Date: 21 Nov 2017
Sources: Medline, Embase.

Low PAPP-A and Growth Scans

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1. Low PAPP-A: The impact of ultrasound to evaluate fetal growth

Author(s): Razavi A.S.; Chasen S.T.

Source: Prenatal Diagnosis; Feb 2016; vol. 36 (no. 2); p. 112-116

Publication Date: Feb 2016

Publication Type(s): Article

PubMedID: 26552045

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

Abstract: Objective: Our objective was to describe utilization and impact of sonographic growth assessment in pregnancies with low pregnancy-associated plasma protein-A (PAPP-A). Methods: Singleton pregnancies with PAPP-A <=5th percentile and no other risk factors for fetal growth restriction from January 2011-June 2013 were included. Antepartum and delivery data were obtained by reviewing medical records. Outcomes of pregnancies referred for sonographic growth assessment were compared with those not referred for ultrasound. Fisher's exact test, chi-square analysis, and Mann-Whitney U were used for statistical comparison. Results: Two hundred ninety-five patients were included. Of 285 pregnancies reaching the third trimester, 77.5% were referred for ultrasound, with the initial scan at a median gestational age of 28weeks [26-29]. Referral for growth scans was associated with earlier gestational age at delivery and higher rates of delivery for fetal indications. Those who did not undergo growth scans were more likely to deliver a small for gestational age infant at term, 20.7% versus 35.0% (p=0.04). There was one third-trimester fetal demise, occurring in a patient who had been undergoing growth scans. Conclusion: Growth scans in those with low PAPP-A were associated with delivery at earlier gestational age, with higher rates of delivery for fetal indications and lower rates of small for gestational age newborns at term. No significant differences in neonatal outcomes were observed.

Database: EMBASE

2. The pregnancy outcome prediction (POP) study: Investigating the relationship between serial prenatal ultrasonography, biomarkers, placental phenotype and adverse pregnancy outcomes

Author(s): Gaccioli F.; Lager S.; Sovio U.; Charnock-Jones D.S.; Smith G.C.S.

Source: Placenta; Nov 2017; vol. 59

Publication Date: Nov 2017

Publication Type(s): Article

Abstract: Placental dysfunction is implicated in many major complications of pregnancy associated with adverse maternal and infant outcome, such as preeclampsia, fetal growth restriction and stillbirth. Yet, despite years of intensive research, screening for these complications is still largely based upon clinical grounds rather than ultrasonic and/or biochemical assessment of placental function. One of the few widely employed methods for assessment of risk, low first trimester levels of PAPP-A (Pregnancy Associated Plasma Protein A), was identified through secondary analysis of data collected to identify new methods of screening for Down's syndrome rather than as a purposeful search for screening tests for abnormal placentation. Development of improved methods for population screening requires better mechanistic understanding of the pathways leading to placentally-related complications of human pregnancy. This is in addition to a need for identification of biomarkers which reflect the underlying pathology, while predicting associated disease with high sensitivity and specificity. In this paper, we outline some of the challenges and opportunities in this area. Furthermore, we illustrate how some of these can be addressed in research studies using the example of the Pregnancy Outcome Prediction (POP) study, a prospective cohort study conducted in Cambridge, UK.

Database: EMBASE

3. Does serial 3rd trimester ultrasound improve detection of small for gestational age babies: Comparison of screening policies in 2 European maternity units

Author(s): Sokol Karadjole V.; Agarwal U.; Poljak B.; Alfirevic Z.; Berberovic E.

Source: European Journal of Obstetrics Gynecology and Reproductive Biology; Aug 2017; vol. 215 ; p. 45-49

Publication Date: Aug 2017

Publication Type(s): Article

Abstract: Objective Methods for the antenatal detection of small for gestational age babies (SGA) differ between countries. The aim of this study was to compare the diagnostic accuracy of routine versus selective small for gestational age babies screening policy using data from two European Maternity Units. Study design This was a retrospective cohort study from Liverpool Women's Hospital, UK, that uses selective third trimester sonography and from the University Hospital Centre Zagreb, Croatia, that uses routine third trimester sonography for SGA detection. Screen positive cases were defined as pregnancies with estimated fetal weight (EFW)

Database: EMBASE

4. First trimester maternal serum analytes and second trimester uterine artery Doppler in the prediction of preeclampsia and fetal growth restriction

Author(s): Yu N.; Cui H.; Chen X.; Chang Y.

Source: Taiwanese Journal of Obstetrics and Gynecology; Jun 2017; vol. 56 (no. 3); p. 358-361

Publication Date: Jun 2017

Publication Type(s): Article

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

Abstract: Objective This study aimed to determine whether pregnancy-associated plasma protein-A (PAPP-A), free beta-human chorionic gonadotropin (beta-hCG), a disintegrin and metalloprotease 12 (ADAM12), and placenta protein 13 (PP13) in the first trimester, and uterine artery Doppler (UAD) in the second trimester, predict preeclampsia and fetal growth restriction (FGR). Materials and methods Maternal serum levels of PAPP-A, free beta-hCG, ADAM12, and PP13 at 11-13+6 weeks of gestation and bilateral uterine artery pulsatility index (PI) at 22-24 weeks of gestation were measured in a nested case-control study within a prospective cohort. The serum analytes and Doppler measurements were compared for uncomplicated pregnancies and pregnancies complicated by preeclampsia and FGR. The efficacy of biochemical and Doppler measurements for the prediction of preelampsia and FGR was investigated. Results Compared with gestational age-matched controls (n = 200), the mean PAPP-A and ADAM12 were lower (P 0.05). In screening for preeclampsia and FGR, assuming a fixed false positive rate (FPR) of 10%, the detection rates were 72% and 68% for a combination of PAPP-A, ADAM12, and UAD, respectively. Conclusion First trimester PAPP-A and ADAM12 levels and second trimester uterine artery PI are associated with adverse pregnancy outcomes. The combination of biochemical markers and UAD improves the screening efficiency for the prediction of preeclampsia and FGR.Copyright © 2017

Database: EMBASE

5. Two year outcome of pregnancies complicated by low PAPP-A (<0.3 MoM) at a tertiary fetal medicine unit

Author(s): Sharp A.; Alfirevic Z.; Denton-Cardew L.; Agarwal U.

Source: BJOG: An International Journal of Obstetrics and Gynaecology; Mar 2017; vol. 124 ; p. 41-42

Publication Date: Mar 2017

Publication Type(s): Conference Abstract

Abstract: Introduction Low first trimester serum PAPP-A is associated with adverse obstetric outcomes, including being small-for-gestational- age (SGA) (birth weight 1.45 MoM deemed significant), serial 3rd trimester growth scans and delivery by 40 weeks of gestation. Methods Retrospective case notes review of all cases with PAPPA 24 weeks. Results 25/76 babies (33%) were SGA at birth, with only 9/25 (36%) recognised as SGA antenatally. 9/76 (12%) women had mean UtA PI >1.45 MoM, of these 4 (44%) were SGA. 67/76 (88%) women had a mean UtA PI <1.45 MoM, of which 21 were SGA (31%). Six women delivered <37 weeks. A single woman developed hypertension. There were no still births in the study cohort. Conclusion Pregnancies with low PAPP-A remain high risk, in particular for SGA. Even with a policy of UtA Doppler and serial growth scans in the third trimester we were only able to detect 31-44% of those who subsequently had an SGA fetus. We suggest that a consistent low PAPP-A policy has benefits but further biomarker based strategies are urgently required to improve detection.

Database: EMBASE

6. Prediction of small-for-gestational-age neonate by third-trimester fetal biometry and impact of ultrasound-delivery interval

Author(s): Reboul Q.; Delabaere A.; Luo Z.C.; Nuyt A.-M.; Wu Y.; Fraser W.; Audibert F.; Chauleur C.

Source: Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology; Mar 2017; vol. 49 (no. 3); p. 372-378

Publication Date: Mar 2017

Publication Type(s): Article

PubMedID: 27153518

Abstract:OBJECTIVES: To compare third-trimester ultrasound screening methods to predict small-for-gestational age (SGA), and to evaluate the impact of the ultrasound-delivery interval on screening performance.METHODS: In this prospective study, data were collected from a multicenter singleton cohort study investigating the links between various exposures during pregnancy with birth outcome and later health in children. We included women, recruited in the first trimester, who had complete outcome data and had undergone third-trimester ultrasound examination. Demographic, clinical and biological variables were also collected from both parents. We compared prediction of delivery of a SGA neonate (birth weight

Database: EMBASE

7. First-trimester maternal serum PIGF, PAPP-A, uterine artery Doppler and maternal history for the prediction of pre-eclampsia/ PIH and IUGR or SGA

Author(s): Harikrishnan K.K.; Wahidah N.

Source: BJOG: An International Journal of Obstetrics and Gynaecology; Mar 2017; vol. 124 ; p. 74

Publication Date: Mar 2017

Publication Type(s): Conference Abstract

Abstract: Introduction The objective was to evaluate the detection of pregnancy hypertensive disorders and intrauterine growth restriction (IUGR) by integrating maternal history, serum biomarkers and uterine artery Doppler in the first trimester. Methods We prospectively recruited 144 women that came to our Early Pregnancy Asessment Unit clinic for early asessment during the first trimester of pregnancy. We gathered information on maternal history, uterine artery Doppler and serum biomarkers. Women that fulfilled all the inclusion and exclusion criteria were followed-up for serial growth scans at 20, 26-28 and 36 weeks of gestation. Result A total of 144 women were enrolled consecutively in our study, we excluded four women due to second-trimester miscarriage. Of the remaining 140 women, four developed preeclampsia (2.78%; with sensitivity 50% and specificity 35%, negative predictive value [NPV] 0.96), 11 women had an IUGR baby (16%; sensitivity 72% and specificity 36% NPV 0.9), 33 women developed pregnancy-induced hypertension (22.9%; with sensitivity 85% and specificity 41.1%, NPV 0.92). In the preeclampsia group placental growth factor (PIGF) and pregnancyassociated plasma protein A (PAPP-A) were lower and uterine artery pulsatility index (PI) was higher than in the controls. PIGF MoM for pre-eclampsia was 0.61 (0.48-0.83), PAPP-A MoM was 0.535 (0.391-0.96), uterine artery PI MoM was 1.51 (1.204-1.653). In the pregnancy-induced hypertension group, there were no significant differences in PIGF, PAPP-A or uterine artery PI. Conclusion An integration of maternal characteristics and firsttrimester maternal serum biomarkers (PIGF and PAPP-A) provide a possible screening for pre-eclampsia and IUGR/small-forgestational- age baby. In the overall pre-eclampsia model terine artery PI turned out to be statistically significant but did not improve the detection rate.

Database: EMBASE

8. Practice Bulletin No. 175: Ultrasound in Pregnancy

Author(s): anonymous

Source: Obstetrics and Gynecology; Dec 2016; vol. 128 (no. 6)

Publication Date: Dec 2016

Publication Type(s): Review

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

Abstract: Obstetric ultrasonography is an important and common part of obstetric care in the United States. The purpose of this document is to present information and evidence regarding the methodology of, indications for, benefits of, and risks associated with obstetric ultrasonography in specific clinical situations. Portions of this Practice Bulletin were developed from collaborative documents with the American College of Radiology and the American Institute of Ultrasound in Medicine (1, 2).

Database: EMBASE

9. Implementing a small-for-gestational age surveillance pathway in women with low PAPP-A: A quality improvement project

Author(s): Ashton-Barnett R.; Walker K.; Chidambaram S.

Source: BJOG: An International Journal of Obstetrics and Gynaecology; Jun 2016; vol. 123 ; p. 212-213

Publication Date: Jun 2016

Publication Type(s): Conference Abstract

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

Abstract: Objectives Low PAPP-A (<0.415 MoM) is associated with an increased risk of fetal growth restriction, placental abruption and stillbirth. According to the RCOG Guideline entitled "The investigation and management of the small for gestational age fetus", it should be considered a major risk factor for a small-forgestational- age fetus, and serial assessment of fetal size and umbilical artery Doppler should be offered from 26 to 28 weeks gestation. Methods We conducted an audit to establish firstly what percentage of women with low PAPP-A in the 1st trimester at Chesterfield Royal Hospital NHS Foundation were being offered serial ultrasounds and secondly what impact the introduction of such a policy would have on the existing sonography workload. We then developed a pathway to implement serial ultrasound scans for women with low PAPP-A. Results Chesterfield Royal Hospital is a District General Hospital with 3000 deliveries per annum. In total 115 women had a low PAPP-A level in the first trimester, between July 2014 and July 2015. Notes were obtained for 99 women. Eighty five women were included in the data analysis. Fourteen women were excluded (two women transferred their care, two medical terminations of pregnancy (T21, T18), nine undelivered at the point of data analysis). Twenty six (31%) of the women were primiparous. Eleven (13%) women had a previous history of fetal growth restriction. Seven (8%) women developed hypertensive disease during pregnancy (five pre-eclampsia, 2 pregnancy induced hypertension). No women were offered growth scans as a result of low PAPP-A levels. Sixty two (73%) women were offered scans for a variety of other reasons. Of those women, seven cases (11%) of fetal growth restriction were reported of which two had an abnormal umbilical artery Doppler. Twelve women (14%) delivered low birth weight babies. There were no stillbirths. Given these findings a pathway to offer serial ultrasound to women with low PAPP-A levels was designed and

implemented in January 2016. Conclusions In our study population more than two thirds of women with a low PAPP-A level in the first trimester required serial growth scans in the third trimester for other indications. Therefore offering serial growth scans to all women with a low PAPP-A level in the first trimester would only result in an additional 20-30 women being scanned per annum which is feasible.

Database: EMBASE

10. Low PAPP-A: The Impact of Ultrasound to Evaluate Fetal Growth

Author(s): Razavi A.S.; Chasen S.T.

Source: Obstetrical and Gynecological Survey; Jun 2016; vol. 71 (no. 6); p. 333-334

Publication Date: Jun 2016

Publication Type(s): Note

Available at Obstetrical & gynecological survey - from Ovid (LWW Total Access Collection 2015 - Q1 with Neurology)

Database: EMBASE

11. Clinical implementation of the RCOG's small-for gestational-age fetus green-top guideline at a tertiary referral hospital for obstetrics

Author(s): Bills V.; Overton T.

Source: BJOG: An International Journal of Obstetrics and Gynaecology; Apr 2016; vol. 123 ; p. 79

Publication Date: Apr 2016

Publication Type(s): Conference Abstract

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

Abstract: Introduction The UK's stillbirth rate is the highest in western Europe. The RCOG's Investigation and Management of the Small-For-Gestational-Age Fetus guideline defines major and minor risk factors for fetal growth restriction (FGR), identifying those pregnancies requiring serial ultrasound scans. Many are concerned that this increased ultrasound scan demand will generate an unmanageable workload for the NHS. Methods We implemented a gap analysis; stillbirth audit; pilot study; pilot study audit; full guideline roll out. Gap analysis There are 4400 pregnancies at St Michael's Hospital annually; 4.5% of all pregnancy-associated plasma protein A (PAPP-A) pregnancies are low <0.0415 multiples of the normal median (nine pregnancies/month). Of these, 80% already received serial scans. Low PAPP-A babies had lower birthweight and increased admission to neonatal intensive care unit (3.12 versus 3.42 kg, 6% versus 4%, respectively). Eighteen percent of pregnancies have minor/major risk factors and 80% of these already received serial scans. Stillbirth audit Of all stillbirths, 36% had autopsy evidence of FGR. All stillbirths had major/minor risk factors, but 42% did not receive serial scans. Pilot study audit Minor risk factors: 141 extra pregnancies to be scanned per year. Major risk factors: 244 extra pregnancies to be scanned per year, 60% are for low PAPP-A. Of low PAPP-A pregnancies (identified by antenatal screening co-ordinator), 13% developed FGR, all diagnosed antenatally. Guideline roll out Uterine artery assessment for three minor risk factors is inefficient. Instead, these pregnancies will receive serial growth scans. Low PAPP-A pregnancies will be scanned in the Fetal Medicine Unit. All other major/minor risk factor pregnancies will be scanned in the Ultrasound Department. Serial scans will occur at 28 and 36 weeks of gestation.

Database: EMBAS

12. The use of first-trimester pregnancy-associated plasma protein A levels to screen for small-for gestational-age: Balancing risk against capacity restrictions

Author(s): Walker S.; Foong T.S.; Sengupta S.

Source: BJOG: An International Journal of Obstetrics and Gynaecology; Apr 2016; vol. 123 ; p. 81-82

Publication Date: Apr 2016

Publication Type(s): Conference Abstract

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

Abstract: Introduction Pregnancy-associated plasma protein A (PAPP-A) levels <0.415 multiples of normal median (MoM) are associated with an increased risk of small-for-gestational-age (SGA) infant defined as birthweight <10th centile (odds ratio 2.7). The RCOG recommends serial growth ultrasound scans (USS) for those with PAPP-A below this level. However, this is not feasible in our unit due to limited capacity. Our aim was to confirm low PAPP-A is associated with increased risk of SGA in our local population and, if so, what PAPP-A level cutoff could feasibly be used in our unit for undertaking serial USS. Methods Retrospective review of birthweight centiles, defined using customised GROW charts, of all pregnancies booking in 2013 with low PAPP-A levels. Results In the 248 pregnancies, consistent with published data, PAPP-A level <0.415 MoM was associated with twice the risk of SGA compared with the overall local population (31% versus 16%). Increasing rates of SGA were seen with decreasing levels of PAPP-A; <0.3 MoM 41% SGA and <0.2 MoM 70% SGA. Conclusion Introduction of serial growth USS for all women in 2013 with low PAPP-A (<0.415 MoM) would have required an additional 744 USS corresponding to 75 extra USS lists. An additional 177 USS would have been required for a cutoff level of <0.3 MoM. However, a cutoff <0.2 MoM would reduce the number of additional USS to 30, which would be feasible within the present capacity. A review of pregnancies with low PAPP-A in 2014 is being undertaken to include neonatal outcome data with the aim of introducing serial USS for women with PAPP-A <0.2 MoM.

Database: EMBASE

13. Screening for fetal growth restriction with universal third trimester ultrasonography in nulliparous women in the Pregnancy Outcome Prediction (POP) study: A prospective cohort study

Author(s): Sovio U.; Dacey A.; Smith G.C.S.; White I.R.; Pasupathy D.

Source: The Lancet; Nov 2015; vol. 386 (no. 10008); p. 2089-2097

Publication Date: Nov 2015

Publication Type(s): Article

PubMedID: 26360240

Abstract: Summary Background Fetal growth restriction is a major determinant of adverse perinatal outcome. Screening procedures for fetal growth restriction need to identify small babies and then differentiate between those that are healthy and those that are pathologically small. We sought to determine the diagnostic effectiveness of universal ultrasonic fetal biometry in the third trimester as a screening test for small-for-gestational-age (SGA) infants, and whether the risk of morbidity associated with being small differed in the presence or absence of ultrasonic markers of fetal growth restriction. Methods The Pregnancy Outcome Prediction (POP) study was a prospective cohort study of nulliparous women with a viable singleton pregnancy at the time of the dating ultrasound scan. Women participating had clinically indicated ultrasonography in the third trimester as per routine clinical care and these results were reported as usual (selective ultrasonography). Additionally, all participants had research ultrasonography, including fetal biometry at 28 and 36 weeks' gestational age. These results were not made available to participants or treating clinicians (universal ultrasonography). We regarded SGA as a birthweight of less than the 10th percentile for gestational age and screen positive for SGA an ultrasonographic estimated fetal weight of less than the 10th percentile for gestational age. Markers of fetal growth restriction included biometric ratios, utero-placental Doppler, and fetal growth velocity. We assessed outcomes for consenting participants who attended research scans and had a livebirth at the Rosie Hospital (Cambridge, UK) after the 28 weeks' research scan. Findings Between Jan 14, 2008, and July 31, 2012, 4512 women provided written informed consent of whom 3977 (88%) were eligible for analysis. Sensitivity for detection of SGA infants was 20% (95% CI 15-24; 69 of 352 fetuses) for selective ultrasonography and 57% (51-62; 199 of 352 fetuses) for universal ultrasonography (relative sensitivity 2.9, 95% CI 2.4-3.5, pinteraction=0.005) if the fetal abdominal circumference growth velocity was in the lowest decile (RR 3.9, 95% CI 1.9-8.1, p=0.0001). 172 (4%) of 3977 pregnancies had both an estimated fetal weight of less than the 10th percentile and abdominal circumference growth velocity in the lowest decile, and had a relative risk of delivering an SGA infant with neonatal morbidity of 17.6 (9.2-34.0, p<0.0001). Interpretation Screening of nulliparous women with universal third trimester fetal biometry roughly tripled detection of SGA infants. Combined analysis of fetal biometry and fetal growth velocity identified a subset of SGA fetuses that were at increased risk of neonatal morbidity. Funding National Institute for Health Research, Medical Research Council, Sands, and GE Healthcare.

Database: EMBASE

14. Impact on obstetric outcome of third-trimester screening for small-for-gestational-age fetuses

Author(s): Callec R.; Lamy C.; Perdriolle-Galet E.; Patte C.; Heude B.; Morel O.

Source: Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology; Aug 2015; vol. 46 (no. 2); p. 216-220

Publication Date: Aug 2015

Publication Type(s): Article

PubMedID: 25487165

Abstract:OBJECTIVES: To evaluate the performance of screening for small-for-gestational-age (SGA) fetuses by ultrasound biometry at 30-35 weeks' gestation, and to determine the impact of screening on obstetric and neonatal outcomes.METHODS: For this prospective cohort study, pregnant women were recruited from two French university maternity centers between 2003 and 2006. Performance measures of third-trimester biometry for the prediction of SGA, defined as estimated fetal weight<10(th) centile, were analyzed. Obstetric outcomes and neonatal health status were compared, first, between SGA neonates diagnosed correctly at ultrasound examination (true positive (TP); n=45) and SGA neonates that went undiagnosed (false negative (FN); n=110) and, second, between non-SGA neonates identified as normal at ultrasound examination (true negative (TN); n=1641) and non-SGA neonates diagnosed incorrectly as SGA (false positive (FP); n=101).RESULTS: In the prediction of SGA, third-trimester ultrasound had a sensitivity of 29.0% (95%CI, 22.5-36.6%) and specificity of 94.2% (95%CI, 93.0-95.2%). Positive and negative predictive values were 30.8% (95%CI, 23.9-38.7%) and 93.7% (95%CI, 92.5-94.8%), respectively. One hundred and ten SGA neonates went undiagnosed at ultrasound. Compared to the TN neonates considered as of normal weight at ultrasound, planned preterm delivery (before 37 weeks) and elective Cesarean section for a fetal growth indication were 2.4 (P=0.01) and 2.85 (P=0.003) times more likely to occur, respectively, in the FP group of non-SGA neonates, diagnosed incorrectly as SGA during the antenatal period. There was no statistically significant difference in 5-min Apgar score<7, cord blood pH at birth<7.15 and need for neonatal resuscitation between the two subgroups (TN vs FP and TP vs FN).CONCLUSIONS: The performance of third-trimester ultrasound screening for SGA seems poor, as it misses the diagnosis of a large number of SGA neonates. The consequences of routine screening for SGA in a low-risk population may lead to unnecessary planned preterm deliveries and elective Cesarean sections in FP pregnancies, without improved neonatal outcome in the FN pregnancies.Copyright © 2014 ISUOG. Published by John Wiley & Sons Ltd.

Database: EMBASE

15. Growth scans for low PAPP-A: Does it make a difference?

Author(s): Razavi A.; Chasen S.

Source: American Journal of Obstetrics and Gynecology; Jan 2015; vol. 212 (no. 1)

Publication Date: Jan 2015

Publication Type(s): Conference Abstract

Abstract:OBJECTIVE: Low PAPP-A is a risk factor for poor outcome, including IUGR and IUFD. Despite this, no studies have identified interventions to improve outcome, and ACOG and SMFM have no management recommendations. Our objective was to describe utilization of growth scans in these patients and to evaluate the impact of growth assessment. STUDY DESIGN: Singleton, euploid pregnancies with PAPP-A<=5th% ile from 1/2012-6/2013 were identified. Those with other risk factors for IUGR were excluded. Follow-up for low PAPP-A was at the discretion of individual providers. Outcome data were obtained by reviewing records. Fisher's exact test and Mann-Whitney U were used for statistical comparison. Continuous data are presented as Median [Interquartile Range]. RESULTS: 295 patients were included. There were 10 IUFDs at <24 weeks. 78% were referred for growth scans in the 3rd trimester, with the initial scan at a median of 28 weeks' gestation [26-29]. Distribution of PAPP-A levels were similar in those who had growth scans vs. those who did not. Those under the care of MFM physicians were more likely to be referred for growth scans (93% vs. 73%; p=.001), and those with Medicaid were less likely to have growth scans (62% vs. 80%; p=.03). Clinical outcomes are seen in Table 1. Referral for growth scans was associated with earlier delivery, and higher rates of delivery for fetal indications. Those who did not undergo growth scans were more likely to deliver an SGA infant at term. There was one 3rd trimester IUFD, in a patient who had undergone growth scans. CONCLUSION: With no guidelines for follow-up of low PAPP-A, we saw significant variation in referral for growth scans based on insurance and provider type. Growth scans in those with low PAPP-A were associated with earlier delivery and higher rates of delivery for fetal indications, with lower rates of SGA at term. While larger studies are needed to rule out higher rates of less common outcomes such as IUFD without fetal surveillance, our data do not identify a clear benefit to growth scans for the indication of low PAPP-A. (Table presented) .

Database: EMBASE

16. 2D-ultrasound and endocrinologic evaluation of placentation in early pregnancy and its relationship to fetal birthweight in normal pregnancies and pre-eclampsia

Author(s): Suri S.; Jauniaux E.; Muttukrishna S.

Source: Placenta; Sep 2013; vol. 34 (no. 9); p. 745-750

Publication Date: Sep 2013

Publication Type(s): Article

PubMedID: 23756051

Abstract: Objectives To study the relationships between 2D ultrasound measurements of placentation and maternal serum (MS) levels of PAPP-A, inhibin A and fbetahCG in early pregnancy and subsequent fetal growth in pregnancies with a normal and abnormal outcome. Study design Prospective population-based cohort study of 301 pregnancies with a normal outcome, 18 with a pregnancy complicated by pre-term delivery (PTD) and 14 with subsequent pre-eclampsia (PE). Main outcome measures Basal placental surface area, placental thickness, ellipsivity and volume; MS PAPP-A and fbetahCG at 11-13 + 6 weeks, MS inhibin A at 15-22 weeks and birthweight centile at delivery. Results In the normal group, the basal surface area showed a significantly ($P < 0.001$) positive correlation with placental thickness and placental ellipsivity. With the exception of placental ellipsivity, all other placental ultrasound parameters were significantly related with birthweight centile. Inhibin A showed a significant ($P < 0.005$) correlation with birthweight centiles. The basal

plate surface area and MS PAPP-A were significantly (P < 0.01 and P < 0.001, respectively) lower and MS inhibin A significantly (P < 0.01) higher in PE than in controls. No changes were found in pregnancies complicated by PTD. Conclusion The basal plate surface area at 11-14 weeks reflects indirectly normal and abnormal placentation and development of the definitive placenta. Combined with MS PAPP-A and/or inhibin A levels this parameter could be useful in identifying from the end of the first trimester, pregnancies subsequently complicated with PE.

Database: EMBASE

17. Audit of pregnancy outcomes and complications in euploid pregnancies with a low PAPP-A (0.3 MoM) at first trimester screening

Author(s): Alldred S.K.; Valjalo B.; Bricker L.; Alfirevic Z.; Agarwal U.

Source: BJOG: An International Journal of Obstetrics and Gynaecology; Jun 2013; vol. 120 ; p. 145

Publication Date: Jun 2013

Publication Type(s): Conference Abstract

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

Abstract: Objective Low first trimester serum PAPP-A is associated with adverse obstetric outcomes, including intrauterine growth restriction (IUGR), preterm labour, fetal death in utero (FDIU), pre-eclampsia and miscarriage. Presently there is no standard national guidance for the management of chromosomally normal pregnancies with a low first trimester serum PAPP-A. We have audited pregnancy outcomes for women with a low first trimester serum PAPP-A in our trust to gain baseline information with the aim of producing a local guideline. Method Retrospective audit of hospital case notes and electronic maternity records (Meditech) from 1st January 2012 to 8th November 2012. Results Sixty women with low PAPP-A were identified. Thirty-six women had a documented pregnancy outcome, 24 women have not yet delivered and are therefore excluded from analysis. Four women had a chromosomal abnormality and are therefore excluded (two miscarriages and two terminations). of the remaining 32 women, there were two miscarriages (6%) and two mid-trimester losses (6%) with normal karyotype. Twenty-eight women had livebirths, there were no fetal deaths in utero. The mean birthweight was 3126 g. There were no babies with IUGR (birthweight <5th centile for gestation). There were six preterm deliveries (<37 weeks) (18.75%) but none at <34 weeks. It is of note that there were a number of women with preterm inductions of labour due to diabetes in pregnancy. Four women (12.5%) developed pre-eclampsia, including one eclamptic seizure. No significant neonatal abnormalities or early neonatal deaths were observed in the 28 live births. Conclusion The adverse obstetric outcomes in our trust are comparable to those noted in a systematic review of pregnancy outcomes associated with a low first trimester serum PAPP-A, with the exceptions that there were no cases of IUGR and FDIU in our patient population. Our preterm labour rate was marginally higher but may be confounded by preterm induction of labour for diabetes in two of our patients. This is a small patient population, and larger numbers are needed for a true reflection of complication rates. These findings warrant the development of a standard protocol in our trust, for monitoring and minimising the risks associated with the pregnancies, which may include aspirin prophylaxis for pre-eclampsia, serial growth scans and timing of induction of labour. A UK survey of current practice is currently in progress.

Database: EMBASE

18. First trimester fetal ultrasound parameters associated with PAPP-A and fbeta-hCG

Author(s): Papastefanou I.; Souka A.; Pilalis A.; Kassanos D.; Eleuftheriades M.

Source: Journal of Maternal-Fetal and Neonatal Medicine; Jul 2012; vol. 25 (no. 7); p. 1029-1033

Publication Date: Jul 2012

Publication Type(s): Article

PubMedID: 21988784

Abstract: Objective: To study the association of fbeta-hCG and PAPP-A measured at 1114 weeks of gestation with delta crown-rump-length (dCRL), delta fetal heart rate (dFHR) and delta nuchal translucency (dNT). To calculate adjusted MoM taking into consideration these associations. Methods: Retrospective cross-sectional study on 5,536 singleton euploid pregnancies participating in a first trimester screening program for chromosomal abnormalities by nuchal translucency and maternal serum biochemistry. Adjusted MoM were calculated for fbeta-hCG and PAPP-A and compared to the observed MoM (calculated by the Fetal Medicine Foundation screening algorithm). Results: fbeta-hCG correlates positively with dCRL and negatively with dNT, whereas PAPP-A shows a positive correlation with dNT and a negative one with dCRL and dFHR. After adjustment for the ultrasound parameters, the median MoM values for fbeta-hCG and PAPP-A changed from 1.02 and 0.92 observed MoM to 0.98 and 0.99 adjusted MoM respectively. The difference between the observed and adjusted MoM was statistically significant ($p<0.001$). Delta CRL increases with gestation and this effect manifests mainly after CRL of 62mm. Conclusions: Adjustment for dCRL, dFHR and dNT improves the calculation of MoM for fbeta-hCG and PAPP-A. CRL measurement overestimates fetal size at the end of the screening period 1114 weeks. © 2012 Informa UK, Ltd.

Database: EMBASE

19. Performance of third-trimester ultrasound for prediction of small-for-gestational-age neonates and evaluation of contingency screening policies

Author(s): Souka A.P.; Papastefanou I.; Pilalis A.; Michalitsi V.; Kassanos D.

Source: Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology; May 2012; vol. 39 (no. 5); p. 535-542

Publication Date: May 2012

Publication Type(s): Article

PubMedID: 21858886

Abstract: To assess the performance of third-trimester fetal biometry and fetal Doppler studies for the prediction of small-for-gestational-age (SGA) neonates, and to explore contingency strategies using a first-trimester prediction model based on maternal and fetal parameters and third-trimester ultrasound. This was an observational cross-sectional study of uncomplicated singleton pregnancies. Risk assessment for chromosomal abnormality was carried out in 4702 pregnancies using a combination of ultrasound markers (fetal nuchal translucency thickness (NT) and nasal bone assessment) and biochemistry (free beta-human chorionic gonadotropin (beta-hCG) and pregnancy-associated plasma protein-A (PAPP-A)) at 11 to 13 + 6 weeks. Maternal demographic characteristics and method of conception were recorded. Third-trimester (30-34 weeks) fetal biometry (biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur length (FL)) and umbilical artery (UA) and middle cerebral artery Doppler studies were performed routinely in a subgroup (n = 2310). Reference ranges for birth weight were constructed using the cohort of 4702

women, and neonates were classified as small (SGA, <= 5th centile) or appropriate (AGA) for gestational age. First-trimester, third-trimester and integrated first- and third-trimester prediction models for SGA were constructed using regression analysis and three different contingency strategies of rescanning in the third trimester were investigated. According to the areas under the receiver-operating characteristics curves (AUCs), AC (AUC = 0.85) and ultrasound-estimated fetal weight (EFW, AUC = 0.87) were equally good predictors of SGA. The model was marginally improved by the addition of UA Doppler, smoking status and first-trimester indices (free beta-hCG and PAPP-A multiples of the median) (combined model, AUC = 0.88), but the difference was not statistically significant. A contingency strategy of rescanning 50% of the population in the third trimester according to the risk estimated by a first-trimester prediction model yielded a detection rate of 79% for a 25% screen-positive rate. Third-trimester ultrasound is effective in screening for SGA in uncomplicated pregnancies. The use of a contingency screening policy can reduce the need for unnecessary examinations.

Database: EMBASE

20. Placental volume and vascularization flow indices by 3D power Doppler US using VOCAL technique and correlation with IGF-1, free beta-hCG, PAPP-A, and uterine artery Doppler at 11-14 weeks of pregnancy.

Author(s): Yigiter, Alin Basgul; Kavak, Zehra Nese; Durukan, Birol; Isci, Herman; Uzuner, Arzu; Uyar, Esra; Gokaslan, Husnu

Source: Journal of perinatal medicine; Mar 2011; vol. 39 (no. 2); p. 137-141

Publication Date: Mar 2011

Publication Type(s): Journal Article

PubMedID: 21241202

Abstract:AIMSThe purpose of this study was to investigate correlations between first trimester placental volume (PV) and blood flow indexes (FIs), bilateral uterine artery pulsatility indexes, notching, and biochemical parameters: pregnancy-associated plasma protein-A (PAPP-A), free beta-human chorionic gonadotropin (f-β-hCG), and insulin-like growth factor-1 (IGF-1) to predict the high-risk pregnancies in the first trimester.METHODSWe prospectively examined 310 patients at 11-14 weeks of pregnancy using transabdominal 3D gray scale and power Doppler ultrasound for assessing PV, vascularization index, FI, and vascularization FI (VFI). The acquired volumes were analyzed using VOCAL™ imaging software. The results were correlated with biochemical parameters.RESULTSWe found significant correlations between PV and biochemical parameters, and between placental blood flow studies and other parameters. Finally, PV/crown-rump length so called the placental quotient is also related to both PAPP-A and VFI.CONCLUSIONSPlacental volumetry, uterine artery Doppler studies, blood flow calculations and biochemical parameters, such as f-β-hCG, PAPP-A, and IGF-1 could be important in the early and rapid diagnosis of high-risk pregnancies. Thus, they may be useful in first trimester prediction of fetal growth restriction presenting with alterations in PV and vascularity.

Database: Medline

21. 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

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

22. First trimester uterine artery Dopplers and PAPP-A in predicting fetal growth restriction in an Indian population

Author(s): Kaul A.; Gupta R.; Acharya V.; Radhakrishnan P.

Source: Prenatal Diagnosis; Jul 2010; vol. 30

Publication Date: Jul 2010

Publication Type(s): Conference Abstract

Abstract:OBJECTIVE: To see whether first trimester uterine artery Dopplers and PAPP-A are predictive of fetal growth restriction. STUDY DESIGN: The study was carried out in a prospectively designed protocol in two tertiary care referral centres for fetal medicine in India. The patients who came for first trimester screening also had their uterine artery PIs measured (according to FMF criteria) at 11-14weeks. The obstetric history and BMI were noted in addition to the parameters of the nuchal translucency scan and serum PAPP-A and beta HCG. Results were correlated to the birth weight percentiles to determine whether first trimester uterine artery Dopplers PI and PAPP-A MoMs could predict fetal growth restriction defined as borth weight of th centile for lowest and highest uterine artery PI were 2.3, and 3.05 respectively. The likelihood ratios on correlating highest and lowest uterine artery PI of more than or equal to 95th centile with fetal growth restriction was 1.26 and 1.11 respectively (positive predictive value of around 20%). On regression analysis PAPP-A did not show significant correlation with the birth weights (p = 0.451 with the Likelihood Ratio of PAPP-A MoMs <0.2 = 0.96). CONCLUSION: In the population studied, first trimester uterine artery Doppler and PAPP-A do not appear to be a good predictor of fetal growth restriction and this will need further evaluation in a larger study.

Database: EMBASE

23. 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

Source: Prenatal diagnosis; Jun 2010; vol. 30 (no. 6); p. 503-508

Publication Date: Jun 2010

Publication Type(s): Journal Article

PubMedID: 20509148

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

24. First-trimester placental volume and vascularization measured by 3-dimensional power Doppler sonography in pregnancies with low serum pregnancy-associated plasma protein a levels.

Author(s): Rizzo, Giuseppe; Capponi, Alessandra; Pietrolucci, Maria Elena; Capece, Antonio; Arduini, Domenico

Source: Journal of ultrasound in medicine : official journal of the American Institute of Ultrasound in Medicine; Dec 2009; vol. 28 (no. 12); p. 1615-1622

Publication Date: Dec 2009

Publication Type(s): Journal Article

PubMedID: 19933473

Abstract:OBJECTIVEThe purpose of this study was to investigate the first-trimester placental volume and 3-dimensional (3D) power Doppler vascularization of pregnancies with low serum pregnancy-associated plasma protein A (PAPP-A) levels and to relate these findings to pregnancy outcomes.METHODSThree-dimensional power Doppler sonography of the placenta was performed at gestational ages of 11 weeks to 13 weeks 6 days in 84 pregnancies with PAPP-A concentrations of less than 0.4 multiple of the median (MoM). With a standardized setting, the placental volume and vascularization index (VI), flow index (FI), and vascularization-flow index (VFI) were calculated and related to pregnancy outcomes.RESULTSPregnancy outcomes were as follows: 57 pregnancies with birth weights at or above the 10th percentile (group A), 16 pregnancies with birth weights below the 10th percentile and normal Doppler findings in the umbilical artery throughout gestation (group B), and 11 pregnancies with birth weights below the 10th percentile and abnormal umbilical Doppler findings later in gestation (group C). No differences were found in PAPP-A levels among groups. Placental volume values were significantly lower than reference limits, but no differences were

found between groups. In groups A and B, there were no significant differences in 3D Doppler indices. However, these indices were significantly lower in group C (VI mean difference, -1.904; P < .001; FI mean difference, -1.939; P < .001; VFI mean difference, -1.944; P < .001). Placental vascular indices were significantly related to the severity of intrauterine growth restriction (IUGR; VI, r = 0.438; P < .001; FI, r = 0.482; P < .001; VFI, r = 0.497; P < .001) but not to the PAPP-A MoM and placental volume values.CONCLUSIONSLow serum maternal PAPP-A levels are associated with altered 3D placental Doppler indices, and these changes are related to subsequent development of IUGR and adverse pregnancy outcomes.

Database: Medline

25. Screening for pre-eclampsia and fetal growth restriction by uterine artery Doppler and PAPP-A at 11-14 weeks' gestation.

Author(s): Pilalis, A; Souka, A P; Antsaklis, P; Daskalakis, G; Papantoniou, N; Mesogitis, S; Antsaklis, A

Source: Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology; Feb 2007; vol. 29 (no. 2); p. 135-140

Publication Date: Feb 2007

Publication Type(s): Journal Article

PubMedID: 17221926

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 assess the role of maternal demographic characteristics, uterine artery Doppler velocimetry, maternal serum pregnancy-associated plasma protein-A (PAPP-A) and their combination in screening for pre-eclampsia and small-for-gestational age (SGA) fetuses at 11-14 weeks.METHODSThis was a prospective study of 878 consecutive women presenting for a routine prenatal ultrasound examination at 11-14 weeks. Pulsed wave Doppler was then used to obtain uterine artery flow velocity waveforms and the mean pulsatility index (PI) of the uterine arteries was calculated. Maternal serum samples for PAPP-A were assayed. Along with maternal history, these measurements were compared in their ability to predict adverse outcome, defined as pre-eclampsia and/or SGA and/or placental abruption.RESULTSMean uterine artery PI > or = 95(th) centile and PAPP-A or = 95(th) centile predicted 23% of cases and PAPP-A or = 95(th) centile (OR, 2.76; 95% CI, 1.11-6.81) and maternal history of pre-eclampsia/hypertension (OR, 50.54; 95% CI, 10.52-242.73). The predicting factors for SGA or = 95(th) centile (OR, 2.0; 95% CI, 1.07-3.74) and low PAPP-A (OR, 0.43; 95% CI, 0.20-0.93). Increased uterine artery PI was the only independent factor in the prediction of placental abruption (OR, 8.49; 95% CI, 2.78-25.94). The combination of uterine artery PI and maternal history of pre-eclampsia/hypertension was better than was using uterine artery Doppler alone in predicting pre-eclampsia. Similarly, for the prediction of SGA < or = 5(th) centile, combining uterine artery Doppler and maternal serum PAPP-A was better than was uterine artery Doppler alone. In both cases, the difference approached statistical significance.CONCLUSIONSThe combination of maternal history with abnormal uterine artery Doppler and low PAPP-A level at 11-14 weeks achieves better results than does either test alone in the prediction of pre-eclampsia and SGA.

Database: Medline

Strategy 318698

#	Database	Search term	Results
1	Medline	("Pregnancy associated plasma protein A").ti,ab	1388
2	Medline	exp "PREGNANCY-ASSOCIATED PLASMA PROTEIN-A"/	1615
3	Medline	("papp-a").ti,ab	1495
4	Medline	(1 OR 2 OR 3)	2124
5	Medline	(serial ADJ2 scan*).ti,ab	2419
6	Medline	(serial ADJ2 ultrasound*).ti,ab	1520
7	Medline	(serial ADJ2 sonography).ti,ab	0
8	Medline	(serial ADJ2 sonogram).ti,ab	3
9	Medline	(serial).ti,ab	105765
10	Medline	(5 OR 6 OR 8 OR 9)	105765
11	Medline	(4 AND 10)	0
12	EMBASE	("Pregnancy associated plasma protein A").ti,ab	1828
13	EMBASE	exp "PREGNANCY-ASSOCIATED PLASMA PROTEIN-A"/	2587
14	EMBASE	("papp-a").ti,ab	2279
15	EMBASE	(12 OR 13 OR 14)	3350
16	EMBASE	(serial ADJ2 scan*).ti,ab	2558
17	EMBASE	(serial ADJ2 ultrasound*).ti,ab	1927
18	EMBASE	(serial ADJ2 sonogram).ti,ab	5

19	EMBASE	(serial).ti,ab	140237
20	EMBASE	(16 OR 17 OR 18 OR 19)	140237
21	EMBASE	(15 AND 20)	55
22	EMBASE	exp "FETUS ECHOGRAPHY"/	22497
23	EMBASE	(15 AND 22)	862
24	EMBASE	*"FETUS ECHOGRAPHY"/ OR *"NUCHAL TRANSLUCENCY MEASUREMENT"/	7065
25	EMBASE	(15 AND 24)	198
26	EMBASE	(20 AND 22)	541
27	EMBASE	(16 AND 22)	39
28	EMBASE	(17 AND 22)	155
29	EMBASE	exp "FETUS GROWTH RETARDATION"/ OR exp "FETUS GROWTH"/	46732
30	EMBASE	exp "SMALL FOR DATE INFANT"/	12366
31	EMBASE	exp "INTRAUTERINE GROWTH RETARDATION"/	36340
32	EMBASE	(29 OR 30 OR 31)	46732
33	EMBASE	(repeat* OR serial).ti,ab	751730
34	EMBASE	(22 AND 32 AND 33)	207
35	EMBASE	exp "THIRD TRIMESTER PREGNANCY"/	23418
36	EMBASE	(15 AND 22 AND 35)	12
37	EMBASE	(22 AND 32 AND 35)	291

38	EMBASE	(serial*).ti,ab	159813
39	EMBASE	(22 AND 32 AND 38)	142
40	EMBASE	(15 AND 22 AND 32)	92
41	Medline	(growth ADJ2 scan*).ti,ab	408
42	Medline	exp "ULTRASONOGRAPHY, PRENATAL"/	29415
45	Medline	((prenatal OR foetal OR fetus) ADJ2 (ultrasound OR ultrasonography OR sonography)).ti,ab	4047
46	Medline	(41 OR 42 OR 45)	31446
47	Medline	(4 AND 46)	521
48	Medline	("foetal growth").ti,ab	0
49	Medline	("fetus growth").ti,ab	56
50	Medline	("fetal growth").ti,ab	12188
51	Medline	exp "FETAL DEVELOPMENT"/	83444
52	Medline	exp "FETAL GROWTH RETARDATION"/	14660
53	Medline	(IUGR).ti,ab	0
54	Medline	(49 OR 50 OR 51 OR 52 OR 53)	101226
55	Medline	(47 AND 54)	149
56	EMBASE	*"PREGNANCY ASSOCIATED PLASMA PROTEIN A"/	1082
57	EMBASE	(24 AND 56)	73
58	Medline	(4 AND 11)	0

59	EMBASE	(15 AND 16)	6
60	Medline	(4 AND 6)	0
61	EMBASE	(interval*).ti,ab	824979
62	EMBASE	(15 AND 22 AND 32 AND 61)	3
63	Medline	(interval*).ti,ab	648239
64	Medline	exp "TIME FACTORS"/	0
65	Medline	(63 OR 64)	0
66	Medline	(4 AND 46 AND 65)	34
67	Medline	(41 OR 42)	29793
68	Medline	(4 AND 67)	519
69	Medline	(4 AND 41)	2
70	EMBASE	(growth ADJ2 scan*).ti,ab	468
71	EMBASE	(15 AND 70)	11
72	EMBASE	*"FETUS GROWTH RETARDATION"/di	1432
73	EMBASE	(15 AND 72)	21
74	EMBASE	*"FETUS ECHOGRAPHY"/	6484
75	EMBASE	(13 AND 74)	90