery were not significantly different across the three subgroups.CONCLUSION The risks of aneuploidy, spontaneous abortion, preterm delivery, and small for gestational age newborn increased with decreasing PAPP-A. © 2016 John Wiley & Sons, Ltd.

Database: Medline

11. Evaluation of biochemical markers combined with uterine artery Doppler parameters in fetuses with growth restriction: a case-control study.

Author(s): Zamarian, Ana Cristina Perez; Araujo Júnior, Edward; Daher, Sílvia; Rolo, Liliam Cristine; Moron, Antonio Fernandes; Nardozza, Luciano Marcondes Machado

Source: Archives of gynecology and obstetrics; Oct 2016; vol. 294 (no. 4); p. 715-723

Publication Date: Oct 2016

Publication Type(s): Journal Article

PubMedID: 26837385

Available at Archives of gynecology and obstetrics - from SpringerLink

Abstract:PURPOSEAssessing the biochemical markers levels and the uterine artery Doppler (UtA) parameters in fetuses with growth restriction (FGR).METHODSProspective case-control study included 66 patients with diagnosis of FGR and 64 healthy pregnancies at 24-41 weeks of gestation. For both groups, maternal circulating concentrations of biochemical factors of soluble fms-like tyrosine kinase-1 (sFlt-1), soluble endoglin(sEng), adiponectin, A disintegrin and metalloproteinases (ADAM-12), pregnancy-associated plasma protein-A (PAPP-A), angiopoietin-2 (ANGI-2), vascular endothelial growth factor (VEGF) and transforming growth factor-β (TGF-β) were assayed by ELISA and UtA by Doppler were performed. ANOVA, Mann-Whitney tests and Pearson correlation coefficient were applied to compare the biochemical factors, UtA Doppler and EFW Z-score between the groups.RESULTSConcentrations of sFlt-1, sEng, PAPP-A were significantly higher in FGR than controls ($p < 0.0001$, $p = 0.02$ and $p = 0.03$, respectively), but concentration of ANGI-2 ($p < 0.0001$) was significantly lower in FGR than controls and ADAM-12 levels had a tendency to be lower in the FGR, though not statistically significant ($p = 0.059$). Increased sEng concentrations were correlated with abnormal UtA Doppler in FGR.CONCLUSIONFetal growth restriction fetuses showed increased serum levels of sFlt-1, sEng and PAPP-A with levels of ANGI-2 decreased and a positive association between elevated concentrations of sEng and changing impedance of UtA Doppler were observed.

Database: Medline

12. Predicting SGA neonates using first-trimester screening: influence of previous pregnancy's birthweight and PAPP-A MoM

Author(s): Krauskopf A.L.; Knippel A.J.; Kozlowski P.; Verde P.E.

Source: Journal of Maternal-Fetal and Neonatal Medicine; Sep 2016; vol. 29 (no. 18); p. 2962-2967

Publication Date: Sep 2016

Publication Type(s): Article

PubMedID: 26551433

Abstract: Objective: Investigating the proportions of anamnestic and biochemical variables of the previous and current pregnancies for the prediction of small for gestational age (SGA) neonates in the current pregnancy. Methods: In this observational retrospective study, 45 029 pregnancies were examined, including 3862 patients with more than one pregnancy. Odds ratios for SGA using anamnestic parameters and pregnancy-associated plasma protein A (PAPP-A) values from all pregnancies were estimated by using a logistic regression model. Results: There were 2552 (5.7%) SGA neonates. Two threshold PAPP-A values were identified at 0.15 MoM and 0.33 MoM with probabilities for SGA of 23% and 17%, respectively. A previous SGA Copyright © 2015 Taylor & Francis.

Database: EMBASE

13. Predictive value of pregnancy-associated plasma protein-A (PAPP-A) and free beta-hCG on fetal growth restriction: results of a prospective study.

Author(s): Cignini, Pietro; Maggio Savasta, Laura; Gulino, Ferdinando Antonio; Vitale, Salvatore Giovanni; Mangiafico, Lucia; Mesoraca, Alvaro; Giorlandino, Claudio

Source: Archives of gynecology and obstetrics; Jun 2016; vol. 293 (no. 6); p. 1227-1233

Publication Date: Jun 2016

Publication Type(s): Journal Article

PubMedID: 26559420

Available at Archives of gynecology and obstetrics - from SpringerLink

Abstract:PURPOSELow levels of plasmatic pregnancy-associated plasma protein-A (PAPP-A) and high levels of free-beta human chorionic gonadotropin (beta-hCG) could influence the outcome of pregnancy. The objective of this study is to assess the correlation between PAPP-A and free beta-hCG and birth weight.MATERIALS AND METHODSProspective follow-up study performed on 3332 patients in the first trimester of pregnancy who were subjected to a screening test focused on evaluation of fetal aneuploidy (SCA-TEST). The values of PAPP-A and free beta-hCG were both analyzed as raw values and subsequently converted to a multiple of the median (MoM). Statistical analysis was performed using SPSS version 17.0.1 (SPSS Inc., Chicago, USA).RESULTSThe incidence of "small for gestational age" in patients with PAPP-A MoM 95th ‰ (7 %; p = 0.03). The values of PAPP-A MoM > 99th ‰ are significantly correlated with an increased risk of "large for gestational age" (16.7 %; p < 0.0001).CONCLUSIONOur study demonstrates that specific values of PAPP-A and free beta-hCG could identify the risk of low or high birth weight since the first trimester of pregnancy.

Database: Medline

14. Correlation of first-trimester serum levels of pregnancy-associated plasma protein A with small-for-gestational-age neonates and preterm births.

Author(s): Gundu, Shridevi; Kulkarni, Mohan; Gupte, Sanjay; Gupte, Asmita; Gambhir, Maitreyee; Gambhir, Prakash

Source: International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics; May 2016; vol. 133 (no. 2); p. 159-163

Publication Date: May 2016

Publication Type(s): Journal Article

PubMedID: 26892697

Available at International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVETo analyze the relationship between first-trimester levels of pregnancy-associated plasma protein A (PAPP-A) and small-for-gestational-age (SGA) neonates and preterm births, and to assess predictive utility for these events.METHODSA prospective study was conducted among women undergoing first-trimester screening between January 1, 2012, and December 31, 2013, at two centers in Pune, India. Serum PAPP-A levels, pregnancy course, and outcome were assessed.RESULTSOverall, 1474 women were included. An association was found between the lowest quintile of PAPP-A levels (<0.4 multiples of median) for both SGA (<10th centile; 20.9% of cases in this PAPP-A quintile) and preterm birth (<37weeks; 15.8%). Women in the lowest quintile of PAPP-A concentration had a significantly increased risk of SGA (<10th centile) than did those with higher concentrations (adjusted odds ratio 2.92, 95% confidence interval 2.00-4.27). Their risk of

preterm birth (<37weeks) was also increased (adjusted odds ratio 1.84, 95% confidence interval 1.25-2.72). The predictive sensitivities of the lowest quintile of PAPP-A were 35.85% for SGA (<10th centile) and 27.92% for preterm birth (<37weeks).CONCLUSIONLow levels of PAPP-A were associated with SGA and preterm births; however, poor predictive sensitivity could restrict clinical utility of this marker when used alone.

Database: Medline

15. The pregnancy outcomes of pregnancy-associated plasma protein A level of 0.4 MoM and below from the perspective of a UK district general hospital

Author(s): Maher M.; Ford J.; Hepworth J.

Abstract: Introduction Pregnancy-associated plasma protein A (PAPP-A) levels <0.4 multiples of the normal median (MoM) have been associated with poor obstetric outcome and are considered a major risk factor for a small-for-gestational-age (SGA) fetus. Despite this, our hospital manages women with a PAPP-A level <0.4 MoM as low risk, and they are not routinely screened for an SGA fetus. Methods We conducted a retrospective study of the outcomes in 70 pregnancies with a PAPP-A level <0.4 MoM (and normal karyotype), to identify whether we could improve care for our local population. Results There was a strong association with an SGA fetus and low PAPP-A level, with 41.4% of babies having a birthweight on or below the 10th centile on their customised growth chart versus a local background risk of 17% (relative risk [RR] 2.44); 27.1% of our study had a birthweight on or below the 5th centile versus a local background risk of 10% (RR 2.71). There was also an association between low PAPP-A and preterm delivery (RR 1.90), but no increased risk of stillbirth. Analysis of ultrasound use showed low sensitivity for identification of growth below the 10th (57%) and 5th centiles (40%). Conclusion Our data support that a PAPP-A result <0.4 MoM is an important risk factor for SGA fetus and preterm delivery. However, ultrasound data suggest a low sensitivity for identifying the SGA fetus, hence we cannot presently justify PAPP-A as a standalone screening test. However, it should be highlighted and further screening for SGA conducted on an individualised basis.

Database: EMBASE

16. First trimester pregnancy-associated plasma protein-A and birth weight.

Author(s): Baer, Rebecca J; Lyell, Deirdre J; Norton, Mary E; Currier, Robert J; Jelliffe-Pawlowski, Laura L

Source: European journal of obstetrics, gynecology, and reproductive biology; Mar 2016; vol. 198 ; p. 1-6

Publication Date: Mar 2016

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 26773241

Abstract:OBJECTIVETo evaluate first trimester pregnancy-associated plasma protein-A (PAPP-A) and birth weight percentile.STUDY DESIGNIncluded were women who underwent first trimester prenatal screening through the California Prenatal Screening Program with expected dates of delivery between August 2009 and December 2010, linked birth certificate and hospital discharge records, known birth weight, and no chromosomal abnormality (n=134.105). PAPP-A results were reported as multiples of the median. The frequency of small or large for gestational age (SGA, ≤10%; LGA, ≥90%) versus appropriately grown for gestational age birth was examined by PAPP-A percentile. Patterns were studied by gestational age at delivery. Relative risks (RRs) and their 95% confidence intervals were adjusted for race/ethnicity.RESULTSWomen with PAPP-A ≤10th percentile and an infant born after 32 weeks were increasingly more likely to have an SGA infant (adjRRs 1.5-4.6) as the PAPP-A percentile declined, and were increasingly less like to have an LGA infant born at term (adjRRs 0.5-0.7) compared to women with PAPP-A measurement >10th to <90th percentile. PAPP-A ≥90th percentile was protective for SGA among infants born after 32 weeks gestation (adjRRs 0.3-0.7) and was associated with LGA among infants born at term (adjRRs 1.2-8.2).CONCLUSION Women with PAPP-A ≤10th percentile are more likely to have an SGA infant at all gestational ages. PAPP-A ≥90th percentile is protective against SGA and is associated with an increased risk of LGA for infants born after 32 weeks gestation.

Database: Medline

17. First trimester PAPP-A2, PAPP-A and hCGβ in small-for-gestational-age pregnancies.

Author(s): Hansen, Young Bae; Myrhøj, Vibeke; Jørgensen, Finn Stener; Oxvig, Claus; Sørensen, Steen

Source: Clinical chemistry and laboratory medicine; Jan 2016; vol. 54 (no. 1); p. 117-123

Publication Date: Jan 2016

Publication Type(s): Journal Article

PubMedID: 26544105

Abstract:BACKGROUNDPregnancy-associated plasma protein-A2 (PAPP-A2) is a recently discovered protease that cleaves a subset of insulin-like growth factor binding proteins (IGFBP). The molecular function suggests its involvement in the IGF system that is vital for fetal growth and development. Our objectives were to establish first trimester median curves of PAPP-A2, PAPP-A and hCGβ for singleton normal pregnancies and to investigate whether an altered level of one or more of the biomarkers is associated with small-for-gestational-age (SGA) neonates before and after stratification according to maternal hypertension and/or proteinuria.METHODSThis was a case-control study based on 985 pregnant women delivering normal-weighted neonates and 170 pregnant women delivering SGA neonates. PAPP-A2 was measured by ELISA. PAPP-A and hCGβ were measured by an automatic analyzer. Median curves from 8+1 to 14+0 were established and all concentration values were converted to multiples of the median (MoM) values.RESULTSBefore stratification the SGA cases had unaffected PAPP-A2 MoM and hCGβ MoM levels but lower PAPP-A

MoM compared with normal controls. After stratification the SGA normotensive subgroup had lower PAPP-A2 MoM and PAPP-A MoM levels than the normal normotensive subgroup. Severe preeclamptic women delivering SGA neonates had higher PAPP-A2 MoM compared to the normotensive women delivering SGA neonates.CONCLUSIONSPregnant women delivering SGA neonates did not have altered levels of PAPP-A2 or hCGβ but had lower PAPP-A level in the first trimester compared with pregnant women delivering normal-weighted neonates. Pregnancies complicated with severe preeclampsia and SGA may be associated with high PAPP-A2 level.

Database: Medline

18. Maternal serum PAPP-A as an early marker of obstetric complications?

Author(s): Quattrocchi, Tommasa; Baviera, Giovanni; Pochiero, Teresa; Basile, Francesca; Rizzo, Laura; Santamaria, Angelo; Corrado, Francesco; D'Anna, Rosario

Available at Fetal Diagnosis and Therapy - from ProQuest (Hospital Premium Collection) - NHS Version

Abstract:OBJECTIVEThe aim of this study was to investigate whether low first-trimester PAPP-A levels are associated with an adverse pregnancy outcome.MATERIALS AND METHODSA retrospective case-control study was carried out using a Down's syndrome assays database over a 6-year period, between the 8th and 11th week of pregnancy. There were 164 women with PAPP-A multiples of median (MoM) levels <0.3 and 1,640 women with PAPP-A MoM levels ≥0.3 who served as a control group. Outcome measures were the prevalence of miscarriages, gestational hypertension, preeclampsia, pre-term delivery, gestational diabetes and intrauterine growth retardation in both groups.RESULTSThe two groups significantly differed only for miscarriages: 29 (17.7%) vs. 159 (9.7%), p = 0.04, OR 1.7; gestational hypertension: 15 (9.1%) vs. 74 (4.5%), p = 0.02, OR 2.1, and preeclampsia: 9 (5.5%) vs. 29 (1.8%), p = 0.02, OR 2.5.DISCUSSIONEven if in this study the PAPP-A cutoff considered was lower and was assayed in an earlier period compared with other studies, the detection rate for adverse pregnancy outcomes did not improve.

Database: Medline

19. Pregnancy-associated plasma protein A gene polymorphism in pregnant women with preeclampsia and intrauterine growth restriction.

Author(s): Ozkan, Sultan; Sanhal, Cem Yasar; Yeniel, Ozgur; Arslan Ates, Esra; Ergenoglu, Mete; Bınbır, Birol; Onay, Huseyin; Ozkınay, Ferda; Sagol, Sermet

Abstract: Preeclampsia (PE) and intrauterine growth restriction (IUGR) are still among the most commonly researched titles in perinatology. To shed light on their etiology, new prevention and treatment strategies are the major targets of studies. In this study, we aimed to investigate the relation between gene polymorphism of one of the products of trophoblasts, pregnancy-associated plasma protein A (PAPP-A) and PE/IUGR.A total of 147 women (IUGR, n = 61; PE, n = 47; IUGR + PE, n = 37; eclampsia, n = 2) were compared with 103 controls with respect to the sequencing of exon 14 of the PAPP-A gene to detect (rs7020782) polymorphism. Genotypes "AA" and "CC" were given in the event of A or C allele homozygosity and "AC" in A and C allele heterozygosity. Our findings revealed that the rate of AA, CC homozygotes, and AC heterozygotes did not differ between groups. Moreover, there was no difference in the distribution of PAPP-A genotypes among the patients with IUGR, PE, IUGR + PE, or eclampsia. Finally, birth weight, rate of the presence of proteinuria, and total protein excretion on 24-hour urine were similar in the subgroups of AA, AC, and CC genotypes in the study group. Our study demonstrated no association between PAPP-A gene rs7020782 polymorphism and PE/IUGR.

Database: Medline

20. Biochemical markers in screening for preeclampsia and intrauterine growth restriction.

Author(s): Litwińska, Ewelina; Litwińska, Magdalena; Oszukowski, Przemysław; Szaflik, Krzysztof; Litwiński, Waldemar; Korcz, Maciej; Kaczmarek, Piotr

Abstract:OBJECTIVESThe aim of the study was to evaluate the relationship between the concentrations of substances released by the placenta: placental growth factor (PIGF), pregnancy-associated plasma protein A (PAPP-A) and free beta-human chorionic gonadotropin (beta-hCG) and the risk of early and late preeclampsia (PE) and intrauterine fetal growth restriction (IUGR).MATERIAL AND METHODSA total of 180 pregnant women between 11+0 and 13+6 weeks gestation were recruited for a case-control study Twenty-two patients suffered from early PE, 29 patients from late PE. Data analyzed during the study included maternal histoty and concentrations of PAPP-A, PlGF beta-hCG.RESULTSThe multiple of the median (MoM) value of the PAPP-A concentrations was 1.01 in the control group (interquartile range (1QR), 0.65-1.55), 0.67 (1QR, 0.382-0.82) in the group of patients with early preeclampsia and 0.74 (IQ, 0.33-1.09) in the group of patients suffering from late preeclampsia. MoM value of the PIGF concentrations was 1.21 in the control group (IQR, 0.93-1.57), 0.62 (IQR, 0.51-0.96) in the group of patients with early preeclampsia and 0.92 (lQR, 0.63-1.09) in the group of patients suffering from late preeclampsia. MoM value of beta-hCG concentrations was 1.14 in the control group (IQR, 0.75-1.49), 1.08(IQR, 0.74-1.23) in the group of patients with early preeclampsia and 1,25(IQR, 1,05-1,49) in the group of patients suffering

from late preeclampsia. The performance of screening was determined by the areas under the curve and detection rates, with a fixed false-positive rate of 10%.CONCLUSIONSDecreased levels of PAPP-A and PIGF are related to an increased risk of preeclampsia and its complications.

Database: Medline

21. Pregnancy-associated plasma protein A for prediction of fetal growth restriction.

Author(s): Lo, Tsz-kin; Chan, Kelvin Yuen-kwong; Chan, Sario Sau-yuk; Kan, Anita Sik-yau; Hui, Amelia Pui-wah; Tang, Mary Hoi-yin

Source: International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics; Aug 2015; vol. 130 (no. 2); p. 200

Publication Date: Aug 2015

Publication Type(s): Journal Article

PubMedID: 25845987

Available at International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Database: Medline

22. Serum screening in first trimester to predict pre-eclampsia, small for gestational age and preterm delivery: systematic review and meta-analysis.

Author(s): Zhong, Yan; Zhu, Fufan; Ding, Yiling

Source: BMC pregnancy and childbirth; Aug 2015; vol. 15 ; p. 191

Publication Date: Aug 2015

Publication Type(s): Meta-analysis Journal Article Review

PubMedID: 26303460

Available at BMC Pregnancy and Childbirth - from BioMed Central

Available at BMC Pregnancy and Childbirth - from Europe PubMed Central - Open Access

Abstract:BACKGROUNDEarly assessment before the establishment of placental dysfunction has the potential to improve treatment and prognosis for clinical practice.The objective of the study is to investigate the accuracy of serum biochemical markers(Pregnancy- Associated Plasma Protein-A (PAPP-A), human Chorionic Gonadotropin (hCG), Placental Growth Factor (PlGF), Placental Protein 13 (PP13) used in first trimester serum screening in predicting preelampsia, small for gestational age (SGA) and preterm delivery.METHODSThe data sources included Medline, Embase, Cochrane library, Medion, hand searching of relevant journals, reference list checking of included articles and contact with experts. Two reviewers independently selected the articles. Two authors independently extracted data on study characteristics, quality and results.RESULTSThe results showed low predictive accuracy overall. For preeclampsia, the best predictor was PlGF; LR + 4.01 (3.74, 4.28), LR-(0.67, 0.64, 0.69). The predictive value of serum markers for early preeclampsia was better than that of late preeclampsia. For SGA the best predictor was PP13; LR+ 3.70 (3.39, 4.03), LR- 0.70 (0.67, 0.73). For preterm delivery, the best predictor was PP13; LR+ 4.16 (2.72, 5.61), LR- 0.56 (0.45, 0.67).CONCLUSIONFirst trimester screening analytes have low predictive accuracy for pre-eclampsia, small for gestational age and preterm delivery. However, the predict value of first trimester analytes is not worse than that of the second trimester markers.

Database: Medline

23. Adverse pregnancy outcome in patients with low pregnancy-associated plasma protein-A: The Indian Experience.

Author(s): Gupta, Sangeeta; Goyal, Manisha; Verma, Deepti; Sharma, Anjana; Bharadwaj, Namita; Kabra, Madhulika; Kapoor, Seema

Source: The journal of obstetrics and gynaecology research; Jul 2015; vol. 41 (no. 7); p. 1003-1008

Publication Date: Jul 2015

Publication Type(s): Journal Article

PubMedID: 25773764

Available at Journal of Obstetrics and Gynaecology Research - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:AIMThe aim of our study was to examine the association of low pregnancy-associated plasma protein-A (PAPP-A) with adverse pregnancy outcome.MATERIAL AND METHODSA total of 1640 consecutive pregnant women between 9(+5) and 13(+6) weeks of pregnancy were recruited. One hundred and thirty women with PAPP-A levels < 0.4 multiple of median were followed till delivery and the outcome information was obtained for fetal loss, birthweight, growth restriction, preterm birth, reduced liquor and development of pre-eclampsia.RESULTSDuring the study period, 130 (7.92%) women had low PAPP-A and were considered as cases and 200 women with normal PAPP-A were controls. Intrauterine growth restriction was observed in 28 (21.54%) cases as compared to 10 (5%) controls. Pre-eclampsia presented in 24 (18.46%) cases and in 18 (9%) controls. Twenty (15.38%) cases had preterm delivery compared to 12 (6%) controls. Fifty-six (43.08%) cases delivered low-birthweight babies compared to 22 (11%) controls. Thus, the incidence of intrauterine growth restriction, preterm birth and low birthweight was significantly more in the cases as compared to the control group.CONCLUSIONSPAPP-A is a valuable analyte for predicting risk of adverse pregnancy outcome and women with low serum PAPP-A levels would benefit from closer surveillance.

Database: Medline

24. Correlation of neonatal weight with maternal serum levels of pregnancy-associated plasma protein-A during the first trimester of pregnancy: A Retrospective study

Author(s): Giudice I.; Benintende G.; Di Nicolo A.M.; Mangiameli D.; Sapuppo I.M.; Gulisano A.; Carrara G.; Randazzo C.

Abstract: Aim: Evaluate the relationship between neonatal weight and pregnancy-associated plasma protein-A. Methods: Retrospective study on 2564 singleton pregnancies with healthy term neonates in three groups of women with different values of pregnancy-associated plasma protein-A who underwent the combined test during the first trimester. Non-parametric test and correlation analysis for statistical elaboration were carried out. Results: There exists a correlation between the serum levels of pregnancy-associated plasma protein-A in the first trimester of pregnancy and neonatal weight. Values of pregnancy-associated plasma protein-A lower than the 25th percentile are associated with neonatal weight in a significant way. There was no significant association between pregnancy-associated plasma protein-A values above 1.50 MoM and neonatal weight. Conclusion: This study confirms the positive correlation between circulating concentrations of pregnancy-associated plasma protein-A and fetal growth. Low neonatal weight and factors that can cause this could be determined from the first trimester by measuring the concentrations of pregnancy-associated plasma protein-A in maternal serum. Even if the association between the levels of pregnancyassociated plasma protein-A and a low neonatal weight has been demonstrated, however, we have to say that the sensitivity of a such screening method for the prediction of low birth weight and perinatal complications seems to be rather low. The variations of pregnancy-associated plasma protein-A during the first trimester cannot be used as a marker of excessive fetal growth.

25. Association of firsttrimester PAPP-a with smallfor-gestational age infant and other adverse pregnancy outcomes

Author(s): Cervino Gomez E.; Gonzalez Rodriguez L.; Cernadas Pires S.; Gonzalez Boubeta R.; Lopez Ramon y Cajal C.N.

Abstract: Brief Introduction: The PAPP-A is produced by the placental syncytiotrophoblasts and works as a protease for IGF binding protein 4. IGF plays a major role in the fetal growth, mediating in the trophoblastic invasion and the glucose and aminoacids transport across the placenta. Levels of PAPP-A=0.41 MoM) are selected on a pairing basis. Statistical analysis: Conducted with a SSPS 19 pack for Windows. A P value<0.05 was deemed to be statistically significant. Clinical Cases or Summary Results: 225 pregnant women were included in the cases group (34 of those 259 were excluded) and 228 in the control group (31 of those 259 were excluded). There were no differences of statistical relevance regarding the age, race, BMI or cigarette smokers. We found relevant differences as for the number of SGA and preterm delivery (p<0.05). 30.9% of newborns with low PAPP-A were SGA (54.36% of those SGA featured a weight below 5st percentile), as opposed to 11% in the controls group. 73% of SGA born during our study featured a low PAPP-A, coming up to 80.4% in SGA below 5st percentile. The incidence of preterm birth was 9.5% in the cases group, compared to 3.6% in the controls group. We did not find differences with regard to adverse outcomes such as

preeclampsia, gestational diabetes or intrauterine fetal birth. Perinatal outcomes were pretty similar concerning the type of birth, Apgar and pH. The number of admissions of newborns was higher in cases group, 13.6% compared to 2.7%. It was somewhat noticeable, though, that there were 3 fetal deaths before week 24 in the cases group as opposed to none in the control group. Conclusions: Low levels of maternal serum PAPP-A are associated with an increased risk of SGA (RR 4.2 for SGA below 5st percentile, RR 2 below10st percentile), preterm delivery (RR 2.6) and admission in neonatal care unit (RR 5). The association for SGA of PAPP-A levels below the 5st percentile suggests that patients within this group may benefit from increased surveillance for this condition.

Database: EMBASE

26. Variation of papp-a level in the first trimester of pregnancy and its clinical outcome.

Author(s): Patil, Mithil; Panchanadikar, T M; Wagh, Girija

Available at The Journal of Obstetrics and Gynecology of India - from SpringerLink

Available at The Journal of Obstetrics and Gynecology of India - from Europe PubMed Central - Open Access

Abstract:INTRODUCTIONAbnormalities in maternal serum marker levels and fetal measurements obtained during the first trimester screening can be a marker not only for certain chromosomal disorders and anomalies in the fetus but also for specific pregnancy complications. In particular, low maternal serum pregnancy-associated plasma protein-A (PAPP-A), at 11-13 weeks of gestation, is associated with stillbirth, infant death, intrauterine growth restriction, preterm birth, and pre-eclampsia in chromosomally normal fetuses, while a raised nuchal translucency is associated with specific structural abnormalities and genetic syndromes. We have studied the serum Papp-A level in 560 pregnant patients (11-13 weeks gestation) registered at Bharati Hospital and Research Centre, Pune. All patients undergoing testing were followed till the delivery and their neonatal outcome was also taken into consideration.AIMS AND OBJECTIVESOur aim is to study the pregnancy outcome in relation to the variations of Papp-A level in the first trimester of pregnancy.MATERIALS AND METHODSEvery patient visiting the antenatal OPD was counseled for testing of First Trimester Screening to assess fetal well-being. Patients who were registered for delivery at our hospital were taken into the trial. Blood samples were taken at 11-13 weeks of pregnancy and sent to the PerkinElmer lab for analysis. Results were expressed in Multiple of Median and patients having MOM value less than 0.5 were carefully observed till the delivery, and a thorough neonatal examination was done by a pediatrician.OBSERVATIONS524 patients were included in the trial out of which 452 patients were found to have a normal Papp-A level of >0.5 MOM. All these patients were followed further during the antenatal period where 18 patients developed preterm labor and few patients developed pregnancy-induced hypertension. The obstetric outcome of patients with a normal Papp-A level was fairly uneventful as compared to others with a low Papp-A level.CONCLUSIONSThough Papp-A level in the first trimester of pregnancy (11-13 weeks) is an important predictor of future obstetric outcome, it has poor positive predictive value. Patients having a Papp-A level less than 0.5 MOM have a high risk for preterm delivery, fetal growth restriction, and stillbirths along with increased incidence of hypertensive disorders of pregnancy. A low Papp-A level is a useful indicator of risk of preterm delivery and future chance of development of pregnancy-induced hypertension.

Database: Medline

27. How low is too low: Does the percentile of low PAPP-A affect pregnancy outcomes?

Author(s): Foroutan J.; Lewis D.; Herrera K.; King L.; Bimson B.

Source: Reproductive Sciences; Mar 2014; vol. 21 (no. 3)

Publication Date: Mar 2014

Publication Type(s): Conference Abstract

Abstract:INTRODUCTION: When screening for aneuploidy, the definition of a low pregnancy-associated plasma protein-A (PAPP-A) depends on the percentile cut-off used. We sought to determine whether a lower percentile cut-off is associated with worse pregnancy outcomes. METHODS: A retrospective cohort study was performed using maternal serum analyte results from first trimester and sequential screening tests from January 2002-December 2012. Low PAPP-A, <=5th percentile, was defined as <=0.4 MOM (multiples of the median). A PAPA-A <=1st percentile was defined as <=0.33 MoM and the 2-5th percentile was defined as 0.34- 0.40 MoM. Patients were excluded if they had known structural and/or chromosomal anomalies, multiple gestations, and pre-gestational diabetes. Women were placed into 2 groups: Group 1, 2-5th percentile and Group 2, <=1st percentile. Low birth weight was defined as <2500g and intrauterine growth restriction (IUGR) was defined as estimated fetal weight or abdominal circumference <10% on ultrasound. Statistical analysis was performed using Wilcoxon signed-rank test and Fisher's exact test to compare pregnancy outcomes among the 2 groups. RESULTS: A total of 11,958 patients had screening tests performed during this time period and 263 patients had a low PAPP-A. Ten patients were excluded, leaving 253 patients for analysis. See table below. (Table Presented) CONCLUSIONS: A PAPP-A <=1st % does not appear to have worse pregnancy outcomes when compared to the 2-5th %. Using a lower cutoff does not appear to have any clinical significance.

Database: EMBASE

28. First trimester maternal lipid levels and serum markers of small- and large-for-gestational age infants

Author(s): Parlakgumus H.A.; Aytac P.C.; Kalayci H.; Tarim E.

Source: Journal of Maternal-Fetal and Neonatal Medicine; Jan 2014; vol. 27 (no. 1); p. 48-51

Publication Date: Jan 2014

Publication Type(s): Article

PubMedID: 23617575

Abstract: Objective: To investigate if first trimester lipids, sonographic parameters and serum markers are related to small- and large-for-gestational age (SGA, LGA) infants. Methods: This study was conducted at Baskent University Adana Research Center between December 2009 and July 2011 and enrolled 433 women. Blood samples were drawn to measure fasting blood glucose, serum triglycerides, cholesterol, very low-density lipoprotein, low-density lipoprotein, high-density lipoprotein, fbeta-hCG and pregnancy associated protein-A (PAPP-A) at the first trimester. Crown rump length and nuchal translucency were measured as suggested by the fetal medicine foundation. Results: LGA group was significantly taller (p=0.016) and SGA group had significantly greater BMI (0.025). SGA fetuses were born at a significantly earlier gestational age (p=0.001). Univariate analysis revealed that LGA group had significantly lower cholesterol (p=0.038) and LDL levels (p=0.041). PAPP-A was significantly lower in SGA Group compared with LGA Group (0.027). After controlling for age, parity, height, pre-pregnant BMI, weight gain during pregnancy and fasting blood sugar, none of the lipids, serum markers or sonographic parameters was related to LGA. PAPP-A was the only

parameter significantly associated with SGA after multivariate analysis (p=0.008). Conclusion: PAPP-A was significantly associated with SGA after controlling for confounders. © 2014 Informa UK Ltd.

Database: EMBASE

29. Association between first-trimester maternal serum pregnancy-associated plasma protein-A and obstetric complications.

Author(s): D'Antonio, Francesco; Rijo, Claudia; Thilaganathan, Basky; Akolekar, Ranjit; Khalil, Asma; Papageourgiou, Aris; Bhide, Amar

Source: Prenatal diagnosis; Sep 2013; vol. 33 (no. 9); p. 839-847

Publication Date: Sep 2013

Publication Type(s): Journal Article Observational Study

PubMedID: 23613261

Available at Prenatal diagnosis - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVEThis study aimed to investigate the relationship between maternal serum pregnancy-associated plasma protein-A (PAPP-A) in the first trimester of pregnancy and the development of preeclampsia (PE), early PE, small-for-gestational age (SGA) fetus and preterm delivery (PD).METHODThis is a retrospective study of 12,355 pregnant women that delivered between 2008 and 2011. We define the first, third and fifth percentiles of maternal serum PAPP-A multiples of the median (MoM). The primary outcome measures were the occurrence of PE, early PE (PE requiring delivery before 34 weeks), SGA fetus (birth weight < 5th centile) and PD. The Mann-Whitney U-test and chi-squared test were used to analyze continuous and dichotomous variables, respectively.RESULTSMaternal serum PAPP-A was significantly lower in women with PE, early PE, SGA fetus and PD (0.91, 0.74, 0.80 and 0.84 MoM, respectively) than in the study population (0.99 MoM) (p < 0.05). The lower the MoM percentile of PAPP-A, the higher are the odds ratio (OR) to develop PE, early PE, SGA fetus and PD.CONCLUSIONSMaternal serum PAPP-A levels are lower in women who develop preeclampsia, those with SGA fetus and those who deliver preterm. However, on its own, maternal serum PAPP-A performs poorly (OR for PE between 1.76 and 2.41 with the lower percentile of PAPP-A) as a screening test for these conditions.

Database: Medline

30. The relationship of low maternal PAPP-A at 11-13+6 weeks of gestation with small for-gestational age newborns and stillbirths

Author(s): Antsaklis P.; Theodora M.; Papanicolaou T.; Daskalakis G.; Mesogitis S.; Papantoniou N.; Antsaklis A.; Iliescu D.

Source: Journal of Perinatal Medicine; Jun 2013; vol. 41

Publication Date: Jun 2013

Publication Type(s): Conference Abstract

Abstract:OBJECTIVE: To assess whether low PAPP-A (Pregnancy associated plasma protein-A) at 11-13+6 weeks of pregnancy is related to bad obstetrical outcome and more specifically small for gestational age newborns and stillbirths. METHODS: A retrospective study, from 2 university hospitals (Athens University-Greece and Craiova University-Romania), which included all women who attended for the first trimester screening for chromosomal abnormalities (Nuchal Translucency, free-shCG and PAPP-A). The study included all women with singleton pregnancies. In total there were 9533 women, while complete data and pregnancy outcome were available in 4012 women. Low PAPP-A (<0,3 MoM) was found in 215 women, while complete data and pregnancy outcome was available in 103 of these pregnancies. RESULTS: From the 9533 pregnancies we identified 215 (2.2%) with low PAPP-A (0,3 MoM). Complete data and outcome of the pregnancy was available for 103 of these pregnancies. From the 103 pregnancies with low PAPP-A we excluded 11 cases who underwent termination of pregnancy for abnormal karyotype. From the remaining 92 pregnancies there were 8 cases of small for gestational age and 2 cases of intrauterine fetal death. There were also 3 cases of preterm delivery and 4 cases of late miscarriage (after 16 weeks). CONCLUSION: Low PAPP-A (< 0,3 MoM) during the first trimester of pregnancy seems to be related with an increased risk of adverse obstetrical outcome and more specifically with small for gestational age fetuses and stillbirth. Pregnancies with low PAPP-A values, even when the risk for chromosomal abnormalities is low should be managed as high-risk pregnancies.

Database: EMBASE

31. Low pregnancy associated plasma protein-A in the 1st trimester: Is it a predictor of poor perinatal outcome?

Author(s): Karim J.N.; Sau A.

Source: Journal of Obstetrics and Gynaecology; May 2013; vol. 33 (no. 4); p. 351-354

Publication Date: May 2013

Publication Type(s): Article

Abstract: The objective of the study was to examine the predictive value of pregnancy associated plasma protein-A (PAPP-A) as a marker of poor pregnancy outcome. Databases at the University Hospital Lewisham, were used retrospectively to identify singleton pregnancies, which underwent 1st trimester combined screening between July 2008 and April 2010 and were found to have PAPP-A levels <= 0.4MoM. The perinatal courses of these pregnancies (n = 315) were evaluated for signs of adverse perinatal outcome and compared with a matched control group of pregnancies (n = 330) with normal PAPP-A levels. Results showed that women with low serum PAPP-A were at increased risk of adverse pregnancy outcome compared with the control group (OR 2.4, p = 000.1). They were also more likely to suffer fetal loss (OR 6.2, p = 0.001) in the form of miscarriage (OR 2.7, p = 0.110) and stillbirth (OR 2.4, p = 0.001). It was concluded that serum PAPP-A is a marker for poor pregnancy outcome and women with low serum PAPP-A levels would benefit from increased monitoring of their pregnancies. © 2013 Informa UK, Ltd.

Database: EMBASE

32. Maternal predictors of intrauterine growth restriction

Author(s): Cetin I.; Mando C.; Calabrese S.

Source: Current Opinion in Clinical Nutrition and Metabolic Care; May 2013; vol. 16 (no. 3); p. 310-319

Publication Date: May 2013

Publication Type(s): Review

PubMedID: 23385473

Available at Current Opinion in Clinical Nutrition and Metabolic Care - from Ovid (LWW Total Access Collection 2015 - Q1 with Neurology)

Abstract:PURPOSE OF REVIEW: Intrauterine growth restriction (IUGR) occurs when fetal growth rate falls below the genetic potential and affects a significant number of pregnancies, but still no therapy has been developed for this pregnancy disease. This article reviews the most recent findings concerning maternal characteristics and behaviours predisposing to IUGR as well as maternal early markers of the disease. A comprehensive understanding of factors associated with IUGR will help in providing important tools for preventing and understanding adverse outcomes. RECENT FINDINGS: Maternal nutritional status, diet and exposure to environmental factors are increasingly acknowledged as potential factors affecting fetal growth both by altering nutrient availability to the fetus and by modulating placental gene expression, thus modifying placental function. SUMMARY: Assessing nutritional and environmental factors associated with IUGR, and the molecular mechanisms by which they may have a role in the disease onset, is necessary to provide comprehensive and common guidelines for maternal care and recommended behaviours. Moreover, maternal genetic predispositions and early serum markers may allow a better and more specific monitoring of high risk pregnancies, optimizing the timing of delivery. © 2013 Wolters Kluwer Health Lippincott Williams &Wilkins.

Database: EMBASE

33. Low maternal serum PAPP-A in the first trimester and pregnancy outcome: An experience over 3 years

Author(s): Weaver A.; Nanda S.; Rozette C.; Kyle P.; Sankaran S.

Source: Archives of Disease in Childhood: Fetal and Neonatal Edition; Apr 2013; vol. 98

Publication Date: Apr 2013

Publication Type(s): Conference Abstract

Available at Archives of Disease in Childhood - Fetal and Neonatal Edition - from BMJ Journals - NHS

Abstract: Introduction Maternal serum PAPP-A (pregnancy associated plasma protein-A) is a part of combined screening. Previous studies have shown correlation between low PAPP-A and adverse pregnancy outcome. Objective The aim of this study is to establish the positive predictive value of low-PAPP-A in prediction of adverse pregnancy outcomes - pre-eclampsia (PET), pregnancy induced hypertension (PIH), delivery of small for gestational age neonates (SGA) and late pregnancy losses. Materials and Methods 16690 women underwent combined screening from 1/8/2008 to 1/8/2011. 326 women with low PAPP-A (=24 weeks).

Database: EMBASE

34. Significance of pregnancy-associated plasma protein A (PAPP-A) concentration determination in the assessment of final outcome of pregnancy.

Author(s): Loncar, Dragan; Varjacić, Mirjana; Arsenijević, Slobodan

Abstract:BACKGROUND/AIMPregnancy-associated plasma protein A (PAPP-A) is high molecular matrix metalloproteinase originally isolated in the serum of pregnant women. The aim of this study was to analyze the values of concentration of PAPP-A in assessment of progress and outcome of pregnancy in pregnant women diagnosed with threatening preterm delivery, preeclampsia and fetal growth restriction in relation to physiological pregnancy of the same gestational age.METHODSThe study included 60 pregnant women that were divided into three groups according to gestational age and the diagnosis of imminent premature birth upon reception, preeclampsia and fetal growth restriction as follows: the group I from 28 to 32 weeks of gestation, a total of 25 pregnant women, the group II from 33 to 36 weeks of gestation, a total of 23 pregnant women, and the group III from 37 to 41 weeks of gestation, a total of 12 pregnant women. The control group consisted of 60 pregnant women without complications of pregnancy that were identically divided into three groups according to gestational age as in the sample. We performed quantitative determination of PAPP-A from the venous blood of patients by using commercial tests of the company Diagnostics Product Corporation (DPC), Los Angeles, California, USA.RESULTSThere was a statistically significant difference in PAPP-A values in the examined groups in all gestational ages (p 0.05).CONCLUSIONDifferences in PAPP-A concentration should point out to the obstetrician the need for more intensive antepartum fetal surveillance in order to increase the chances of favorable perinatal outcome, regardless gestational age.

Database: Medline

35. Association of first trimester low PAPP-A levels with adverse pregnancy outcomes.

Author(s): Saruhan, Z; Ozekinci, M; Simsek, M; Mendilcioglu, I

Abstract:OBJECTIVETo investigate whether first trimester low PAPP-A levels are associated with adverse pregnancy outcomes.METHODSA case control retrospective study including 663 pregnant women whose gestational age ranged between 11 and 14 weeks attending prenatal care at Akdeniz University Hospital was carried out. Chromosomal abnormalities, spontaneous abortions, and multiple pregnancies were excluded from the study. Finally 318 singleton pregnancies were included in this study. Pregnant women whose PAPP-A levels were 10'h percentile for the frequency of pregnancy complications such as SGA, preeclampsia, preterm delivery, gestational diabetes mellitus and gestational hypertension.RESULTSThe most common complication of pregnancy was SGA (9.4%, n=30). There was no significant association between low PAPP-A levels and incidence of subsequent pregnancy outcomes. Maternal age was found to be a risk factor for gestational diabetes (p = 0.00). Small for gestational age was significantly associated with nulliparity and smoking during pregnancy (p = 0.03 and p = 0.01, respectively).CONCLUSIONFirst trimester of low PAPP-A level (< or = 10th percentile) was not associated with SGA, preeclampsia, preterm delivery, gestational hypertension or gestational diabetes mellitus.

Database: Medline

36. Efficiency of first-trimester growth restriction and low pregnancy-associated plasma protein-A in predicting small for gestational age at delivery.

Author(s): Carbone, Jeanine F; Tuuli, Methodius G; Bradshaw, Rachael; Liebsch, Julie; Odibo, Anthony O

Available at Prenatal diagnosis - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVETo evaluate the efficiency of first-trimester fetal growth restriction (FGR), low pregnancy-associated plasma protein A (PAPP-A), and their combination for predicting small for gestational age (SGA) at delivery.METHODSRetrospective cohort study of women undergoing first-trimester aneuploidy screening. Fetal crown-rump lengths (CRLs) were at 10 to 14 weeks' gestation and converted to gestational age adjusted Z-scores. Low PAPP-A was defined as levels<5th percentile for GA. Receiver-operating characteristic curves were used to assess screening efficiencies.RESULTSAmong 3269 pregnancies meeting the inclusion criteria 185 (5.7%) infants were SGA. CRL Z-score< -1.0 standard deviation was identified as the optimal definition of early FGR. Using either CRL Z-score< -1.0 standard deviation or PAPP-A<5th percentile had the highest sensitivity (33%) with a specificity of 82.1% when screening for SGA. Using a combination resulted in an increased association (adjusted odds ratio 4.23[confidence interval 1.37-13.03]) at the expense of significantly reduced sensitivity (3.13%).CONCLUSIONSFirst-trimester FGR and PAPP-A<5th percentile are associated with delivery of an SGA infant. Neither of these parameters or the combination of the two are sufficient powerful predictors of SGA to be clinically useful screening tools.

Database: Medline

37. Combinations of maternal serum markers to predict preeclampsia, small for gestational age, and stillbirth: a systematic review.

Author(s): Hui, Dini; Okun, Nan; Murphy, Kellie; Kingdom, John; Uleryk, Elizabeth; Shah, Prakesh S

Abstract:OBJECTIVEAbnormal serum screening markers have been associated with adverse pregnancy outcomes. We sought to review the performance of combined abnormal first and/or second trimester maternal serum markers used in prenatal screening for aneuploidy and open neural tube defects for predicting preeclampsia (PET), small for gestational age (SGA), and stillbirth beyond 24 weeks' gestation.DATA SOURCES AND STUDY SELECTIONMedline, EMBASE, and Cochrane Library databases were searched for studies from 1970 to May 2010 that analyzed predictive abilities of combined serum markers for defined outcomes.DATA EXTRACTION AND SYNTHESISData were extracted independently by two authors, and 15 studies were included. Eight studies of 115,290 pregnancies, 11 studies of 144 853 pregnancies, and seven studies of 80 274 pregnancies examined PET, SGA, and stillbirth respectively. Because of the heterogeneity of marker combinations and thresholds, outcome definitions, and analytic methods, limited meta-analysis was possible for the outcomes of PET and SGA only. Three relatively homogeneous studies on prediction of PET, and two on prediction of SGA were meta-analyzed. Several single studies demonstrated utility in combining markers to predict adverse outcome; however, this effect was not confirmed after meta-analysis. The most common combination of markers evaluated was alpha fetoprotein and human chorionic gonadotrophin for all outcomes. The highest positive likelihood ratios for predicting PET (5.68; 95% CI 0.73 to 43.97) and SGA (6.18; 95% CI 1.84 to 20.85) were seen with combined alpha fetoprotein and human chorionic gonadotrophin (> 2.5 multiples of the median).CONCLUSIONSCurrently, no identifiable combination of serum markers performs well as a screening test for preeclampsia, small for gestational age, and stillbirth beyond 24 weeks. Large cohort studies with standardized screening test parameters and outcomes are needed.

Database: Medline

38. Placental protein-13 and pregnancy-associated plasma protein-A as first trimester screening markers for hypertensive disorders and small for gestational age outcomes.

Author(s): Stamatopoulou, Anastasia; Cowans, Nicholas J; Matwejew, Elisabet; von Kaisenberg, Constantine; Spencer, Kevin

Abstract:OBJECTIVETo investigate the role of placenta protein 13 (PP13) and pregnancy-associated plasma protein-A (PAPP-A) in hypertensive disorders and small for gestational age (SGA) during first trimester of pregnancy.METHODSIn this case-control study, first trimester serum samples (11(+0) to 13(+6) weeks) were retrieved from frozen storage of which 452 were from normal pregnancies and 47 samples were identified to have pregnancies with at least one of the following adverse outcomes: SGA, preeclampsia (PE), hemolysis, elevated liver enzymes, and low platelets (HELLP), or gestational hypertension (GH). PP13 concentrations were measured by a new AutoDELFIA method. Levels of PAPP-A were measured for a first trimester screening program using Kryptor analyzer.RESULTSFirst trimester levels of PAPP-A are significantly lower in cases of SGA, PE, and most subgroups including HELLP. Levels of PP13 were not found to differ between control and affected pregnancies.CONCLUSIONPP13 needs to be studied further as our results contrast the majority of previous studies.

39. First trimester screening for intra-uterine growth restriction and early-onset pre-eclampsia.

Author(s): Vandenberghe, G; Mensink, I; Twisk, J W R; Blankenstein, M A; Heijboer, A C; van Vugt, J M G

Available at Prenatal diagnosis - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVETo assess first trimester placental growth factor (PlGF) and pregnancy-associated plasma protein-A (PAPP-A) as screening markers for early-onset pre-eclampsia (PE) and intra-uterine growth restriction (IUGR).METHODSPlGF concentration was retrospectively measured in first trimester serum specimens of 23 cases of early-onset PE (<34 weeks), 26 cases of IUGR (birth weight < 5th centile) and 5 controls per case. Levels were adjusted for gestational age (GA), ethnicity and smoking to obtain multiples of the expected median (MoM). Logistic regression was used to assess PlGF, PAPP-A and maternal characteristics as potential predictors of early-onset PE and IUGR.RESULTSPlGF MoM levels were significantly lower in the early-onset PE group (P < 0.0001) compared with controls, but not in the IUGR group. PAPP-A MoM levels were significantly lower in the IUGR group (P < 0.01) compared with controls but not in the early-onset PE group. PlGF significantly improved the ability of systolic blood pressure at the first prenatal visit to predict early-onset PE [achieving a receiver-operating characteristics curve with area under the curve (AUC) of 0.8]. Combining systolic blood pressure at the first prenatal visit and PlGF did not significantly improve the predictive ability compared with PlGF alone (AUC = 0.83).CONCLUSIONSerum PlGF is an

acceptable marker in first trimester screening for early-onset PE, but a poor marker in screening for IUGR. Screening performance of serum PAPP-A is poor for both early-onset PE and IUGR.

Database: Medline

40. Decreased PAPP-A is associated with preeclampsia, premature delivery and small for gestational age infants but not with placental abruption.

Author(s): Ranta, Jenni K; Raatikainen, Kaisa; Romppanen, Jarkko; Pulkki, Kari; Heinonen, Seppo

Abstract:OBJECTIVETo investigate links between first trimester Down's syndrome screening markers and adverse pregnancy outcomes; preeclampsia (PE), small for gestational age (SGA), preterm delivery (PD) and placental abruption (PA) in spontaneous, chromosomally normal pregnancies.STUDY DESIGNCohort study in a university hospital. Data during pregnancy were routinely collected from a total study population of 2844 pregnant women between 2005 and 2007. Four study groups were pregnancies with PE (N=175), PA (N=17), PD (N=213) and SGA (N=275) plus a reference group with normal outcome (N=2164). The median MOMs of maternal serum concentrations of pregnancy associated plasma protein A (PAPP-A) and free beta human chorionic gonadotropin (fβ-hCG) were compared using two-tailed pooled t-tests, continuous variables were compared using Student's two-way t-tests, and Chi-square tests were used to analyse dichotomous variables. Fisher's exact test was used when there were fewer than five units in any of the classes.RESULTSThe median MOM of maternal serum PAPP-A was significantly lower in women with PE, PD and SGA (0.79, 0.80 and 0.79 MOM, respectively) than in the reference group (0.99 MOM) (p<0.01). The median MOM of maternal serum fβ-hCG was also significantly lower in the SGA group (0.90 MOM) and in the PE and PD groups (0.86 and 0.92 MOM) than in the reference group (0.99 MOM, p=0.02). There was no detectable difference between the biochemical markers in the PA group and the reference group. No statistical difference was found between NT MOMs in the reference and study groups.CONCLUSIONThe concentrations of first trimester screening (FTS) serum markers were lower in pregnancies where PE, PD and SGA occurred. In the latter two cases, there was an inverse association between incidence and PAPP-A and fβ-hCG values. However, the development of PA during pregnancy could not be predicted from biochemical marker concentrations. The mechanism behind PA is probably less dependent on the placenta than on the decidua.

Database: Medline

41. Early fetal growth, PAPP-A and free β-hCG in relation to risk of delivering a small-for-gestational age infant.

Author(s): Kirkegaard, I; Henriksen, T B; Uldbjerg, N

Available at Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVESTo examine early fetal growth, pregnancy-associated plasma protein-A (PAPP-A) and free β-human chorionic gonadotropin (β-hCG) in relation to the risk of delivering a small-for-gestational age (SGA) infant.METHODSIncluded in the study were 9450 singleton pregnant women who attended the prenatal screening program at Aarhus University Hospital, Denmark, between January 2005 and December 2007. Maternal serum levels of PAPP-A and free β-hCG were measured between gestational weeks 8 and 13. Two ultrasound examinations were performed, the first at 11-13 weeks and the second at 18-22 weeks, from which gestational age was estimated based on crown-rump length and biparietal diameter, respectively. Early fetal growth was expressed as an index: the ratio between the estimated number of days from the first to the second scan and the actual calendar time elapsed in days. SGA was defined as birth weight < 5(th) centile for gestational age, and the risk of SGA was evaluated according to different cut-offs of the early fetal growth index and the serum markers.RESULTSPAPP-A < 0.4 MoM combined with an early fetal growth index < 10(th) centile resulted in an increased risk of SGA (odds ratio (OR), 5.8; 95% CI, 2.7-12.7). Low PAPP-A, low free β-hCG and slow early fetal growth were statistically, independently associated with SGA, and the association between free β-hCG < 0.3 MoM and SGA was as strong as that between PAPP-A < 0.3 MoM and SGA (OR, 3.1 and 3.0, respectively).CONCLUSIONThe combination of slow early fetal growth and low PAPP-A resulted in a nearly six-fold increased risk of delivery of an SGA infant. These findings might improve our chances of early identification of fetuses at increased risk of growth restriction.

Database: Medline

42. PAPP-A and free beta-hCG measured prior to 10 weeks is associated with preterm delivery and small-for-gestational-age infants

Author(s): Kirkegaard I.; Uldbjerg N.; Henriksen T.B.; Torring N.

Source: Prenatal Diagnosis; Feb 2011; vol. 31 (no. 2); p. 171-175

Publication Date: Feb 2011

Publication Type(s): Article

PubMedID: 21268036

Available at Prenatal diagnosis - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract: Objective: To evaluate whether measuring pregnancy-associated plasma protein A (PAPP-A) and free beta-human chorionic gonadotrophin (beta-hCG) before 10 weeks of gestation affect the association between these biomarkers and adverse pregnancy outcomes. Methods: Singleton pregnant women (9450) who attended the prenatal screening program, Aarhus University Hospital, Denmark, were included. Maternal serum levels of PAPP-A and free beta-hCG were measured between week 8 and 13 weeks and 6 days. The risk of preterm delivery (=10 weeks) biochemical testing. Results: A stronger association between low PAPP-A and SGA was found with early serum sampling compared to late, but the difference was not statistically significant [odds ratio (OR) 3.2 vs 1.8; P value = 0.11]. This difference did not apply to PAPP-A and preterm delivery. For free beta-hCG, a stronger association with preterm delivery was found with early testing (OR 1.9 vs 1.1; P value = 0.31), whereas this difference was not found regarding SGA. Conclusion: Biochemical testing before 10 weeks does not affect the association between low PAPP-A and free beta-hCG and adverse pregnancy outcomes. Whether the association is actually stronger with early testing, requires further study. Copyright © 2011 John Wiley & Sons, Ltd.

Database: EMBASE

43. First-trimester umbilical vein blood flow in pregnancies with low serum pregnancy-associated plasma protein-A levels: an early predictor of fetal growth restriction.

Author(s): Rizzo, G; Capponi, A; Pietrolucci, M E; Capece, A; Arduini, D

Source: Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology; Oct 2010; vol. 36 (no. 4); p. 433-438

Publication Date: Oct 2010

Publication Type(s): Journal Article Evaluation Studies

PubMedID: 20509137

Available at Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVETo investigate umbilical vein blood flow (UVBF) during the first trimester in pregnancies with low serum pregnancy-associated plasma protein-A (PAPP-A) levels and to relate umbilical vein (UV) diameter, time-averaged maximum velocity (TAMXV) and UVBF values to the subsequent development of fetal intrauterine growth restriction (IUGR).METHODSUVBF assessment was performed at 11 + 0 to 13 + 6 weeks' gestation in 102 singleton pregnancies with PAPP-A concentrations of < 0.3 multiples of the median. UV diameter, UV-TAMXV and UVBF were calculated and analyzed in relation to pregnancy outcome.RESULTSPregnancy outcomes were: 51 pregnancies with birth weight ≥ 10(th) centile (Group A), 30 pregnancies with birth weight < 10(th) centile with normal Doppler in the umbilical artery throughout gestation (Group B) and 21 pregnancies with birth weight < 10(th) centile and abnormal umbilical artery Doppler later in gestation (Group C). No

differences were found in PAPP-A levels between groups. Group C fetuses exhibited significantly lower values of UV-TAMXV (z-score - 1.99 SDs, t = 8.527, P ≤ 0.0001) and UVBF (z-score - 0.97 SDs, t = 7.420, P ≤ 0.0001) in comparison with normal reference ranges, while no differences were found in Groups A or B.CONCLUSIONSDecreased UV-TAMXV and UVBF at 11 + 0 to 13 + 6 weeks' gestation identify fetuses at risk of developing IUGR among pregnancies with low levels of PAPP-A.

Database: Medline

44. Distinction between fetal growth restriction and small for gestational age newborn weight enhances the prognostic value of low PAPP-A in the first trimester.

Author(s): Conserva, V; Signaroldi, M; Mastroianni, C; Stampalija, T; Ghisoni, L; Ferrazzi, E

Source: Prenatal diagnosis; Oct 2010; vol. 30 (no. 10); p. 1007-1009

Publication Date: Oct 2010

Publication Type(s): Letter

PubMedID: 20721875

Available at Prenatal diagnosis - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Database: Medline

45. Low maternal PAPP-A is associated with small-for-gestational age newborns and stillbirths.

Author(s): Marttala, Jaana; Peuhkurinen, Sini; Laitinen, Paivi; Gissler, Mika; Nieminen, Pentti; Ryynanen, Markku

Source: Acta obstetricia et gynecologica Scandinavica; Sep 2010; vol. 89 (no. 9); p. 1226-1228

Publication Date: Sep 2010

Publication Type(s): Journal Article

PubMedID: 20590503

Available at Acta obstetricia et gynecologica Scandinavica - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract: We investigated the association of first trimester low maternal serum pregnancy-associated plasma protein-A (PAPP-A) levels with small-for-gestational age (SGA) newborns and stillbirths (SBs) in a retrospective national population-based register study. The study group comprised 921 women with the lowest 5% PAPP-A levels (0.3 MoM. In the study group there were 35 (3.8%) and in the control group 213 SGA newborns (1.1%), respectively (OR, 3.41; 95% CI, 2.37-4.91). There were 9 (1.0%) and 51 (0.3%) cases of SBs in the study and control groups, respectively (p < 0.002; OR, 3.59; 95% CI, 1.76-7.32). Low PAPP-A is a risk factor for SGA and SB.

Database: Medline

46. The relationship between first trimester fetal growth, pregnancy-associated plasma protein A levels and birthweight

Author(s): Habayeb O.; Hackett G.A.; Lees C.C.; Daemen A.; De Moor B.; Timmerman D.; Bourne T.

Available at Prenatal diagnosis - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract: Objective: We sought to define the relationship between first trimester fetal growth, pregnancy-associated plasma protein A (PAPP-A) levels and birthweight. Methods: Two-hundred and one women with repeat first trimester crown-rump length (CRL) measurements were included. In 194, the first trimester PAPP-A value was known and in 169 there was complete data including birthweight. Fetal growth curves were derived using functional linear discriminant analysis (FLDA) and growth compared between those with 90th percentile PAPP-A multiple of median (MoM) levels and birthweight percentiles. Results: Median maternal age was 35 years, gestation at PAPP-A sampling and of first scan was 11 weeks. Median delivery gestation was 40 weeks and birthweight 3425 g. There was no association between first trimester fetal CRL growth and either PAPP-A MoM percentile or birthweight percentile. There was a significant positive correlation between PAPP-A MoM and birthweight percentile ($p = 0.0004$). Conclusions: First trimester fetal growth rate is not related to birthweight percentile or first trimester PAPP-A levels. Irrespective of gestation, a low PAPP-A is associated with delivery of a smaller baby, and a high PAPP-A with a larger baby. Copyright © 2010 John Wiley & Sons, Ltd.

Database: EMBASE

47. Low PAPP-A in the first trimester is associated with reduced fetal growth rate prior to gestational week 20.

Author(s): Salvig, J D; Kirkegaard, I; Winding, T N; Henriksen, T B; Tørring, N; Uldbjerg, N

Available at Prenatal diagnosis - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVETo evaluate the association between maternal pregnancy-associated plasma protein-A (PAPP-A) and fetal growth from the first to the second trimester.METHODSA prospective cohort study including 8347 pregnant women attending prenatal care at Aarhus University Hospital were conducted. PAPP-A was measured during 8 to 14 gestational weeks. Fetal growth between the two scans in the first and second trimesters was estimated by (GA(20)- GA(12))/Days(calendar), where GA(12) reflects gestational age in days calculated from crown-rump length at a 12-week scan, GA(20) reflects gestational age in days calculated from biparietal diameter at a 20-week scan, and Days(calendar) reflects the number of calendar days between the two scans.RESULTSFetal growth rate from the first to the second trimester was correlated with PAPP-A, with a regression coefficient of 0.009 (95% CI, 0.007-0.012, P < 0.001). PAPP-A below 0.30 MoM was associated with a fetal growth rate below the tenth centile, with an adjusted OR of 2.05 (95% CI, 1.24-3.38).CONCLUSIONLow levels of PAPP-A are associated not only with low birth weight at term but also with slower fetal growth prior to 20 weeks of gestation.

Database: Medline

48. Low PAPPA-A and neonatal outcomes

Author(s): Quezada Rojas M.S.; Vizcaino Martinez A.; Carretero Lucena P.; Blazquez Ruiz A.R.; Fresneda Jaimez M.D.; Padilla Vinuesa C.

Abstract: Brief introduction: Recent research conclude that the biochemical markers can have influence in neonatal outcomes. There is a relation between a low Papp-A (<0.3 MoM)in the chromosomal abnormalities screening in the first trimester and a low weight of the newborns. Our main aim is to check if this condition appears in our population with a low PAPP-A. Materials and Methods: We study 206 pregnant women who had a low PAPP-A (<0.3 MoM) in the chromosomal abnormalities screening in the first trimester. Descriptive Study Clinical cases or summary results: From the 206 women with low PAPP-A, 113 had a high risk of chromosomal abnormalities, from this 113 pregnants, 75 had normal cariotype and 17 had an abnormal results: trisomy 21 (9), trisomy 13 (2), trisomy 18 (6). From the 206 women with low PAPP-A, 17 had a termination, 6 had a late miscarriage, 2 had fetal death, and 2 still pregnant and 126 had live-birth babies. The other 49 pregnant women had delivery in other hospital From the 126 women with low PAPP-A who had delivery in our hospital, 6 cases were CIR (4,8%), 14 cases (11,1%) were below P10, 27 cases (21.4%) were between P10-25, and 76 had a normal weight between P25-75. Conclusions: Low PAPP A is a useful marker to predict an adverse perinatal outcome. In fetus with normal kariotype and low PAPP-A, it would be advisable to make a antenatal surveillance as a scan at 28 weeks pregnancy in order to improve the diagnostic accuracy of intrauterine growth restriction.

Database: EMBASE

49. The impact of first-trimester serum free beta-human chorionic gonadotropin and pregnancy-associated plasma protein A on the diagnosis of fetal growth restriction and small for gestational age infant.

Author(s): Montanari, Laura; Alfei, Alessandro; Albonico, Giulia; Moratti, Remigio; Arossa, Alessia; Beneventi, Fausta; Spinillo, Arsenio

Source: Fetal diagnosis and therapy; 2009; vol. 25 (no. 1); p. 130-135

Publication Date: 2009

Publication Type(s): Journal Article

PubMedID: 19279389

Available at Fetal Diagnosis and Therapy - from ProQuest (Hospital Premium Collection) - NHS Version

Abstract:OBJECTIVETo evaluate the risk of fetal growth restriction (FGR) associated with first-trimester maternal serum concentrations of pregnancy-associated plasma protein A (PAPP-A) and free beta-human chorionic gonadotropin (beta-hCG).METHODSA longitudinal study of 2,178 women who underwent first-trimester evaluation of serum PAPP-A and free beta-hCG. FGR was defined as a decrement of the fetal abdominal circumference to below the 10th percentile of our standard growth curve in the presence of Doppler signs of impaired placental perfusion. Logistic regression was used to compute multivariable odds ratios and the estimated prevalences of outcomes associated with first-trimester serum marker concentrations.RESULTSThe prevalences of small for gestational age (SGA, <10th percentile birth-weight) neonates and FGR were significantly higher among women with serum PAPP-A concentrations below the 10th percentile than in controls: 40/206 compared to 183/1,928, for SGA, adjusted odds ratio = 2.1, 95% confidence intervals (CI) 1.4-3.03; 24/75 compared to 182/1,900, for FGR, adjusted odds ratio = 3.9, 95% CI 2.3-6.5. The adjusted prevalences of FGR and SGA among women with simultaneous low first-trimester values of PAPP-A and free beta-hCG were 0.21 (95% CI 0.13-0.33) and 0.26 (95% CI 0.17-0.36), respectively.CONCLUSIONLow first-trimester maternal serum PAPP-A concentrations are significantly associated with reduced fetal size and increased risk of FGR with Doppler signs of impaired placental perfusion.

Database: Medline

50. First trimester pregnancy associated plasma protein-A as a marker for poor pregnancy outcome in patients with early-onset fetal growth restriction.

Author(s): Fox, Nathan S; Chasen, Stephen T

Source: Prenatal diagnosis; Dec 2009; vol. 29 (no. 13); p. 1244-1248

Publication Date: Dec 2009

Publication Type(s): Journal Article

PubMedID: 19862778

Available at Prenatal diagnosis - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVETo determine whether pregnancy associated plasma protein-A (PAPP-A) can be used to identify pregnancies at risk for poor perinatal outcomes among patients with second trimester fetal growth restriction (FGR).METHODSWe analyzed outcomes for singleton pregnancies of patients with evidence of FGR in the second trimester who also had first trimester serum PAPP-A measured for aneuploidy risk assessment. We excluded pregnancies with aneuploidy, major anomalies, fetal infection, or second trimester premature rupture of membranes (PPROM).RESULTSOne hundred and ninety eight pregnancies with second trimester FGR and first trimester serum PAPP-A measurements were identified. PAPP-A below the fifth percentile was associated with an increased rate of third trimester SGA (50% vs 11%, p = 0.012), preterm birth (33.3% vs 8%, p = 0.039), NICU admission (33.3% vs 8%, p = 0.039), intrauterine or neonatal death (20% vs 0%, p = 0.002), smaller median birth weight (2975g vs 3085g, p = 0.026), and earlier median gestational age at delivery (38.14 weeks vs 39.86 weeks, p = 0.004). PAPP-A values below the 10th percentile and below the 25th percentile were also associated with poor outcomes.CONCLUSIONPAPP-A appears to be a useful marker for neonatal outcome in patients diagnosed with second trimester FGR.

Database: Medline

51. The efficiency of first-trimester serum analytes and maternal characteristics in predicting fetal growth disorders.

Author(s): Goetzinger, Katherine R; Singla, Ashima; Gerkowicz, Sabrina; Dicke, Jeffrey M; Gray, Diana L; Odibo, Anthony O

Source: American journal of obstetrics and gynecology; Oct 2009; vol. 201 (no. 4); p. 412

Publication Date: Oct 2009

Publication Type(s): Journal Article

PubMedID: 19716535

Abstract:OBJECTIVETo evaluate the association between first-trimester serum analytes, pregnancy-associated plasma protein A and free beta-human chorionic gonadotropin, and fetal growth disorders, and to determine whether a prediction model for these growth disorders can be developed.STUDY DESIGNRetrospective cohort study of patients seen for first-trimester aneuploidy screening. Pregnancy-associated plasma protein A and free beta-human chorionic gonadotropin multiples of the median were evaluated for association with small- and large-for-gestational-age infants in combination with maternal characteristics. Univariate and backward stepwise logistic regression analyses were performed and the area under the receiver-operator curves used to determine the best prediction models.RESULTSNeither pregnancy-associated plasma protein A nor free beta-human chorionic gonadotropin levels were associated with an increased risk of large-for-gestational-age infants. For small-for-gestational-age infants, the final model included black race, free beta-human chorionic gonadotropin multiples of the median >90th percentile, and pregnancy-

associated plasma protein A multiples of the median <5th percentile as significant predictors (area under the curve = 0.58).CONCLUSIONLow pregnancy-associated plasma protein A and high free beta-human chorionic gonadotropin levels are associated with a small-for-gestational-age growth pattern; however, additional factors to improve the prediction model are needed.

Database: Medline

52. Pregnancy outcome in the setting of extremely low first trimester PAPP-A levels.

Author(s): Scott, Fergus; Coates, Anne; McLennan, Andrew

Source: The Australian & New Zealand journal of obstetrics & gynaecology; Jun 2009; vol. 49 (no. 3); p. 258-262

Publication Date: Jun 2009

Publication Type(s): Journal Article

PubMedID: 19566556

Available at Australian and New Zealand Journal of Obstetrics and Gynaecology - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:BACKGROUNDSerum pregnancy-associated plasma protein-A (PAPP-A) is part of first trimester Down syndrome screening. Low levels have been associated with adverse outcome as well as chromosomal abnormality.AIMSTo assess the incidence of adverse outcome when PAPP-A levels are at or below 0.2 multiples of the median (MoM).METHODSData on consecutive patients attending a first trimester screening program were collected. Those with PAPP-A levels < or = 0.2 MoM were divided into three groups: < or = 0.1 MoM; 0.11-0.15 MoM; and 0.16-0.2 MoM.RESULTSScreening 44 535 patients resulted in 197 with PAPP-A levels < or = 0.2 MoM. The incidence of karyotypic abnormality increased with decreasing PAPP-A levels. In the absence of chromosome abnormality, pregnancy outcomes were defined as 'normal' in at least 30% and 'good' in at least 60%, with both percentages increasing as the PAPP-A level rose. The PAPP-A levels were significantly lower in the group with a poor outcome. The incidence of prematurity was similar in the three groups, but higher than the statewide average, while the incidence of extreme prematurity appeared to be related to reducing PAPP-A levels. The incidence of growth restriction in the three groups was similar, but was still double the incidence in the normal population.CONCLUSIONIf the PAPP-A level is < or = 0.2 MoM and the karyotype is normal, there is an increased risk of adverse outcome. Even with PAPP-A below 0.1 MoM, a good outcome can be expected in 60% of cases. Careful morphological assessment is suggested and later monitoring of fetal growth and well-being.

Database: Medline

53. Obstetrical Complications Associated With Abnormal Maternal Serum Markers Analytes

Author(s): Gagnon A.; Langlois S.; Wilson R.D.; Douglas Wilson R.; Audibert F.; Desilets V.A.; Allen V.M.; Blight C.; Brock J.-A.; Johnson J.-A.; Summers A.; Wyatt P.

Abstract: Objective: To review the obstetrical outcomes associated with abnormally elevated or decreased level of one or more of the most frequently measured maternal serum marker analytes used in screening for aneuploidy. To provide guidance to facilitate the management of pregnancies that have abnormal levels of one of more markers and to assess the usefulness of these markers as a screening test. Options: Perinatal outcomes associated with abnormal levels of maternal serum markers analytes are compared with the outcomes of pregnancies with normal levels of the same analytes or the general population. Evidence: The Cochrane Library and Medline were searched for English-language articles published from 1966 to February 2007, relating to maternal serum markers and perinatal outcomes. Search terms included PAPP-A (pregnancy associated plasma protein A), AFP (alphafetoprotein), hCG (human chorionic gonadotropin), estriol, unconjugated estriol, inhibin, inhibin-A, maternal serum screen, triple marker screen, quadruple screen, integrated prenatal screen, first trimester screen, and combined prenatal screen. All study types were reviewed. Randomized controlled trials were considered evidence of the highest quality, followed by cohort studies. Key individual studies on which the recommendations are based are referenced. Supporting data for each recommendation are summarized with evaluative comments and references. The evidence was evaluated using the guidelines developed by the Canadian Task Force on Preventive Health Care. Values: The evidence collected was reviewed by the Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada. Benefits, Harms, and Costs: The benefit expected from this guideline is to facilitate early detection of potential adverse pregnancy outcomes when risks are identified at the time of a maternal serum screen. It will help further stratification of risk and provide options for pregnancy management to minimize the impact of pregnancy complications. The potential harms resulting from such practice are associated with the so called false positive (i.e., uncomplicated pregnancies labelled at increased risk for adverse perinatal outcomes), the potential stress associated with such a label, and the investigations performed for surveillance in this situation. No cost-benefit analysis is available to assess costs and savings associated with this guideline. Summary Statements: 1.An unexplained level of a maternal serum marker analyte is defined as an abnormal level after confirmation of gestational age by ultrasound and exclusion of maternal, fetal, or placental causes for the abnormal level. (III)2.Abnormally elevated levels of serum markers are associated with adverse pregnancy outcomes in twin pregnancies, after correction for the number of fetuses. Spontaneous or planned mutifetal reductions may result in abnormal elevations of serum markers. (II-2). Recommendations: 1.In the first trimester, an unexplained low PAPP-A (2.5 MoM), hCG (> 3.0 MoM), and/or inhibin-A (>=22.0 MoM) or a decreased level of maternal serum AFP (< 0.25 MoM) and/or unconjugated estriol (< 0.5 MoM) are associated with an increased frequency of adverse obstetrical outcomes, and, at present, no specific protocol for treatment is available. (II-2A)2.Pregnant woman with an unexplained elevated PAPP-A or hCG in the first trimester and an unexplained low hCG or inhibin-A and an unexplained elevated unconjugated estriol in the second trimester should receive normal antenatal care, as this pattern of analytes is not associated with adverse perinatal outcomes. (II-2A)3.The combination of second or third trimester placenta previa and an unexplained elevated maternal serum AFP should increase the index of suspicion for placenta accreta, increta, or percreta. (II-2B) An assessment (ultrasound, MRI) of the placental-uterine interface should be performed. Abnormal invasion should be strongly suspected, and the planning of delivery location and technique should be done accordingly. (III-C)4.A prenatal consultation with the medical genetics department is recommended for low unconjugated

estriol levels (<0.3 MoM), as this analyte pattern can be associated with genetic conditions. (II-2B)5.The clinical management protocol for identification of potential adverse obstetrical outcomes should be guided by one or more abnormal maternal serum marker analyte value rather than the false positive screening results for the trisomy 21 and/or the trisomy 18 screen. (II-2B)6.Pregnant woman who are undergoing renal dialysis or who have had a renal transplant should be offered maternal serum screening, but interpretation of the result is difficult as the level of serum hCG is not reliable. (II-2A)7.Abnormal maternal uterine artery Doppler in association with elevated maternal serum AFP, hCG, or inhibin-A or decreased PAPP-A identifies a group of women at greater risk of IUGR and gestational hypertension with proteinuria. Uterine artery Doppler measurements may be used in the evaluation of an unexplained abnormal level of either of these markers. (II-2B)8.Further research is recommended to identify the best protocol for pregnancy management and surveillance in women identified at increased risk of adverse pregnancy outcomes based on an abnormality of a maternal serum screening analyte. (III-A)9.In the absence of evidence supporting any specific surveillance protocol, an obstetrician should be consulted in order to establish a fetal surveillance plan specific to the increased obstetrical risks (maternal and fetal) identified. This plan may include enhanced patient education on signs and symptoms of the most common complications, increased frequency of antenatal visits, increased ultrasound (fetal growth, amniotic fluid levels), and fetal surveillance (biophysical profile, arterial and venous Doppler), and cervical length assessment. (III-A)10.Limited information suggests that, in women with elevated hCG in the second trimester and/or abnormal uterine artery Doppler (at 22-24 weeks), low-dose aspirin (60-81 mg daily) is associated with higher birthweight and lower incidence of gestational hypertension with proteinuria. This therapy may be used in women who are at risk. (II-2B)11.Further studies are recommended in order to assess the benefits of low-dose aspirin, low molecular weight heparin, or other therapeutic options in pregnancies determined to be at increased risk on the basis of an abnormal maternal serum screening analyte. (III-A)12.Multiple maternal serum markers screening should not be used at present as a population-based screening method for adverse pregnancy outcomes (such as preeclampsia, placental abruption, and stillbirth) outside an established research protocol, as sensitivity is low, false positive rates are high, and no management protocol has been shown to clearly improve outcomes. (II-2D) When maternal serum screening is performed for the usual clinical indication (fetal aneuploidy and/or neural tube defect), abnormal analyte results can be utilized for the identification of pregnancies at risk and to direct their clinical management. (II-2B) Further studies are recommended to determine the optimal screening method for poor maternal and/or perinatal outcomes. (III-A).Copyright © 2008 Society of Obstetricians and Gynaecologists of Canada.

Database: EMBASE

54. First trimester maternal serum PAPP-A, beta-hCG and ADAM12 in prediction of small-for-gestational-age fetuses.

Author(s): Pihl, Kasper; Larsen, Torben; Krebs, Lone; Christiansen, Michael

Source: Prenatal diagnosis; Dec 2008; vol. 28 (no. 12); p. 1131-1135

Publication Date: Dec 2008

Publication Type(s): Journal Article Evaluation Studies

PubMedID: 19003798

Available at Prenatal diagnosis - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVETo examine the ability of predicting fetuses being small-for-gestational-age (SGA) at delivery with the maternal serum markers pregnancy-associated plasma protein A (PAPP-A), beta-human chorionic gonadotrophin (beta-hCG) and A disintegrin and metalloprotease 12 (ADAM12) in first trimester.METHODSIn all,36 cases being SGA (birth weight < 5th centile) and 108 controls being non-SGA were matched on ethnicity (only Caucasians), smoking status (only nonsmokers), body mass index (BMI), age and parity. Stored blood samples from PAPP-A and beta-hCG testing obtained at gestational age (GA) of 8 weeks to 13 weeks and 6 days were analyzed for ADAM12. Median MoM values were compared using Mann-Whitney test. Monte Carlo estimation and receiver-operator-characteristics curves were used to asses screening performance.RESULTSMedian MoM values of PAPP-A (0.64 vs 1.02, $p < 0.001$), beta-hCG (0.74 vs 1.04, $p = 0.007$) and ADAM12 (0.74 vs 0.97, $p = 0.004$) were significantly reduced in cases compared to controls. The combination of PAPP-A MoM and beta-hCG MoM yielded a detection rate (DR) for SGA of 26% for a 5% false-positive rate (FPR). Addition of ADAM12 only improved (28% DR for a 5% FPR) screening performance modestly.CONCLUSIONEarly prediction of fetuses being SGA is feasible with the combination of first trimester PAPP-A, beta-hCG and ADAM12. Screening performance is approaching clinical relevance. The inclusion of further markers is an attractive option.

Database: Medline

55. Low levels of maternal serum PAPP-A in early pregnancy and the risk of adverse outcomes.

Author(s): Spencer, C A; Allen, V M; Flowerdew, G; Dooley, K; Dodds, L

Source: Prenatal diagnosis; Nov 2008; vol. 28 (no. 11); p. 1029-1036

Publication Date: Nov 2008

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 18925584

Available at Prenatal diagnosis - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVESTo determine if low maternal serum level of pregnancy associated plasma protein A (PAPP-A) measured in early pregnancy can predict adverse pregnancy outcomes and to examine the gestational age (GA) sampling interval for these outcomes.METHODSThis was a nested case-control study from a prospective cohort of women recruited at 0.4 MoM). However, performance as a screening test was poor [sensitivity=38.7%; specificity=81.6%; positive likelihood ratio (LR)=2.1; negative LR=0.75]. In the adjusted model, the 10- to 14-week GA period was the only time period where low PAPP-A was significantly associated with adverse outcomes.CONCLUSIONSWomen with a low PAPP-A early in their pregnancy have twice the risk of an adverse outcome, though PAPP-A as a one-time single marker test has limited value.

Database: Medline

56. First-trimester pregnancy-associated plasma protein A and subsequent abnormalities of fetal growth.

Author(s): Peterson, Suzanne E; Simhan, Hyagriv N

Source: American journal of obstetrics and gynecology; May 2008; vol. 198 (no. 5); p. e43

Publication Date: May 2008

Publication Type(s): Journal Article

PubMedID: 18295168

Abstract:OBJECTIVEThe purpose of this study was to describe the relationship between first-trimester pregnancy-associated plasma protein A (PAPP-A) and birthweight along its continuum and at its extremes.STUDY DESIGNThis was a retrospective cohort of 1371 women who underwent first-trimester screening for fetal aneuploidy and who delivered at our hospital.RESULTSFirst-trimester PAPP-A has a positive relationship with birthweight. As PAPP-A decreases, the risk of small-for-gestational-age (SGA) infants increases. PAPP-A of 90% were associated with an adjusted odds ratio for birthweight of >4500 g of 2.9 (95% CI, 1.02-8.17; P = 0.046).CONCLUSIONFirst-trimester PAPP-A is a marker of placental function that correlates with birthweight along its continuum and at its extremes. The strong association between low PAPP-A and SGA warrants further investigation of its usefulness as a screening tool.

Database: Medline

57. Association between birth weight and first-trimester free beta-human chorionic gonadotropin and pregnancy-associated plasma protein A.

Author(s): Canini, Silvana; Prefumo, Federico; Pastorino, Daniela; Crocetti, Lucia; Afflitto, Calogero Gallo; Venturini, Pier Luigi; De Biasio, Pierangela

Source: Fertility and sterility; Jan 2008; vol. 89 (no. 1); p. 174-178

Publication Date: Jan 2008

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 17509577

Abstract:STUDY OBJECTIVETo assess the relationship between first-trimester maternal serum PAPP-A and free beta-hCG and birth weight.DESIGNObservational study.SETTINGTeaching hospital.PATIENT(S)Singleton pregnancies (n = 1,630) at 10-14 weeks of gestation.INTERVENTION(S)Fluorimetric immunoassays for maternal serum pregnancy-associated plasma protein A (PAPP-A) and free beta-hCG.MAIN OUTCOME MEASURE(S)Customized birth weight percentiles, calculated taking into account maternal height, weight, ethnic origin, parity, smoking status, and fetal gender.RESULT(S)There was a significant positive correlation between birth weight and PAPP-A, but not free beta-hCG levels. Maternal serum levels of PAPP-A were significantly lower in small-for-gestation (SGA) newborns than in control subjects and were significantly higher in large-for-gestation (LGA) newborns than in control subjects. Maternal serum free beta-hCG levels were lower in pregnancies complicated by pre-eclampsia than in normotensive ones. Multivariable analysis found PAPP-A to be an independent predictor of absolute birth weight, SGA, and LGA. Free beta-hCG was found to be an independent predictor of gestational hypertension and pre-eclampsia. Neither of the two markers was associated with preterm delivery.CONCLUSION(S)Maternal serum PAPP-A levels in the late first trimester of pregnancy are associated with subsequent fetal growth (including both physiologic variation and abnormal growth), and decreased free beta-hCG is more predictive of hypertensive disorders of pregnancy.

Database: Medline

58. First-trimester biochemical markers of aneuploidy and the prediction of small-for-gestational age fetuses.

Author(s): Spencer, K; Cowans, N J; Avgidou, K; Molina, F; Nicolaides, K H

Source: Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology; Jan 2008; vol. 31 (no. 1); p. 15-19

Publication Date: Jan 2008

Publication Type(s): Research Support, Non-u.s. Gov't Multicenter Study Journal Article Evaluation Studies

PubMedID: 17999381

Available at Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVESTo examine the clinical utility of the first-trimester biochemical markers of aneuploidy in their ability to predict subsequent delivery of a small-for-gestational age (SGA) infant.METHODSWe examined singleton pregnancies with no chromosomal abnormality and with complete outcome data that had undergone screening for trisomy 21 by a combination of fetal nuchal translucency (NT) thickness and maternal serum free beta-human chorionic gonadotropin (beta-hCG) and pregnancy-associated plasma protein-A (PAPP-A) at 11 + 0 and 13 + 6 weeks' gestation. The biochemical markers were converted to multiples of the expected normal median (MoM) for a pregnancy of the same gestation. The association between free beta-hCG and PAPP-A and the incidence of SGA were assessed by comparing the relative incidence at MoM cut-offs and birth-weight centile cut-offs. At various marker levels the likelihood ratios (LR) for SGA were also calculated after excluding other adverse pregnancy complications.RESULTSThere were 46,262 pregnancies resulting in live births with birth weight at or above the 10(th) centile, and 3,539 below the 10(th) centile for gestation (SGA). There was a significant inverse association between the risk for SGA and maternal serum PAPP-A MoM but not free beta-hCG MoM. At the 5(th) centile of the normal outcome group for PAPP-A (0.415 MoM) the odds ratios for SGA below the 10(th), 5(th) and 3(rd) centiles of normal were 2.70, 3.21 and 3.66 and the respective detection rates for SGA were 12.0%, 14.0% and 16.0%.CONCLUSIONSLow levels of maternal serum PAPP-A are associated, in the absence of an abnormal karyotype, with an increased risk for subsequent delivery of an SGA infant.

Database: Medline

59. Prediction of birth weight by fetal crown-rump length and maternal serum levels of pregnancy-associated plasma protein-A in the first trimester.

Author(s): Leung, T Y; Sahota, D S; Chan, L W; Law, L W; Fung, T Y; Leung, T N; Lau, T K

Available at Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVETo determine whether the first trimester crown-rump length (CRL), maternal serum levels of pregnancy-associated plasma protein A (PAPP-A) and free beta-human chorionic gonadotropin (fbeta-hCG) are independent predictors of birth weight.METHODSThis was an observational study over 1.5 years in Chinese patients who underwent first-trimester combined screening for Down syndrome in a University fetal medicine unit. After excluding cases with multiple pregnancies, congenital malformations and in-utero deaths, the relationship between fetal CRL (expressed as standardized Z-score (Z-CRL)), maternal PAPP-A and fbeta-hCG levels (expressed as log(10) of multiples of the median) and birth weight (Z-BW) were analyzed by Pearson's correlation test followed by multiple regression to check for their independency. The predictive power of the independent predictors for small-for-gestational age (SGA, defined as birth weight < 10(th) centile) was then assessed using receiver-operating characteristics (ROC) curves, and the likelihood ratios were derived.RESULTSA total of 2760 cases were included. Z-CRL, log(10) PAPP-A(MoM), and log(10) fbeta-hCG were positively correlated with Z-BW (P < 0.0001), but only Z-CRL and log(10) PAPP-A(MoM) were independent predictors (P < 0.0001). The areas under the ROC curves of PAPP-A(MoM) and Z-CRL were 0.608 and 0.593, respectively (P < 0.0001). Likelihood ratios increased with decreasing PAPP-A(MoM) and Z-CRL, but were around 1 when the markers were at or above the mean.CONCLUSIONFirst-trimester CRL and PAPP-A are independent factors that influence final birth weight. The lower the PAPP-A and the smaller the CRL, the higher the risk of a fetus becoming SGA. However, their predictive powers are not sufficiently good for them to be used alone for SGA screening.

Database: Medline

60. Is there a relationship between cord blood pregnancy-associated plasma protein-A and birth weight and length?

Author(s): Senses, Dursun A; Coskun, Abdurrahman; Kiseli, Mine; Berberoglu, Murat; Kandemir, Omer; Yalvac, Serdar; Duran, Sadik

Abstract:BACKGROUNDInfants whose mothers had low serum pregnancy-associated plasma protein-A (PAPP-A) in the first trimester were observed to have intrauterine growth retardation.AIMSuggesting that PAPP-A plays an important role in the availability and activity of insulin-like growth factors (IGFs), which affect growth, we aimed to investigate cord blood PAPP-A levels of infants with different birth lengths and weights. STUDY DESIGN AND OUTCOME MEASURES: The study included 97 full-term, live-birth neonates. After birth, their lengths and weights were measured. Cord blood PAPP-A levels were measured with an ultra sensitive enzyme-linked immunosorbent assay (ELISA).RESULTSThere was a significant negative correlation between cord blood PAPP-A levels and birth weight (r=-0.23; P=0.023) and length (r=-0.24; P=0.016). Using the classification made according to their length, it was found that newborns with short lengths had significantly higher mean PAPP-A levels than neonates with normal and long lengths (P=0.022; P=0.002, respectively), whereas the difference between infants with normal lengths and infants with long lengths was not found to be statistically significant (P>0.05). On the other hand, there was a difference between the mean PAPP-A levels of the neonate groups classified according to weight; however, these differences were not statistically significant (P>0.05).CONCLUSIONWe concluded that increased cord blood PAPP-A levels were associated with birth length and weight decreases; however, PAPP-A levels affected birth length more than birth weight.

Database: Medline

61. First-trimester ADAM12 and PAPP-A as markers for intrauterine fetal growth restriction through their roles in the insulin-like growth factor system.

Author(s): Cowans, Nicholas J; Spencer, Kevin

Available at Prenatal diagnosis - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:BACKGROUNDPAPP-A is a marker used as part of the most effective method of screening for chromosomal anomalies in the first trimester. ADAM12 is a recently discovered pregnancy associated member of the ADAM (a multidomain glycoprotein metalloprotease) family. Recently, ADAM12 has been shown as a potential marker for early screening for chromosomal anomalies. Both PAPP-A and ADAM12 have been identified as proteases to insulin-like growth factor binding proteins. In this role, they may have a regulatory function in controlling the amount of free bioactive insulin-like growth factor (IGF). We therefore wish to examine if the levels of either of these proteases are related to various growth related adverse pregnancy outcomes.MATERIALS AND METHODSPAPP-A and ADAM12 were measured in a subset of samples collected at 11 to 14 weeks as part of an OSCAR clinic screening for chromosomal anomalies. Follow-up of pregnancies screened between September 1999 and August 2003 identified 1705 pregnancies with an outcome of intrauterine fetal demise on or after 24 weeks, preterm delivery at 24-34 weeks or 35-36 weeks, very low birthweight (4.5 kg), and birth weight below the 3rd or 5th or 10th centile for gestation. A series of 414 normal outcome pregnancies constituted the control group. Marker levels were adjusted for gestation and maternal weight and the log MoM of the markers were compared using t-test of unequal variance between the control group and the various adverse outcome groups.RESULTSADAM12 and PAPP-A concentrations were reduced in low for gestational age birth weights and in all births with weights below 2.5 kg. There was a linear relationship between the severity of the IUGR and the decrease in PAPP-A and ADAM12. In the larger babies, only ADAM12 was found to be significantly increased in babies above the 90th centile of weight for gestation.CONCLUSIONSThe results of our study are compatible with the proposed role of ADAM12 and PAPP-A in promoting growth and development by breaking down IGF binding proteins and causing the release of free IGF for uptake into cells to promote growth. In those cases that eventually result in poor fetal growth, levels of PAPP-A and ADAM12 at 11-14 weeks are significantly lower than normal-in this instance, lowered PAPP-A and ADAM12 would result in less free IGF being available for cell uptake and growth stimulation. Further studies may elucidate if screening using such modalities can lead to new potential treatments for poorly growing fetuses.

Database: Medline

62. First-trimester maternal serum levels of placental hormones are independent predictors of second-trimester fetal growth parameters.

Author(s): Leung, T Y; Chan, L W; Leung, T N; Fung, T Y; Sahota, D S; Lau, T K

Available at Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVETo determine whether first-trimester maternal serum levels of pregnancy-associated plasma protein-A (PAPP-A) and free beta-human chorionic gonadotropin (fbeta-hCG) are independent predictors of second-trimester fetal growth parameters.METHODSThis was a cohort study over a 1-year period involving 594 Chinese women who underwent both first-trimester combined screening for Down syndrome and a routine second-trimester ultrasound examination. Maternal PAPP-A and fbeta-hCG levels (expressed in log(10) of multiples of median (MoM)), crown-rump length (CRL) (expressed in standardized Z-score (Z-CRL)), and maternal height and weight, were correlated with the Z-score of biparietal diameter (Z-BPD), femur length (Z-FL) and abdominal circumference (Z-AC) measured in the second trimester, using the Pearson test, followed by multiple regression analysis.RESULTSZ-BPD, Z-FL and Z-AC were positively correlated with log(10) PAPP-A MoM, CRL and maternal height (all $P < 0.05$), while log(10) fbeta-hCG MoM was negatively correlated with Z-AC ($P < 0.05$). After controlling for the effects of CRL, maternal height and weight, log(10) PAPP-A MoM was found to be an independent positive predictor of Z-FL ($r = 0.797$, $P < 0.001$) and Z-AC ($r = 0.305$, $P = 0.049$), and log(10) fbeta-hCG MoM was an independent negative predictor of Z-FL ($r = -0.381$, $P = 0.023$) and Z-AC ($r = -0.418$, $P = 0.002$). Neither hormonal level was related to Z-BPD.CONCLUSIONSFirst-trimester PAPP-A and fbeta-hCG are independent factors that influence subsequent fetal growth. PAPP-A level is positively correlated with FL and AC in the second trimester, while fbeta-hCG level is negatively correlated with them. However, BPD is not affected by either of the hormones.

Database: Medline

63. Pregnancy-associated plasma protein A and alpha-fetoprotein and prediction of adverse perinatal outcome.

Author(s): Smith, Gordon C S; Shah, Imran; Crossley, Jennifer A; Aitken, David A; Pell, Jill P; Nelson, Scott M; Cameron, Alan D; Connor, Michael J; Dobbie, Richard

Available at Obstetrics and gynecology - from Ovid (LWW Total Access Collection 2015 - Q1 with Neurology)

Abstract:OBJECTIVETo describe the association between pregnancy associated plasma protein A (PAPP-A), alpha-fetoprotein (AFP) and adverse perinatal outcome.METHODSWe conducted a multicenter prospective cohort study of 8,483 women attending for prenatal care in southern Scotland between 1998 and 2000. The risk of delivering a small for gestational age infant, delivering preterm, and stillbirth were related to maternal serum levels of PAPP-A and AFP.RESULTSWomen with a low PAPP-A were not more likely to have elevated levels of AFP. Compared with women with a normal PAPP-A and a normal AFP, the odds ratio for delivering a small for gestational age infant for women with a high AFP was 0.9 (95% confidence interval [CI] 0.5-1.6), for women with a low PAPP-A was 2.8 (95% CI 2.0-4.0), and for women with both a high AFP and a low PAPP-A was 8.5 (95% CI 3.6-20.0). The odds ratio for delivering preterm for women with a high AFP was 1.8 (95% CI 1.3-2.7), for women with a low PAPP-A was 1.9 (95% CI 1.3-2.7), and for women with both a low PAPP-A and a high AFP was 9.9 (95% CI 4.4-22.0). These interactions were statistically significant for both outcomes (P = .03 and .04, respectively). There was a nonsignificant trend toward a similar interaction in relation to stillbirth risk. Of the women with the combination of a low PAPP-A and high AFP, 32.1% (95% CI 15.9-52.4) delivered a low birth weight infant.CONCLUSIONLow maternal serum levels of PAPP-A between 10 and 14 weeks and high levels of AFP between 15 and 21 weeks gestation are synergistically associated with adverse perinatal outcome.LEVEL OF EVIDENCEII-2.

Database: Medline

64. Prediction of pregnancy complications by first-trimester maternal serum PAPP-A and free beta-hCG and with second-trimester uterine artery Doppler.

Author(s): Spencer, Kevin; Yu, Christina K H; Cowans, Nicholas J; Otigbah, Chineze; Nicolaides, Kypros H

Available at Prenatal diagnosis - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:BACKGROUNDPrevious studies have shown an association between low first trimester maternal serum free beta-hCG and PAPP-A and subsequent development of pregnancy complications. Similarly, uterine artery Doppler in the late second trimester has shown that high impedance to flow is associated with increased risk for preeclampsia and fetal growth restriction. The objective of this study is to determine whether there is an association between the maternal serum concentration of PAPP-A and free beta-hCG at 11-13(+6) weeks with the uterine artery pulsatility index (PI) at 22-24 weeks, and secondly, to compare the screening characteristics of the two methods in the prediction of adverse pregnancy outcome.METHODSMaternal serum PAPP-A and free beta-hCG at 11-13(+6) weeks and uterine artery PI at 22-24 weeks were measured in 4390 women with singleton pregnancies. Pregnancies with chromosomal defects or fetal anomalies were excluded. The biochemical and Doppler measurements were compared between those with normal outcome and those resulting in spontaneous preterm delivery, pre-eclampsia and fetal growth restriction (FGR). Detection rates using a combination of the biochemical and Doppler measurements were investigated.RESULTSIn the pregnancies resulting in pre-eclampsia (n = 64) and FGR (n = 172), the median PAPP-A was lower (0.844 and 0.813 MoM), the median uterine artery mean PI was higher (1.56 and 1.18) but the median free betahCG was not significantly different (0.923 and 0.933 MoM) than in the normal outcome group. In the preterm delivery group (n = 159), the median free beta-hCG (0.944 MoM) and uterine artery mean PI (1.06) were not significantly different from normal but the median PAPP-A (0.928 MoM) was significantly lower than normal. In screening for pre-eclampsia, the detection rate, for a 5% false-positive rate, was 14.1% for PAPP-A, 54.7% for uterine artery mean PI and 62.1% for a combination of PAPP-A and uterine artery mean PI.CONCLUSIONMaternal serum PAPP-A at 11-13(+6) of gestation is significantly lower in adverse pregnancy outcomes. The combination of first trimester serum PAPP-A and uterine artery mean PI at 22-24 weeks improves the screening efficacy for the prediction of pre-eclampsia.

Database: Medline

65. Can first-trimester maternal serum level of pregnancy-associated plasma protein-A predict subsequent fetal growth restriction?

Author(s): Cheong M.-L.; She B.-Q.; Tsai M.-S.; Chen S.-C.; Lee F.-K.

Source: Taiwanese Journal of Obstetrics and Gynecology; Jun 2005; vol. 44 (no. 2); p. 148-152

Publication Date: Jun 2005

Publication Type(s): Article

Available at Taiwanese Journal of Obstetrics and Gynecology - from Free Medical Journals . com

Abstract: Objective: To evaluate whether the maternal serum level of pregnancy-associated plasma protein-A (PAPP-A) in the first trimester can predict pregnancy complicated by low birth weight (LBW) and fetal growth restriction (FGR). Materials and Methods: This retrospective analysis enrolled 3,089 women with singleton pregnancy who underwent screening for Down syndrome in the first trimester of pregnancy and who delivered at Cathay General Hospital. They were divided into five groups according to the birth weight of their infants: three FGR groups of birth weight less than the 10th, 5th, and 3rd centiles, a LBW group of birth weight less than 2,500 g, and a control group of all other women. Results: The mean multiples of median (MoM) values of PAPP-A were significantly lower in the LBW group (0.98) and the three FGR groups (th centile, 1.03; th centile, 0.96; and rd centile, 0.99) than in the control group (1.15). Women with PAPP-A less than 0.3 MoM, 0.5 MoM or in the 5th centile (0.32 MoM) also had a significantly higher relative risk of pregnancy complicated by LBW and FGR, but the sensitivity of detection was low. The highest sensitivity using a cut-off at 0.5 MoM was 22.5%. Conclusion: Our study demonstrated that a low maternal serum PAPP-A level in the first trimester is associated with pregnancy complicated by LBW and FGR, but the sensitivity was low. As a single marker, PAPP-A is not sufficient to predict LBW and FGR.

Database: EMBASE

66. Association of extreme first-trimester free human chorionic gonadotropin-beta, pregnancy-associated plasma protein A, and nuchal translucency with intrauterine growth restriction and other adverse pregnancy outcomes.

Author(s): Krantz, David; Goetzl, Laura; Simpson, Joe Leigh; Thom, Elizabeth; Zachary, Julia; Hallahan, Terrence W; Silver, Richard; Pergament, Eugene; Platt, Lawrence D; Filkins, Karen; Johnson, Anthony; Mahoney, Maurice; Hogge, W Allen; Wilson, R Douglas; Mohide, Patrick; Hershey, Douglas; Wapner, Ronald; First Trimester Maternal Serum Biochemistry and Fetal Nuchal Translucency Screening (BUN) Study Group

Source: American journal of obstetrics and gynecology; Oct 2004; vol. 191 (no. 4); p. 1452-1458

Publication Date: Oct 2004

Publication Type(s): Journal Article Research Support, U.s. Gov't, P.h.s.

PubMedID: 15507982

Abstract:OBJECTIVEThe purpose of this study was to determine the association between first-trimester trisomy 21 screening markers (free human chorionic gonadotropin-beta [hCG], pregnancy-associated plasma protein A [PAPP-A], and nuchal translucency) and adverse pregnancy outcome.STUDY DESIGNThis was a cohort study of 8012 patients enrolled in a National Institute of Child Health and Human Development-sponsored study of first-trimester trisomy 21 and 18 screening. Trisomy 21 and 18 risk results and individual marker levels in unaffected pregnancies and pregnancies with adverse outcomes were evaluated.RESULTSPAPP-A 99th percentile (OR 3.5, 95% CI 1.1-11.3) were associated with increased risk of preterm delivery before 34 weeks. Increased risk at screening for trisomy 21 and 18 identified 16 of the 29 other chromosomal abnormalities (55%). Low free beta-hCG, low PAPP-A, and increased nuchal translucency were all associated with an increased

rate of fetal abnormality.CONCLUSIONExtreme values of first-trimester free beta-hCG, PAPP-A, and nuchal translucency are all associated with adverse outcomes. The especially high predictive value for IUGR of PAPP-A levels below the 1st percentile suggests that patients within this group may benefit from increased surveillance for this condition.

Database: Medline

67. Second- and third-trimester serum levels of placental proteins in preeclampsia and small-for-gestational age pregnancies.

Author(s): Bersinger, Nick A; Ødegård, Rønnaug A

Source: Acta obstetricia et gynecologica Scandinavica; Jan 2004; vol. 83 (no. 1); p. 37-45

Publication Date: Jan 2004

Publication Type(s): Comparative Study Journal Article

PubMedID: 14678084

Available at Acta obstetricia et gynecologica Scandinavica - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:BACKGROUNDPoor placentation may perpetuate preeclampsia, but the presence of a major placental pathology has been questioned in cases of preeclampsia where the newborn has an appropriate birthweight for gestational age. On the other hand, poor placentation is also observed in the absence of preeclampsia, in pregnancies with small-for-gestational-age (SGA) fetuses. In late gestation, maternal serum levels of placental protein hormones are changed in both preeclampsia and SGA, but no longitudinal pre-onset studies are available for pregnancy-associated plasma protein A (PAPP-A), pregnancy-specific beta1-glycoprotein (SP1) or human placental lactogen (HPL).METHODSIn a nested case-control study we compared maternal serum levels of PAPP-A, SP1, HPL and placenta growth factor (PLGF) at 17, 25 and 33 weeks in pregnancies developing preeclampsia without fetal growth restriction (n = 28), or characterized by a growth-retarded fetus (n = 25), with gestation-matched controls (n = 65). The proteins were quantified using microplate enzyme immunometric assays and the serum levels at 17, 25 and 33 weeks compared between the three groups by nonparametric statistical tests.RESULTSIn pregnancies with subsequent preeclampsia PAPP-A, SP1, HPL and PLGF were reduced at 17 weeks of gestation whereas at 25 and 33 weeks only PLGF remained below the controls. In growth-restricted pregnancies PAPP-A, SP1 and HPL were reduced at 17 weeks, and only HPL continued to be strongly affected thereafter.CONCLUSIONThe reduced serum levels of the placental proteins PAPP-A, SP1 and HPL in the early second trimester (17 weeks) in pregnancies with subsequent preeclampsia or with fetal growth restriction involve an underlying role for the placenta in either pathology independent from the other.

Database: Medline

68. Association between first trimester maternal serum pregnancy associated plasma protein-A and adverse pregnancy outcome.

Author(s): Kwik, Michele; Morris, Jonathan

Available at Australian and New Zealand Journal of Obstetrics and Gynaecology - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:AIMSTo investigate whether low pregnancy associated plasma protein-A (PAPP-A) levels in the first trimester of pregnancy are associated with subsequent intrauterine fetal growth restriction, stillbirth and preterm delivery.METHODSA retrospective review of pregnancy outcomes was undertaken in women who had PAPP-A carried out in the first trimester of pregnancy at the time of nuchal translucency scan. Pregnancy outcomes were assessed by the review of medical records, and postal questionnaires. Delivery details were collected, including livebirth, neonatal birthweight and gestational age at delivery. The chi2 test was used to investigate the association between low first trimester serum PAPP-A levels and adverse fetal outcomes. Unpaired t-test was used for continuous variables. Sensitivities and specificities were then calculated.RESULTSA total of 894 women who had blood collected for PAPP-A were identified, and data was obtained for 827 deliveries. Each had a normal karyotype. There were six intrauterine deaths, 13 babies with birthweights below the 3rd centile, 55 babies weighing below the 10th centile, and 96 women who delivered prematurely. Four of six intrauterine deaths had low PAPP-A levels (<0.5 multiples of the median), with a relative risk of 13.75. Low PAPP-A levels were associated with fetal weight below the 10th centile (P = 0.01) but not the 3rd centile. There was no statistically significant association between low maternal serum PAPP-A levels and preterm delivery.CONCLUSIONAt 11-13 weeks' gestation, low maternal serum PAPP-A levels are associated with fetal death in utero and birthweight below the 10th centile. First trimester PAPP-A may be a useful tool for identifying pregnancies at risk of adverse fetal outcomes.

Database: Medline

69. Decreased first trimester PAPP-A is a predictor of adverse pregnancy outcome.

Author(s): Yaron, Yuval; Heifetz, Sigal; Ochshorn, Yifat; Lehavi, Ofer; Orr-Urtreger, Avi

Available at Prenatal diagnosis - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVELow levels of maternal serum pregnancy associated plasma protein-A (PAPP-A) have been linked to chromosome anomalies such as trisomy 21, 13 and 18, triploidy and sex chromosome aneuploidy. Low levels of PAPP-A have also been implicated in spontaneous miscarriage. The purpose of this study was to evaluate whether low levels of first trimester PAPP-A are predictive of other adverse pregnancy outcomes.STUDY DESIGNThe study included patients with singleton pregnancies who underwent combined first trimester screening using nuchal translucency (NT) and maternal serum free beta-human chorionic gonadotrophin (free beta-hCG) and PAPP-A at 10-13 weeks' gestation. Patients with chromosome aberrations or fetal anomalies were excluded. Serum marker levels were expressed as gestational age-specific multiples of the median (MoMs). The incidences of various adverse pregnancy outcomes (spontaneous preterm labor, fetal growth restriction (FGR), proteinuric and non-proteinuric pregnancy induced hypertension (PIH), intrauterine fetal demise, oligohydramnios, spontaneous miscarriage and placental abruption) were evaluated, according to maternal PAPP-A MoM levels.RESULTSOf the 1622 patients in the study, pregnancy complications were observed in 184 (11.3%). Patients with PAPP-A < or =0.25 MoM had significantly higher rates of FGR (RR = 3.12), proteinuric PIH (RR = 6.09), spontaneous miscarriage (RR = 8.76). No statistically significant differences were noted for other adverse outcomes evaluated Women with PAPP-A < or =0.50 MoM also had significantly higher rates of FGR (RR = 3.30) and spontaneous miscarriage (RR = 3.78).CONCLUSIONSWe conclude that decreased levels of first trimester maternal serum PAPP-A are predictive not only of chromosome anomalies but also of adverse pregnancy outcome.

Database: Medline

70. Early pregnancy levels of pregnancy-associated plasma protein a and the risk of intrauterine growth restriction, premature birth, preeclampsia, and stillbirth.

Author(s): Smith, Gordon C S; Stenhouse, Emily J; Crossley, Jennifer A; Aitken, David A; Cameron, Alan D; Connor, J Michael

Source: The Journal of clinical endocrinology and metabolism; Apr 2002; vol. 87 (no. 4); p. 1762-1767

Publication Date: Apr 2002

Publication Type(s): Research Support, Non-u.s. Gov't Multicenter Study Journal Article

PubMedID: 11932314

Abstract: The risk of adverse perinatal outcome among 8839 women recruited to a multicenter, prospective cohort study was related to maternal circulating concentrations of trophoblast-derived proteins at 8-14 wk gestation. Women with a pregnancy-associated plasma protein A (PAPP-A) in the lowest fifth percentile at 8-14 wk gestation had an increased risk of intrauterine growth restriction [adjusted odds ratio, 2.9; 95% confidence interval (CI), 2.0-4.1], extremely premature delivery (adjusted odds ratio, 2.9; 95% CI, 1.6-5.5), moderately premature delivery (adjusted odds ratio, 2.4; 95% CI, 1.7-3.5), preeclampsia (adjusted odds ratio, 2.3; 95% CI, 1.6-3.3), and stillbirth (adjusted odds ratio, 3.6; 95% CI, 1.2-11.0). The strengths of the associations were similar when the test was performed before 13 wk gestation or between 13 and 14 wk gestation. In contrast, levels of free beta-human CG, another circulating protein synthesized by the syncytiotrophoblast, were not predictive of later outcome in multivariate analysis. PAPP-A has been identified as a protease specific for IGF binding proteins. We conclude that control of the IGF system in the first and early second trimester trophoblast may have a key role in determining subsequent pregnancy outcome.

Database: Medline

71. First trimester maternal serum free beta human chorionic gonadotrophin and pregnancy associated plasma protein A as predictors of pregnancy complications.

Author(s): Ong, C Y; Liao, A W; Spencer, K; Munim, S; Nicolaides, K H

Source: BJOG : an international journal of obstetrics and gynaecology; Oct 2000; vol. 107 (no. 10); p. 1265-1270

Publication Date: Oct 2000

Publication Type(s): Journal Article

PubMedID: 11028579

Available at BJOG : an international journal of obstetrics and gynaecology - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract:OBJECTIVETo examine the value of first trimester maternal serum free beta human chorionic gonadotrophin (beta hCG) and pregnancy associated plasma protein A (PAPP-A) as predictors of pregnancy complications.DESIGNScreening study.SETTINGAntenatal clinics.POPULATIONSingleton pregnancies at 10-14 weeks of gestation.METHODSMaternal serum free beta hCG and PAPP-A were measured at 10-14 weeks of gestation in 5,584 singleton pregnancies. In the 5,297 (94.9%) pregnancies with complete follow up free beta hCG and PAPP-A were compared between those with normal outcome and those resulting in miscarriage, spontaneous preterm delivery, pregnancy induced hypertension or fetal growth restriction and in those with pre-existing or gestational diabetes.RESULTSMaternal serum PAPP-A increased and beta hCG decreased with gestation. The multiple of median maternal serum PAPP-A was significantly lower in those pregnancies resulting in miscarriage, pregnancy induced hypertension, growth restriction and in those with pre-existing or gestational diabetes mellitus, but not in those complicated by spontaneous preterm delivery. The level was < 10th centile of the reference range in

about 20% of the pregnancies that subsequently resulted in miscarriage or developed pregnancy induced hypertension or growth restriction, and in 27% of those that developed gestational diabetes. Maternal serum free beta hCG was < 10th centile of the reference range in about 15% of the pregnancies that subsequently resulted in miscarriage or developed pregnancy induced hypertension or growth restriction, and in 20% of those that developed gestational diabetes.CONCLUSIONLow maternal serum PAPP-A or beta hCG at 10-14 weeks of gestation are associated with subsequent development of pregnancy complications.

Database: Medline

72. Maternal serum levels of free beta-hCG and PAPP-A in the first trimester of pregnancy are not associated with subsequent fetal growth retardation or preterm delivery.

Author(s): Morssink, L P; Kornman, L H; Hallahan, T W; Kloosterman, M D; Beekhuis, J R; de Wolf, B T; Mantingh, A

Available at Prenatal diagnosis - from Wiley Online Library Medicine and Nursing Collection 2017 - NHS

Abstract: The purpose of this case-control study was to examine the association of first-trimester concentrations of free beta-human chorionic gonadotropin (free beta-hCG) and pregnancy-associated plasma protein A (PAPP-A) in maternal serum with subsequent preterm delivery or small-for-gestational age (SGA) fetuses. We collected all the blood samples before chorionic villus sampling in the first trimester. Concentrations of free beta-hCG and PAPP-A were expressed in multiples of the median (MOM) for gestational age. We compared the levels of both analytes in 73 SGA pregnancies (birth weight below the fifth percentile) with those in 292 normal controls, who were matched for gestational age, maternal age, parity, maternal weight, and smoking habits. We also compared the levels in 87 pregnancies with a preterm delivery (delivery before 37 completed weeks) with those in 348 matched controls. The median concentrations of PAPP-A and free beta-hCG, expressed in MOMs, in the 73 SGA pregnancies were 0.83 and 0.95, respectively, compared with 0.98 and 1.01, respectively, in the 292 matched controls (P=0.08 and 0.19, respectively). In the 87 pregnancies with a preterm delivery, the median concentrations of PAPP-A and free beta-hCG were 0.98 and 0.94, respectively, compared with 0.99 and 0.99, respectively, in the 348 matched controls (P=0.82 and 0.10, respectively). In contrast with the maternal serum analytes used in second-trimester screening--alpha-fetoprotein and human chorionic gonadotropin--this study showed that concentrations of PAPP-A and free beta-hCG in the first trimester were not associated with subsequent fetal growth retardation or preterm delivery.

Database: Medline

#	Database	Search term	Results
1	Medline	("Pregnancy associated plasma protein A").ti,ab	1388
2	Medline	("PAPP-A").ti,ab	1495
3	Medline	exp "PREGNANCY-ASSOCIATED PLASMA PROTEIN-A"/	1615
4	Medline	(1 OR 2 OR 3)	2124
5	Medline	(growth ADJ2 restrict*).ti,ab	13402
6	Medline	exp "FETAL GROWTH RETARDATION"/	14660
8	Medline	(IUGR).ti,ab	4798
9	Medline	(retard*).ti,ab	102948
10	Medline	(5 OR 6 OR 8 OR 9)	121095
11	Medline	(4 AND 10)	158
12	Medline	exp "INFANT, SMALL FOR GESTATIONAL AGE"/	6234
13	Medline	("small for gestational age").ti,ab	8147
14	Medline	(12 OR 13)	0
15	Medline	(4 AND 14)	104
16	EMBASE	("Pregnancy associated plasma protein A").ti,ab	1828
17	EMBASE	("PAPP-A").ti,ab	2279
18	EMBASE	exp "PREGNANCY ASSOCIATED PLASMA	2587

		PROTEIN A"/	
19		(16 OR 17 OR 18)	3350
20	EMBASE	(growth ADJ2 restrict*).ti,ab	18390
21	EMBASE	(IUGR).ti,ab	8059
22	EMBASE	exp "INTRAUTERINE GROWTH RETARDATION"/	36340
23	EMBASE	exp "FETUS GROWTH"/	13334
24	EMBASE	(growth ADJ2 restrict*).ti,ab	18390
25	EMBASE	(growth ADJ2 retard*).ti,ab	28540
26	EMBASE	(20 OR 21 OR 22 OR 23 OR 24 OR 25)	75811
27	EMBASE	(19 AND 26)	464
28	EMBASE	(18 AND 26)	361
29	EMBASE	(serial* ADJ2 scan*).ti,ab	2668
30	EMBASE	(16 OR 17 OR 18)	3350
31	EMBASE	(29 AND 30)	6
32	EMBASE	(serial ADJ2 ultraso*).ti,ab	2600
33	EMBASE	(30 AND 32)	9