Welcome to the 4th issue of Obstetrics and Gynaecology Research Review.

A landmark study from Canada found no associations between exposure to pH1N1 influenza vaccine during pregnancy and most five year paediatric health outcomes. Another Canadian study reported cannabis use was significantly associated with an increased risk of preterm birth. A population-based retrospective cohort study reported smoking during the first trimester of pregnancy is associated with increased risk of some birth defects. The authors also noted smoking during the few months before conception, even with cessation in the first trimester, may also pose a risk for birth defects.

A meta-analysis identified a 264% increase in the odds of child obesity when mothers have obesity before conception. The concluding article found maternal pre-pregnancy BMI and gestational weight gain are associated with risks of pregnancy complications. Furthermore, obese mothers with high gestational weight gain are at the highest risk of pregnancy complications.

I hope you find the research in this issue useful to you in your practice and I look forward to your comments and feedback.

Kind Regards,

Associate Professor Mark Erian
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Health outcomes of young children born to mothers who received 2009 pandemic H1N1 influenza vaccination during pregnancy: Retrospective cohort study

Authors: Walsh LK, et al

Summary: This retrospective cohort study analysed registry and administrative databases including 104,249 live births with 5 year follow up. Of the study cohort 30% were exposed to pH1N1 influenza vaccination in utero. The authors concluded prenatal pH1N1 vaccination had no significant associations with respiratory infections, otitis media, any infectious diseases, neoplasms, sensory disorders, urgent and inpatient health services use, paediatric complex chronic conditions, or mortality. They noted weak associations with increased asthma and reduced gastrointestinal infections.

Comment: Influenza can be a serious viral infection and many obstetricians would encourage their patients to receive immunisation against influenza during pregnancy. But, would influenza vaccination cause a health problem for newborns during their early childhood?

In a landmark retrospective study from Ontario, Canada, 104,204 live births from November 2009 through October 2010 were analysed and 31,295 (30%) were exposed to pH1N1 influenza vaccination in utero. The authors concluded prenatal pH1N1 vaccination had no significant associations with respiratory infections, otitis media, any infectious diseases, neoplasms, sensory disorders, urgent and inpatient health services use, paediatric complex chronic conditions, or mortality. They noted weak associations with increased asthma and reduced gastrointestinal infections.

There was no association between exposure to pH1N1 influenza vaccine during pregnancy and most 5 year paediatric health outcomes. Residual confounding may explain the small associations observed with increased asthma and reduced gastrointestinal infections; these outcomes should be assessed in future studies.

Reference: BMJ 2019 Jul 10;366:l4151

Abstract
Association between self-reported prenatal cannabis use and maternal, perinatal, and neonatal outcomes

Authors: Corsi DJ, et al

Summary: This population-based retrospective cohort study assessed births among a cohort of 661,617 women; of whom 9,427 (1.4%) reported cannabis use during pregnancy. The investigators addressed the imbalance in obstetrical and sociodemographic characteristics between users and nonusers by using matching; yielding a sample of 5,639 reported users and 92,873 nonusers. They found the crude rate of preterm birth less than 37 weeks’ gestation was 6.1% among nonusers and 12.0% among users in the unmatched cohort (risk difference, 5.88% [95% CI, 5.22%-6.54%]). In the matched cohort, reported cannabis exposure was significantly associated with a risk difference of 2.98% (95% CI, 2.63%-3.34%) and a relative risk of 1.41 (95% CI, 1.36-1.47) for preterm birth. Furthermore, cannabis exposure was significantly associated with greater frequency of small for gestational age, placental, transfer to neonatal intensive care, and S-5-minute Apgar score less than 4.

Comment: There is some social evidence that the use of cannabis is on the rise. However, our knowledge about perinatal outcome following in utero exposure remains limited.

In interesting research from Ontario, Canada, the association between self-reported prenatal cannabis use and adverse maternal and perinatal outcomes were evaluated. Population-based retrospective cohort study was designed and covered live births and stillbirths among women aged 15 years and older in Ontario, Canada. In a cohort of 661,617 women the mean gestational age was 39.4 weeks and 51% of infants were male. Mothers had a mean age of 30.4 years and 9,427 (1.4%) reported cannabis use during pregnancy. Imbalance in measured maternal obstetrical and sociodemographic characteristics between reported cannabis users and nonusers was attenuated using matching. Reported cannabis use was associated with increased risk of preterm labour, small for gestational age, placental abruption, transfer to neonatal intensive care and lower S-5-minute Apgar score less than in non users.

Reference: JAMA 2019 Jul 9;322(2):145-152

Association of preterm birth and low birth weight with romantic partnership, sexual intercourse, and parenthood in adulthood: A systematic review and meta-analysis

Authors: Mendonça M, et al

Summary: The meta-analysis included 21 prospective longitudinal and registry studies reporting on selected social outcomes in adults who were born preterm or with low birth weight compared with control individuals born at term. Of the 4,423,798 participants 179,724 were preterm or low birth weight. The researchers found adults born preterm or with low birth weight were less likely to have ever experienced a romantic partnership, to have had sexual intercourse, or to have become parents than adults born full-term. In addition, a dose-response association according to degree of prematurity was found for romantic partnership and parenthood.

Comment: Social relationships are important indicators of well-being, health and quality of life. This is interesting research from the Department of Psychology, University of Warwick, United Kingdom, to systematically investigate the association between preterm birth or low birth weight and social outcomes in adulthood.

The data sources PubMed, PsycINFO, web of Science and Embase were searched for peer-reviewed articles published through August 5, 2018. Prospective longitudinal and registry studies reporting on selected social outcomes in adults who were born preterm or with low birth weight (mean age sample age 18 years and above) were compared with control individuals born at term.

Meta-analysis followed Preferred Reporting Items for Systematic Review and Meta-analysis guidelines and collected and extracted by 2 independent reviewers. Twenty-one studies were included of the 1,829 articles screened. Summary data described a maximum of 4,423,798 adult participants (179,724 preterm or low birth weight). The findings suggest that adults born preterm or with low birth weight are less likely to experience a romantic partnership, sexual intercourse, or to become parents. However, preterm birth or low birth weight does not seem to impair the quality of relationships with partners and friends.

Reference: JAMA Netw Open 2019 Jul 3;2(7):e196961

The association between maternal body mass index and child obesity: A systematic review and meta-analysis

Authors: Heslehurst N, et al

Summary: This systematic review and meta-analysis included 20 studies of obese children (n=88,872), 22 studies of overweight/obese children (n=181,800) and 10 studies of overweight children (n=53,238). The authors concluded there were significantly increased odds of child obesity with maternal obesity (OR 3.64, 95% CI 2.68-4.95) and maternal overweight (OR 1.89, 95% CI 1.62-2.19). Furthermore, there were significantly increased odds for child overweight/obesity (OR 2.69, 95% CI 2.10-3.46) and for child overweight (OR 1.80, 95% CI 1.25, 2.59) with maternal obesity.

Comment: Obesity is a global health problem. Association between maternal body mass index (BMI) and childhood obesity in the offspring is interesting. Searches in MEDLINE, Child Development & Adolescent Studies, CINAHL, Embase and Psych Info were carried out and updated in March 2019. Supplementary searches included hand-searching reference lists, performing citation searching and contacting authors.

Categorical outcomes were child obesity (at or above 95th percentile), overweight/obesity (at or more than 85th percentile) and overweight (85th to 95th percentile). Linear and nonlinear dose-response meta-analysis were summarised narratively. Seventy-nine of 41,301 studies met the criteria. Meta-analysis of child obesity included 20 studies (n=88,872), child overweight/obesity 22 studies (n=181,800) and overweight 10 studies (n=53,238). A limitation of this research was that the included studies did not always report the data in a format that enabled inclusion in this complex meta-analysis.

This research has identified a 264% increase in the odds of child obesity when mothers have obesity before conception. This study throws light on the valuable prevention of pre-conception obesity so that intergenerational obesity may be better managed.


Independent commentary by Associate Professor Mark Erian

A/Prof Mark Erian, MD (High Doctorate of Medicine, Queensland University), is a senior consultant obstetrician and gynaecologist based in Brisbane, Australia. He has been in specialist practice for more than 25 years. He has a wide range of experiences in obstetrics and gynaecology and related surgical specialties through a variety of appointments in Ireland, the UK and Australia. A/Prof Mark Erian has many years of experience in a full range of intensive labour ward management. He is well versed in managing high-risk pregnancy in labour and management of both spontaneous and induced labour. In addition, he performs all the major elective gynaecological surgical procedures, including laparoscopic hysterectomy and laparoscopic excision of endometriosis, myomectomy and vaginal repairs. He has extensive experience in grave emergency gynaecological surgery including laparoscopy for ruptured ectopic pregnancy and other adnexal and appendix conditions. Because of his knowledge in this specialist field, A/Prof Mark Erian is an accredited trainer at minimally-invasive gynaecological surgery, and has been actively involved in the teaching of trainees, fellows, undergraduate and postgraduate trainees in advanced laparoscopic procedures both in Australia and the US. He regularly lectures in the US in advanced hysteroscopic surgery and has published numerous papers.
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* Recurrent UTIs ≥2 in 6 months or ≥3 in 12 months
† Hiprex should be started after finishing treatment for an acute UTI

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Azithromycin vs erythromycin for the management of preterm premature rupture of membranes

Authors: Navathe R, et al

Summary: The investigators evaluated whether there are differences in the latency from preterm premature rupture of membranes to delivery in patients treated with different dosing regimens of azithromycin versus erythromycin. The cohort consisted of 453 women with singleton pregnancies with confirmed rupture of membranes between 23 and 33 weeks + 6 days. Seventy-eight patients received azithromycin for 1 day, 191 patients received azithromycin for 5 days, 52 patients received azithromycin for 7 days, and 132 patients received erythromycin. The investigators observed no statistical difference in median latency time of azithromycin 1 day (4.9 days), azithromycin 5 days (5.0 days), or azithromycin 7 days (4.9 days) when compared with erythromycin (5.1 days). Respiratory distress syndrome was increased in the azithromycin 5 day group vs azithromycin 1 day vs erythromycin (44% vs 29% and 29%, P =.005, respectively).

Comment: Preterm premature rupture of membranes complicates about 3% of pregnancies. Many obstetric units opted for the use of azithromycin instead of erythromycin. That is probably due to occasional national shortfalls of erythromycin, ease of administration, better side effect profile and decreased cost of azithromycin as compared with erythromycin.

This is a multicentre, retrospective cohort of women with singleton pregnancies with confirmed rupture of membranes between 23 to 36 weeks +6 days from January 2010 to June 2015 and there were no contraindications to expectant management. Patients received 1 of 4 antibiotic regimens: (1) azithromycin 1g orally stat; (2) azithromycin 500mg orally, followed by 250mg orally daily for 4 days; (3) azithromycin 500mg intravenously for 2 days followed by azithromycin 500mg orally for 5 days; (4) erythromycin intravenously for 2 days followed by oral erythromycin for 5 days. 453 patients were recruited in the study and randomly selected to one of the aforementioned groups.

There was no difference in latency to delivery, incidence of chorioamnionitis, or neonatal outcomes when comparing different dosing regimens of the azithromycin with erythromycin with the exception of respiratory distress syndrome being more common in the 5 days azithromycin (2) group.


Abstract

Cervical pessary for preventing preterm birth in twin pregnancies with maternal short cervix after an episode of threatened preterm labor: Randomised controlled trial

Authors: Mercad C, et al

Summary: Women with twin pregnancies who had not delivered 48 hours after a threatened preterm labour episode and had a short cervix remaining were randomly assigned to cervical pessary (n = 67) or routine management (n = 65). The authors concluded pessary use significantly lowered the spontaneous preterm birth rate before 34 weeks. Pessary use also reduced the threatened preterm labour recurrence and neonates' weight less than 2500g.

Comment: Preterm birth is one of the main causes of neonatal morbidity and mortality. No intervention (expectant approach) may be adopted in some cases to minimise the risk of preterm birth in twin pregnancy. This study was designed to establish the value of cervical pessaries in preventing preterm birth in twin pregnancy.

132 pregnant women were included in this open, randomised, controlled trial who had not delivered 48 hours after a threatened preterm labour episode and had a short cervix (<20mm between 24 and 29+6 weeks and <10mm between 30 and 33+6 weeks). Women were randomly assigned to the cervical pessary (n=67) or routine (non-intervention) management (n=65). The primary outcome was the spontaneous preterm birth rate before 34 weeks.

Significant difference were noted in the spontaneous preterm birth rate before 34 weeks between the pessary and routine management groups; 16.4% and 32.3% in the pessary and control groups respectively. No significant differences were observed in the preterm rate <28 weeks or <37 weeks between groups. The pessary group less frequently required readmission for new threatened preterm labour episodes; 5.6% and 21.5% respectively. Significant reduction was observed in the number of neonates weighing less than 2500g; 17.9% in the pessary group and 70.8% in the routine management group.

Pessary use may be considered for the management of preterm birth in twin pregnancy.


Abstract

Oral vs intravenous iron therapy for postpartum anaemia: A systematic review and meta-analysis

Authors: Sultan P, et al

Summary: The team analysed 15 randomised trials comparing oral iron (n=1,001) versus intravenous (IV) iron (n=1,181) to treat postpartum anaemia. They reported haemoglobin concentrations at 6 weeks postpartum were almost 1g/dL higher in women who received IV iron compared to oral iron. Furthermore, women receiving IV iron had higher haemoglobin concentrations at postpartum weeks 1, 2, and 3; higher ferritin concentrations at postpartum weeks 1, 2, 4, and 6; an increased likelihood of skin flushing and a decreased likelihood of constipation and dyspepsia. A systematic review and meta-analysis included randomised trials comparing oral vs IV iron monotherapy to treat postpartum anaemia (classified as a haemoglobin less than 12g/dL). The primary outcome was haemoglobin concentration at 6 weeks postpartum. Secondary outcomes included haemoglobin concentration at 1-5 weeks postpartum, ferritin concentration at 1-6 weeks postpartum, and maternal adverse outcomes.

A total of 15 randomised trials were evaluated and included. Higher postpartum week 6 haemoglobin concentrations were in the IV iron group (mean difference 0.9g/dL; 95% CI, 0.41-1.3; P =.0003). Compared to oral iron, women receiving IV iron had a higher haemoglobin concentration at postpartum weeks 1, 2 and 3; higher ferritin concentrations at postpartum weeks 1, 2, 4 and 6; increased likelihood of skin flushing; decreased likelihood of constipation and dyspepsia. The reported event rate for anaphylaxis among women receiving IV iron was 0.6%. In this systematic review, IV iron therapy produced a higher rise of haemoglobin in postpartum anaemic women. In addition, the safety profile of IV iron was reassuring.


Abstract
Influence of periconception smoking behavior on birth defect risk

Authors: Perry MF, et al

Summary: Rates of cardiovascular, musculoskeletal, gastrointestinal, and neural tube birth defects were compared between a group of women who did not smoke and a group of women who smoked during the preconception period of 3 months before conception only and in the preconception period plus throughout the first trimester of pregnancy. The researchers found smoking during the preconception period only was associated with a 40% increased risk of gastroschisis. Smoking during preconception only was not associated with any other individual birth defects. In contrast, smoking through the first trimester was associated with a statistically significant increased risk of several defects that included gastrochisis and limb reduction.

Comment: Smoking is one of the risky lifestyles and is associated with many health hazards to the smoker and those in his/her vicinity. This study aims at assessing the association of maternal smoking and the timing of periconception exposure with congenital birth defects.

The study was a population--based retrospective cohort of live births in Ohio, USA, from 2006-2015 (inclusive) with the use of data from birth certificates. Rates of birth defects were compared between a referent group of women who did not smoke and a group of women who smoked (1) during the preconception period of 3 months before conception only, not in the first trimester and (2) in the preconception period plus throughout the first trimester of pregnancy. Multivariate logistic regression was used to quantify the relationship between periconception smoking and the rate of birth defects after adjustment.

Of 1,436,036 live births in the study period 75% of mothers did not smoke during preconception nor during pregnancy; 23.3% who smoked during pregnancy; 6.0% of the population smoked during preconception only; 17.3% smoked both during the preconception period plus through the first trimester. Smoking during the preconception period only was associated with a 40% increased risk of gastrochisis. Smoking during the first trimester (period of organogenesis) was associated with statistically significant increased risk of several birth defects that included gastrochisis and a composite outcome of any defect. Smoking during the period of fetal organogenesis is associated with increased risk of some birth defects.


Abstract

Neonatal and maternal adverse outcomes among low-risk parous women at 39-41 weeks of gestation

Authors: Chen HY, et al

Summary: The study cohort included low-risk parous women with nonanomalous singleton gestations who delivered at 39, 40, or 41 weeks of gestation. Of the 5.4 million live births included in the analysis 54.4% delivered at 39 weeks of gestation, 35.7% at 40 weeks, and 9.9% at 41 weeks. The overall rate of the composite neonatal adverse outcome was 4.86 per 1,000 live births. The rates of the composite neonatal and maternal adverse outcomes modestly increased from 39 through 41 weeks of gestation.

Comment: Induction of labour at 39-41 weeks of gestation for low-risk pregnancies has been a long standing debate regarding the best time to do so considering the neonatal or maternal outcome.

This retrospective cohort study used the USA vital statistics data sets (2012-2016, inclusive). Low-risk women with nonanomalous singleton gestations who delivered at 39-41 weeks of gestation were evaluated. The primary outcome was the composite neonatal outcome included Apgar score less than 5 at 5 minutes, assisted ventilation for more than 6 hours, neonatal seizures/mortality. The secondary outcome was the composite maternal adverse outcome included admission to intensive care unit, blood transfusion, uterine rupture or unplanned hysterectomy. Multivariable Poisson regression analysis was employed.

19.9 million live births were evaluated, 5.4 million met inclusion criteria. The overall rate of composite neonatal adverse outcome was 4.86 per 1000 live births. The risk was higher for those delivered at 40 and 41 weeks of gestation compared with 39 weeks. The overall rate of composite maternal adverse outcome was 2.31 per 1000 live births. Similarly, the risk of the composite maternal adverse outcome was significantly higher with delivery at 40 and 41 weeks of gestation than 39 weeks.

The rates of composite neonatal and maternal adverse outcomes increase from 39 through 41 weeks of gestation.


Abstract

Impact of maternal body mass index and gestational weight gain on pregnancy complications: An individual participant data meta-analysis of European, North American and Australian cohorts

Authors: Santos S, et al

Summary: The meta-analysis included 39 cohorts with a total of 265,270 births. The researchers found higher maternal pre-pregnancy BMI and gestational weight gain were associated with higher risks of gestational hypertensive disorders, gestational diabetes, and large for gestational age at birth. They also noted obese mothers with high gestational weight gain had the highest risk of any pregnancy complication. The researchers estimated that 23.9% of any pregnancy complication was attributable to maternal overweight/obesity and 31.6% of large for gestational age infants was attributable to excessive gestational weight gain.

Comment: In clinical obstetrical practice it is prudent to manage maternal pre-pregnancy BMI and gestational weight gain to prevent associated complications.

Meta-analysis of 39 cohorts from Europe, North America and Oceania were evaluated, that included 265,270 births. Information on maternal pre-pregnancy BMI, gestational weight gain, and pregnancy complications were obtained and multilevel binary logistic regression models were employed. The main outcome measures were gestational hypertension, pre-eclampsia, gestational diabetes, preterm birth, small and large for gestational age at birth.

Higher maternal pre-pregnancy BMI and gestational weight gain were associated with higher risks of gestational hypertensive disorders, gestational diabetes, and large for gestational age at birth. Promoting a healthy pre-pregnancy BMI and gestational weight gain may reduce the potential risks of pregnancy complications and consequently the problems of maternal and neonatal morbidity.

Reference: BJOG 2019 Jul;126(8):984-995

Abstract