February 2016 Literature Alert

1.

[Angiogenic factor imbalance early in pregnancy predicts adverse outcomes in patients with lupus and antiphospholipid antibodies: results of the PROMISSE study.](#)

Kim MY, Buyon JP, Guerra MM, Rana S, Zhang D, Laskin CA, Petri M, Lockshin MD, Sammaritano LR, Branch DW, Porter TF, Merrill JT, Stephenson MD, Gao Q, Karumanchi SA, Salmon JE.

Abstract

BACKGROUND:

Over 20% of pregnancies in patients with systemic lupus erythematosus (SLE) and/or antiphospholipid antibodies (APL) result in an adverse pregnancy outcome (APO) related to abnormal placentation. The ability to identify, early in pregnancy, patients who are destined for poor outcomes would significantly impact care of this high-risk population. In nonautoimmune patients, circulating angiogenic factors are dysregulated in disorders of placentation, such as preeclampsia (PE) and fetal growth restriction.

OBJECTIVE:

We sought to determine whether early dysregulation of circulating angiogenic factors can predict APO in high-risk SLE and/or APL pregnancies.

STUDY DESIGN:

We used data and samples from the Predictors of Pregnancy Outcome: Biomarkers in APL Syndrome and SLE (PROMISSE), a multicenter prospective study that enrolled 492 pregnant women with SLE and/or APL from September 2003 through August 2013. Patients were followed through pregnancy from <12 weeks gestation. Circulating levels of soluble fms-like tyrosine kinase-1 (sFlt1), placental growth factor (PlGF), and soluble endoglin were measured monthly and subjects followed up for APO, classified as severe (PE <34 weeks, fetal/neonatal death, indicated preterm delivery <30 weeks) or moderate (PE ≥34 weeks, indicated preterm delivery 30-36 weeks, growth restriction without PE).

RESULTS:

Severe APOs occurred in 12% and moderate APOs in 10% of patients. By 12-15 weeks, sFlt1, PlGF, and soluble endoglin levels were markedly altered in women who developed severe APO. After adjusting for clinical risk factors, sFlt1 was the strongest predictor of severe APO among 12-15 week measures (odds ratio, 17.3 comparing highest and lowest quartiles; 95% confidence interval [CI], 3.5-84.8; positive predictive value [PPV], 61%; negative predictive value [NPV], 93%). At 16-19 weeks, the combination of sFlt1 and PlGF was most predictive of severe APO, with risk greatest for subjects with both PlGF in lowest quartile (<70.3 pg/mL) and sFlt1 in highest quartile (>1872 pg/mL; odds ratio, 31.1; 95% CI, 8.0-121.9; PPV, 58%; NPV, 95%). Severe APO rate in this high-risk subgroup was 94% (95% CI, 70-99.8%), if lupus anticoagulant or history of high blood pressure was additionally present. In contrast, among patients with both sFlt1 <1872 pg/mL and PlGF >70.3 pg/mL, rate of severe APO was only 4.6% (95% CI, 2.1-8.6%).

CONCLUSION:

Circulating angiogenic factors measured during early gestation have a high NPV in ruling out the

development of severe adverse outcomes among patients with SLE and/or APL syndrome. Timely risk stratification of patients is important for effective clinical care and optimal allocation of health care resources.

2.
Fetal and Neonatal Effects of N-Acetylcysteine When Used for Neuroprotection in Maternal Chorioamnionitis.
Jenkins DD, Wiest DB, Mulvihill DM, Hlavacek AM, Majstoravich SJ, Brown TR, Taylor JJ, Buckley JR, Turner RP, Rollins LG, Bentzley JP, Hope KE, Barbour AB, Lowe DW, Martin RH, Chang EY.

Abstract
OBJECTIVE:
To evaluate the clinical safety of antenatal and postnatal N-acetylcysteine (NAC) as a neuroprotective agent in maternal chorioamnionitis in a randomized, controlled, double-blinded trial.
STUDY DESIGN:
Twenty-two mothers >24 weeks gestation presenting within 4 hours of diagnosis of clinical chorioamnionitis were randomized with their 24 infants to NAC or saline treatment. Antenatal NAC (100 mg/kg/dose) or saline was given intravenously every 6 hours until delivery. Postnatally, NAC (12.5-25 mg/kg/dose, n = 12) or saline (n = 12) was given every 12 hours for 5 doses. Doppler studies of fetal umbilical and fetal and infant cerebral blood flow, cranial ultrasounds, echocardiograms, cerebral oxygenation, electroencephalograms, and serum cytokines were evaluated before and after treatment, and 12, 24, and 48 hours after birth. Magnetic resonance spectroscopy and diffusion imaging were performed at term age equivalent. Development was followed for cerebral palsy or autism to 4 years of age.
RESULTS:
Cardiovascular measures, cerebral blood flow velocity and vascular resistance, and cerebral oxygenation did not differ between treatment groups. Cerebrovascular coupling was disrupted in infants with chorioamnionitis treated with saline but preserved in infants treated with NAC, suggesting improved vascular regulation in the presence of neuroinflammation. Infants treated with NAC had higher serum anti-inflammatory interleukin-1 receptor antagonist and lower proinflammatory vascular endothelial growth factor over time vs controls. No adverse events related to NAC administration were noted.
CONCLUSIONS:
In this cohort of newborns exposed to chorioamnionitis, antenatal and postnatal NAC was safe, preserved cerebrovascular regulation, and increased an anti-inflammatory neuroprotective protein.
TRIAL REGISTRATION:
ClinicalTrials.gov: NCT00724594.

3.

Global, regional, and national levels and trends in maternal mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Maternal Mortality Estimation Inter-Agency Group.

Alkema L, Chou D, Hogan D, Zhang S, Moller AB, Gemmill A, Fat DM, Boerma T, Temmerman M, Mathers C, Say L; United Nations Maternal Mortality Estimation Inter-Agency Group collaborators and technical advisory group.
Collaborators (14)

Abstract
BACKGROUND:
Millennium Development Goal 5 calls for a 75% reduction in the maternal mortality ratio (MMR) between 1990 and 2015. We estimated levels and trends in maternal mortality for 183 countries to assess progress made. Based on MMR estimates for 2015, we constructed projections to show the requirements for the Sustainable Development Goal (SDG) of less than 70 maternal deaths per 100,000 livebirths globally by 2030.
METHODS:
We updated the UN Maternal Mortality Estimation Inter-Agency Group (MMEIG) database with more than 200 additional records (vital statistics from civil registration systems, surveys, studies, or reports). We generated estimates of maternal mortality and related indicators with 80% uncertainty intervals (UIs) using a Bayesian model. The model combines the rate of change implied by a multilevel regression model with a time-series model to capture data-driven changes in country-specific MMRs, and includes a data model to adjust for systematic and random errors associated with different data sources.
RESULTS:
We had data for 171 of 183 countries. The global MMR fell from 385 deaths per 100,000 livebirths (80% UI 359-427) in 1990, to 216 (207-249) in 2015, corresponding to a relative decline of 43·9% (34·0-48·7), with 303,000 (291,000-349,000) maternal deaths worldwide in 2015. Regional progress in reducing the MMR since 1990 ranged from an annual rate of reduction of 1·8% (0·0-3·1) in the Caribbean to 5·0% (4·0-6·0) in eastern Asia. Regional MMRs for 2015 ranged from 12 deaths per 100,000 livebirths (11-14) for high-income regions to 546 (511-652) for sub-Saharan Africa. Accelerated progress will be needed to achieve the SDG goal; countries will need to reduce their MMRs at an annual rate of reduction of at least 7·5%.
INTERPRETATION:
Despite global progress in reducing maternal mortality, immediate action is needed to meet the ambitious SDG 2030 target, and ultimately eliminate preventable maternal mortality. Although the rates of reduction that are needed to achieve country-specific SDG targets are ambitious for most high mortality countries, countries that made a concerted effort to reduce maternal mortality between 2000 and 2010 provide inspiration and guidance on how to accomplish the acceleration necessary to substantially reduce preventable maternal deaths.
FUNDING:
National University of Singapore, National Institute of Child Health and Human Development, USAID, and the UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction.
Comment in
Modest global achievements in maternal survival: more focus on sub-Saharan Africa is needed. [Lancet.

4.
Immediate delivery compared with expectant management after preterm pre-labour rupture of the membranes close to term (PPROMT trial): a randomised controlled trial.
Morris JM, Roberts CL, Bowen JR, Patterson JA, Bond DM, Algert CS, Thornton JG, Crowther CA; PPROMT Collaboration.

Abstract
BACKGROUND:
Preterm pre-labour ruptured membranes close to term is associated with increased risk of neonatal infection, but immediate delivery is associated with risks of prematurity. The balance of risks is unclear. We aimed to establish whether immediate birth in singleton pregnancies with ruptured membranes close to term reduces neonatal infection without increasing other morbidity.
METHODS:
The PPROMT trial was a multicentre randomised controlled trial done at 65 centres across 11 countries. Women aged over 16 years with singleton pregnancies and ruptured membranes before the onset of labour between 34 weeks and 36 weeks and 6 days weeks who had no signs of infection were included. Women were randomly assigned (1:1) by a computer-generated randomisation schedule with variable block sizes, stratified by centre, to immediate delivery or expectant management. The primary outcome was the incidence of neonatal sepsis. Secondary infant outcomes included a composite neonatal morbidity and mortality indicator (ie, sepsis, mechanical ventilation ≥24 h, stillbirth, or neonatal death); respiratory distress syndrome; any mechanical ventilation; and duration of stay in a neonatal intensive or special care unit. Secondary maternal outcomes included antepartum or intrapartum haemorrhage, intrapartum fever, postpartum treatment with antibiotics, and mode of delivery. Women and caregivers could not be masked, but those adjudicating on the primary outcome were masked to group allocation. Analyses were by intention to treat. This trial is registered with the International Clinical Trials Registry, number ISRCTN44485060.
FINDINGS:
Between May 28, 2004, and June 30, 2013, 1839 women were recruited and randomly assigned: 924 to the immediate birth group and 915 to the expectant management group. One woman in the immediate birth group and three in the expectant group were excluded from the primary analyses. Neonatal sepsis occurred in 23 (2%) of 923 neonates whose mothers were assigned to immediate birth and 29 (3%) of 912 neonates of mothers assigned to expectant management (relative risk [RR] 0·8, 95% CI 0·5-1·3; p=0·37). The composite secondary outcome of neonatal morbidity and mortality occurred in 73 (8%) of 923 neonates of mothers assigned to immediate delivery and 61 (7%) of 911 neonates of mothers assigned to expectant management (RR 1·2, 95% CI 0·9-1·6; p=0·32). However, neonates born to mothers in the immediate delivery group had increased rates of respiratory distress (76 [8%] of 919 vs 47 [5%] of 910, RR 1·6, 95% CI 1·1-2·30; p=0·008) and any mechanical ventilation (114 [12%] of 923 vs 83 [9%] of 912, RR 1·4, 95% CI 1·0-1·8; p=0·02) and spent more time in intensive care (median 4·0 days [IQR 0·0-10·0] vs 2·0 days [0·0-7·0]; p<0·0001) compared with neonates born to mothers in the expectant management group. Compared with women assigned to the immediate delivery group, those assigned to the expectant management group had higher risks of antepartum or intrapartum haemorrhage (RR 0·6, 95% CI 0·4-0·9), intrapartum fever (0·4, 0·2-0·9), and use of postpartum antibiotics (0·8, 0·7-1·0), and longer hospital stay (p<0·0001), but a lower risk of caesarean delivery (RR 1·4, 95% CI 1·2-1·7).

INTERPRETATION:
In the absence of overt signs of infection or fetal compromise, a policy of expectant management with appropriate surveillance of maternal and fetal wellbeing should be followed in pregnant women who present with ruptured membranes close to term.

Comment in
Late preterm rupture of membranes: it pays to wait. [Lancet. 2016]
PMID: 26564381 [PubMed - in process]

5.

Shared Genetic Predisposition in Peripartum and Dilated Cardiomyopathies.

Ware JS, Li J, Mazaika E, Yasso CM, DeSouza T, Cappola TP, Tsai EJ, Hilfiker-Kleiner D, Kamiya CA, Mazzarotto F, Cook SA, Halder I, Prasad SK, Pisarcik J, Hanley-Yanez K, Alharethi R, Damp J, Hsich E, Elkayam U, Sheppard R, Kealey A, Alexis J, Ramani G, Safirstein J, Boehmer J, Pauly DF, Wittstein IS, Thohan V, Zucker MJ, Liu P, Gorcsan J 3rd, McNamara DM, Seidman CE, Seidman JG, Arany Z; IMAC-2 and IPAC Investigators.
Collaborators (155)

Abstract
Background
Peripartum cardiomyopathy shares some clinical features with idiopathic dilated cardiomyopathy, a disorder caused by mutations in more than 40 genes, including TTN, which encodes the sarcomere protein titin.
Methods
In 172 women with peripartum cardiomyopathy, we sequenced 43 genes with variants that have been associated with dilated cardiomyopathy. We compared the prevalence of different variant types (nonsense, frameshift, and splicing) in these women with the prevalence of such variants in persons with dilated cardiomyopathy and with population controls.
Results
We identified 26 distinct, rare truncating variants in eight genes among women with peripartum cardiomyopathy. The prevalence of truncating variants (26 in 172 [15%]) was significantly higher than that in a reference population of 60,706 persons (4.7%, P=1.3×10(-7)) but was similar to that in a cohort of patients with dilated cardiomyopathy (55 of 332 patients [17%], P=0.81). Two thirds of identified truncating variants were in TTN, as seen in 10% of the patients and in 1.4% of the reference population (P=2.7×10(-10)); almost all TTN variants were located in the titin A-band. Seven of the TTN truncating variants were previously reported in patients with idiopathic dilated cardiomyopathy. In a clinically well-characterized cohort of 83 women with peripartum cardiomyopathy, the presence of TTN truncating variants was significantly correlated with a lower ejection fraction at 1-year follow-up (P=0.005).
Conclusions
The distribution of truncating variants in a large series of women with peripartum cardiomyopathy was remarkably similar to that found in patients with idiopathic dilated cardiomyopathy. TTN truncating variants were the most prevalent genetic predisposition in each disorder.
PMID: 26735901 [PubMed - in process]

6.

Predictive Value of the sFlt-1:PlGF Ratio in Women with Suspected Preeclampsia.

Zeisler H, Llurba E, Chantraine F, Vatish M, Staff AC, Sennström M, Olovsson M, Brennecke SP, Stepan H, Allegranza D, Dilba P, Schoedl M, Hund M, Verlohren S.
Author information

Abstract

BACKGROUND:

The ratio of soluble fms-like tyrosine kinase 1 (sFlt-1) to placental growth factor (PlGF) is elevated in pregnant women before the clinical onset of preeclampsia, but its predictive value in women with suspected preeclampsia is unclear.

METHODS:

We performed a prospective, multicenter, observational study to derive and validate a ratio of serum sFlt-1 to PlGF that would be predictive of the absence or presence of preeclampsia in the short term in women with singleton pregnancies in whom preeclampsia was suspected (24 weeks 0 days to 36 weeks 6 days of gestation). Primary objectives were to assess whether low sFlt-1:PlGF ratios (at or below a derived cutoff) predict the absence of preeclampsia within 1 week after the first visit and whether high ratios (above the cutoff) predict the presence of preeclampsia within 4 weeks.

RESULTS:

In the development cohort (500 women), we identified an sFlt-1:PlGF ratio cutoff of 38 as having important predictive value. In a subsequent validation study among an additional 550 women, an sFlt-1:PlGF ratio of 38 or lower had a negative predictive value (i.e., no preeclampsia in the subsequent week) of 99.3% (95% confidence interval [CI], 97.9 to 99.9), with 80.0% sensitivity (95% CI, 51.9 to 95.7) and 78.3% specificity (95% CI, 74.6 to 81.7). The positive predictive value of an sFlt-1:PlGF ratio above 38 for a diagnosis of preeclampsia within 4 weeks was 36.7% (95% CI, 28.4 to 45.7), with 66.2% sensitivity (95% CI, 54.0 to 77.0) and 83.1% specificity (95% CI, 79.4 to 86.3).

CONCLUSIONS:

An sFlt-1:PlGF ratio of 38 or lower can be used to predict the short-term absence of preeclampsia in women in whom the syndrome is suspected clinically. (Funded by Roche Diagnostics.).

Comment in

Improving the Prediction of Preeclampsia. [N Engl J Med. 2016]

PMID: 26735990 [PubMed - indexed for MEDLINE]

7.

Prenatal Diagnosis of DNA Copy Number Variations by Genomic Single-Nucleotide Polymorphism Array in Fetuses with Congenital Heart Defects.

Tang S, Lv J, Chen X, Bai L, Li H, Chen C, Wang P, Xu X, Lu J.

Abstract

OBJECTIVES:

To evaluate the usefulness of single-nucleotide polymorphism (SNP) array for prenatal genetic diagnosis of congenital heart defect (CHD), we used this approach to detect clinically significant copy number variants (CNVs) in fetuses with CHDs.

METHODS:

A HumanCytoSNP-12 array was used to detect genomic samples obtained from 39 fetuses that exhibited cardiovascular abnormalities on ultrasound and had a normal karyotype. The relationship between CNVs

and CHDs was identified by using genotype-phenotype comparisons and searching of chromosomal databases. All clinically significant CNVs were confirmed by real-time PCR.
RESULTS:
CNVs were detected in 38/39 (97.4%) fetuses: variants of unknown significance were detected in 2/39 (5.1%), and clinically significant CNVs were identified in 7/39 (17.9%). In 3 of the 7 fetuses with clinically significant CNVs, 3 rare and previously undescribed CNVs were detected, and these CNVs encompassed the CHD candidate genes FLNA (Xq28 dup), BCOR (Xp11.4 dup), and RBL2 (16q12.2 del).
CONCLUSION:
Compared with conventional cytogenetic genomics, SNP array analysis provides significantly improved detection of submicroscopic genomic aberrations in pregnancies with CHDs. Based on these results, we propose that genomic SNP array is an effective method which could be used in the prenatal diagnostic test to assist genetic counseling for pregnancies with CHDs.
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PMID: 26184588 [PubMed - in process]

8.
Prenat Diagn. 2016 Jan;36(1):40-8. doi: 10.1002/pd.4708. Epub 2015 Nov 20.
<u>Prevalence of defined ultrasound findings of unknown significance at the second trimester fetal anomaly scan and their association with adverse pregnancy outcomes: the Welsh study of mothers and babies population-based cohort.</u>
Hurt L, Wright M, Dunstan F, Thomas S, Brook F, Morris S, Tucker D, Wills MA, Davies C, John G, Fone D, Paranjothy S.

Abstract
OBJECTIVE:
The aim of this article was to estimate the population prevalence of seven defined ultrasound findings of uncertain significance ('markers') in the second trimester and the associated risk of adverse pregnancy outcomes.
METHOD:
A prospective record-linked cohort study of 30 078 pregnant women who had second trimester anomaly scans between July 2008 and March 2011 in Wales was conducted.
RESULTS:
The prevalence of markers ranged from 43.7 per 1000 singleton pregnancies for cardiac echogenic foci [95% confidence interval (CI): 38.8, 51.1] to 0.6 for mild-to-moderate ventriculomegaly (95% CI: 0.3, 1.0). Isolated echogenic bowel was associated with an increased risk of congenital anomalies [risk ratio (RR) 4.54, 95% CI: 2.12, 9.73] and preterm birth (RR 2.30, 95% CI: 1.08, 4.90). Isolated pelvicalyceal dilatation was associated with an increased risk of congenital anomalies (RR 3.82, 95% CI: 2.16, 6.77). Multiple markers were associated with an increased risk of congenital anomalies (RR 5.00, 95% CI: 1.35, 18.40) and preterm birth (RR 3.38, 95% CI 1.20, 9.53).
CONCLUSIONS:
These data are useful for counselling families and developing clinical guidance and care pathways following the detection of markers in clinical practice, particularly the need for follow-up scans to monitor placental function and growth in pregnancies with isolated echogenic bowel, and further investigation for multiple markers. © 2015 The Authors. Prenatal Diagnosis published by John Wiley & Sons Ltd.
© 2015 The Authors. Prenatal Diagnosis published by John Wiley & Sons Ltd.
PMID: 26475362 [PubMed - in process]

9.

Associations of maternal prepregnancy body mass index and gestational weight gain with cardio-metabolic risk factors in adolescent offspring: a prospective cohort study.

Gaillard R, Welten M, Oddy WH, Beilin LJ, Mori TA, Jaddoe V, Huang RC.

Abstract
OBJECTIVE:
To assess the associations of maternal prepregnancy body mass index (BMI) and rates of early-pregnancy, mid-pregnancy and total gestational weight gain with adolescent body fat distribution and cardio-metabolic outcomes.
DESIGN:
Population-based prospective cohort study.
SETTING:
Western Australia.
POPULATION:
Thousand three hundred and ninety-two mothers and their children.
METHODS:
Maternal prepregnancy weight was assessed by questionnaire. Maternal weights at a mean of 16.5 ± 2.2 SD and 34.1 ± 1.5 SD weeks of gestation were obtained from medical records. Offspring adiposity and cardio-metabolic outcomes were assessed at a median age 17.0 years [95% confidence interval (CI) range: 16.7, 17.7].
MAIN OUTCOME MEASURES:
Adolescent BMI, waist circumference (WC), waist-to-hip ratio (WHR), blood pressure, total and HDL-cholesterol, triglycerides, insulin, glucose and HOMA-IR.
RESULTS:
Higher prepregnancy BMI was associated with higher adolescent BMI, WC, WHR, systolic blood pressure, insulin, glucose and HOMA-IR levels (P-values <0.05). Adjustment for adolescent current BMI attenuated the associations of prepregnancy BMI with adolescent cardio-metabolic outcomes. Higher weight gain in early-pregnancy, but not mid-pregnancy, was associated with higher adolescent BMI, WC and WHR (P-values <0.05), but not with other cardio-metabolic risk factors. Total gestational weight gain was associated with adolescent BMI and WC (P-values <0.05). Higher prepregnancy BMI and early-pregnancy weight gain were associated with increased risks of the high-metabolic risk cluster in adolescents (OR 1.57, 95% CI 1.33, 1.85 and OR 1.23, 95% CI 1.03, 1.47 per SD increase in prepregnancy BMI and early-pregnancy weight gain, respectively).
CONCLUSIONS:
Higher maternal prepregnancy BMI and early-pregnancy weight gain rate are associated with an adverse adolescent cardio-metabolic profile. These associations are largely mediated by adolescent BMI.
TWEETABLE ABSTRACT:
Prepregnancy BMI and early-pregnancy WG rate are associated with adverse adolescent cardio-metabolic profile.

PMID: 26525168 [PubMed - in process]

10.

[Term elective induction of labour and perinatal outcomes in obese women: retrospective cohort study.](#)

Lee VR, Darney BG, Snowden JM, Main EK, Gilbert W, Chung J, Caughey AB.

Abstract
OBJECTIVE:
To compare perinatal outcomes between elective induction of labour (eIOL) and expectant management in obese women.
DESIGN:
Retrospective cohort study.
SETTING:
Deliveries in California in 2007.
POPULATION:
Term, singleton, vertex, nonanomalous deliveries among obese women (n = 74 725).
METHODS:
Women who underwent eIOL at 37 weeks were compared with women who were expectantly managed at that gestational age. Similar comparisons were made at 38, 39, and 40 weeks. Results were stratified by parity. Chi-square tests and multivariable logistic regression were used for statistical comparison.
MAIN OUTCOME MEASURES:
Method of delivery, severe perineal lacerations, postpartum haemorrhage, chorioamnionitis, macrosomia, shoulder dystocia, brachial plexus injury, respiratory distress syndrome.
RESULTS:
The odds of caesarean delivery were lower among nulliparous women with eIOL at 37 weeks [odds ratio (OR) 0.55, 95% confidence interval (CI) 0.34-0.90] and 39 weeks (OR 0.77, 95% CI 0.63-0.95) compared to expectant management. Among multiparous women with a prior vaginal delivery, eIOL at 37 (OR 0.39, 95% CI 0.24-0.64), 38 (OR 0.65, 95% CI 0.51-0.82), and 39 weeks (OR 0.67, 95% CI 0.56-0.81) was associated with lower odds of caesarean. Additionally, eIOL at 38, 39, and 40 weeks was associated with lower odds of macrosomia. There were no differences in the odds of operative vaginal delivery, lacerations, brachial plexus injury or respiratory distress syndrome.
CONCLUSIONS:
In obese women, term eIOL may decrease the risk of caesarean delivery, particularly in multiparas, without increasing the risks of other adverse outcomes when compared with expectant management.
TWEETABLE ABSTRACT:
Elective induction of labour in obese women does not increase risk of caesarean or other perinatal morbidities.
© 2015 Royal College of Obstetricians and Gynaecologists.
KEYWORDS:
Caesarean delivery; elective induction of labour; maternal obesity

11.

[Oral nifedipine versus intravenous labetalol for severe hypertension during pregnancy: a systematic review and meta-analysis.](#)

Shekhar S, Gupta N, Kirubakaran R, Pareek P.

Abstract
BACKGROUND:
Oral nifedipine is recommended along with labetalol and hydralazine for treatment of severe hypertension during pregnancy by most authorities. Although nifedipine is cheap and easily administered, the usage pattern among health care providers suggests a strong preference for labetalol despite lack of evidence for the same.
OBJECTIVES:
To determine the efficacy and safety of oral nifedipine for treatment of severe hypertension of pregnancy compared with intravenous labetalol.
SEARCH STRATEGY:
We systematically searched for articles comparing oral nifedipine with intravenous labetalol for the treatment of severe hypertension during pregnancy in any language, over Medline, Cochrane Central Register of Clinical Trials and Google Scholar from inception till February 2014.
SELECTION CRITERIA:
We included all RCTs that compared intravenous labetalol with oral nifedipine for treatment of severe hypertension during pregnancy, addressing relevant efficacy and safety outcomes.
DATA COLLECTION AND ANALYSIS:
Eligible studies were reviewed, and data were extracted onto a standard form. We used Cochrane review manager software for quantitative analysis. Data were analysed using a fixed effect model.
MAIN RESULTS:
The pooled analysis of seven trials (four from developing countries) consisting of 363 woman-infant pairs showed that oral nifedipine was associated with less risk of persistent hypertension (RR 0.42, 95% CI 0.18-0.96) and reported maternal side effects (RR 0.57, 95% CI 0.35-0.94). However, on sensitivity analysis the outcome 'persistent hypertension' was no longer significant. Other outcomes did not reach statistical significance.
CONCLUSION:
Oral nifedipine is as efficacious and safe as intravenous labetalol and may have an edge in low resource settings.
TWEETABLE ABSTRACT:
Although studies to date are few in number and small, nifedipine shows promise for severe hypertension in pregnancy.

12.
Effect of Vitamin D3 Supplementation During Pregnancy on Risk of Persistent Wheeze in the Offspring: A Randomized Clinical Trial.
Chawes BL, Bønnelykke K, Stokholm J, Vissing NH, Bjarnadóttir E, Schoos AM, Wolsk HM, Pedersen TM, Vinding RK, Thorsteinsdóttir S, Arianto L, Hallas HW, Heickendorff L, Brix S, Rasmussen MA, Bisgaard H.

Abstract
IMPORTANCE:
Observational studies have suggested that increased dietary vitamin D intake during pregnancy may

protect against wheezing in the offspring, but the preventive effect of vitamin D supplementation to pregnant women is unknown.

OBJECTIVE:

To determine whether supplementation of vitamin D3 during the third trimester of pregnancy reduces the risk of persistent wheeze in the offspring.

DESIGN, SETTING, AND PARTICIPANTS:

A double-blind, single-center, randomized clinical trial conducted within the Copenhagen Prospective Studies on Asthma in Childhood 2010 cohort. Enrollment began March 2009 with a goal of 708 participants, but due to delayed ethical approval, only 623 women were recruited at 24 weeks of pregnancy. Follow-up of the children (N = 581) was completed when the youngest child reached age 3 years in March 2014.

INTERVENTIONS:

Vitamin D3 (2400 IU/d; n = 315) or matching placebo tablets (n = 308) from pregnancy week 24 to 1 week postpartum. All women received 400 IU/d of vitamin D3 as part of usual pregnancy care.

MAIN OUTCOMES AND MEASURES:

Age at onset of persistent wheeze in the first 3 years of life. Secondary outcomes included number of episodes of troublesome lung symptoms, asthma, respiratory tract infections, and neonatal airway immunology. Adverse events were assessed.

RESULTS:

Of the 581 children, persistent wheeze was diagnosed during the first 3 years of life in 47 children (16%) in the vitamin D3 group and 57 children (20%) in the control group. Vitamin D3 supplementation was not associated with the risk of persistent wheeze, but the number of episodes of troublesome lung symptoms was reduced, and the airway immune profile was up-regulated (principal component analysis, P = .04). There was no effect on additional end points. Intrauterine death was observed in 1 fetus (<1%) in the vitamin D3 group vs 3 fetuses (1%) in the control group and congenital malformations in 17 neonates (5%) in the vitamin D3 group vs 23 neonates (8%) in the control group. [table: see text].

CONCLUSIONS AND RELEVANCE:

The use of 2800 IU/d of vitamin D3 during the third trimester of pregnancy compared with 400 IU/d did not result in a statistically significant reduced risk of persistent wheeze in the offspring through age 3 years. However, interpretation of the study is limited by a wide CI that includes a clinically important protective effect.

TRIAL REGISTRATION:

clinicaltrials.gov Identifier: NCT00856947.

Comment in

Inconclusive Results of Randomized Trials of Prenatal Vitamin D for Asthma Prevention in Offspring: Curbing the Enthusiasm. [JAMA. 2016]

PMID: 26813208 [PubMed - indexed for MEDLINE]

13.

Primary Care Screening for and Treatment of Depression in Pregnant and Postpartum Women: Evidence Report and Systematic Review for the US Preventive Services Task Force.

O'Connor E, Rossom RC, Henninger M, Groom HC, Burda BU.

Author information

Abstract

IMPORTANCE:

Depression is a source of substantial burden for individuals and their families, including women during

the pregnant and postpartum period.

OBJECTIVE:

To systematically review the benefits and harms of depression screening and treatment, and accuracy of selected screening instruments, for pregnant and postpartum women. Evidence for depression screening in adults in general is available in the full report.

DATA SOURCES:

MEDLINE, PubMed, PsycINFO, and the Cochrane Collaboration Registry of Controlled Trials through January 20, 2015; references; and government websites.

STUDY SELECTION:

English-language trials of benefits and harms of depression screening, depression treatment in pregnant and postpartum women with screen-detected depression, and diagnostic accuracy studies of depression screening instruments in pregnant and postpartum women.

DATA EXTRACTION AND SYNTHESIS:

Two investigators independently reviewed abstracts and full-text articles and extracted data from fair- and good-quality studies. Random-effects meta-analysis was used to estimate the benefit of cognitive behavioral therapy (CBT) in pregnant and postpartum women.

MAIN OUTCOMES AND MEASURES:

Depression remission, prevalence, symptoms, and related measures of depression recovery or response; sensitivity and specificity of selected screening measures to detect depression; and serious adverse effects of antidepressant treatment.

RESULTS:

Among pregnant and postpartum women 18 years and older, 6 trials (n = 11,869) showed 18% to 59% relative reductions with screening programs, or 2.1% to 9.1% absolute reductions, in the risk of depression at follow-up (3-5 months) after participation in programs involving depression screening, with or without additional treatment components, compared with usual care. Based on 23 studies (n = 5398), a cutoff of 13 on the English-language Edinburgh Postnatal Depression Scale demonstrated sensitivity ranging from 0.67 (95% CI, 0.18-0.96) to 1.00 (95% CI, 0.67-1.00) and specificity consistently 0.87 or higher. Data were sparse for Patient Health Questionnaire instruments. Pooled results for the benefit of CBT for pregnant and postpartum women with screen-detected depression showed an increase in the likelihood of remission (pooled relative risk, 1.34 [95% CI, 1.19-1.50]; No. of studies [K] = 10, $I2$ = 7.9%) compared with usual care, with absolute increases ranging from 6.2% to 34.6%. Observational evidence showed that second-generation antidepressant use during pregnancy may be associated with small increases in the risks of potentially serious harms.

CONCLUSIONS AND RELEVANCE:

Direct and indirect evidence suggested that screening pregnant and postpartum women for depression may reduce depressive symptoms in women with depression and reduce the prevalence of depression in a given population. Evidence for pregnant women was sparser but was consistent with the evidence for postpartum women regarding the benefits of screening, the benefits of treatment, and screening instrument accuracy.