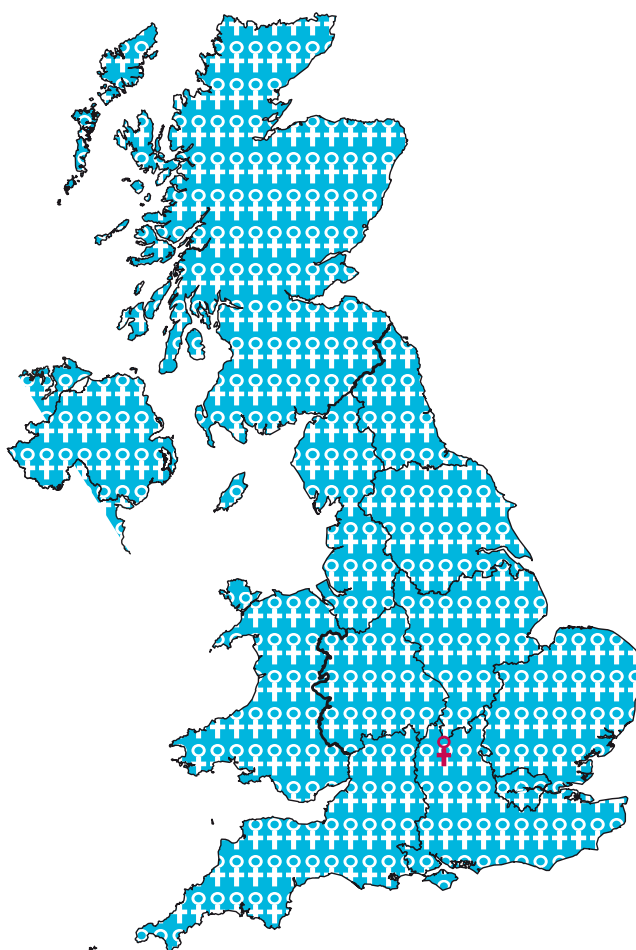


UK Obstetric Surveillance System

Fifth Annual Report 2011

We would like to thank all the reporting anaesthetists, midwives, obstetricians, risk managers and other clinicians throughout the UK who have contributed to UKOSS, without whom this work would not have been possible



Royal College of
Obstetricians and
Gynaecologists



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1. Introduction

The UK Obstetric Surveillance System (UKOSS), a joint initiative between the National Perinatal Epidemiology Unit and the Royal College of Obstetricians and Gynaecologists, was launched in February 2005. The system is designed to be used to survey a range of rare conditions in pregnancy. The system is also supported by the Royal College of Midwives, the Obstetric Anaesthetists Association, the NCT, the Faculty of Public Health, the Department of Health and the Health Protection Agency.

Rare conditions are difficult to study because the identification of even a small number of affected women requires collaboration between large numbers of investigators. Such collaborations are difficult to establish and may be costly, hence uncommon disorders are rarely studied comprehensively on a population basis. The information available about the natural history, prognosis, risk factors and evidence-based practice is therefore very limited. UKOSS draws together clinicians from all hospitals with consultant-led maternity units in the UK in a routine reporting system, thus allowing the straightforward conduct of a changing programme of studies of rare disorders of pregnancy. The information gained from these studies may be used to inform counselling of women, development of guidelines for prevention or treatment and for service planning. Completed studies have demonstrated the efficacy of the system for generating this information¹⁻⁶.

Studies using UKOSS may be undertaken by any investigator who identifies a suitable topic⁷. Suitable disorders to study are those which are uncommon (usually no more than one case per 2000 births annually in the UK); are an important cause of maternal or perinatal morbidity or mortality; and which have research questions that can be suitably addressed using the UKOSS methodology (prospective descriptive, cohort or case-control studies). This report outlines the studies undertaken during the sixth year of surveillance using UKOSS.

2. Methods

Up to four nominated clinicians (anaesthetists, midwives, obstetricians and risk managers) in each hospital with a consultant-led maternity unit in the UK report to UKOSS. Every month, the nominated individuals are sent a report card with a list of conditions currently under surveillance (Figure 1). They are asked to complete a tick box indicating the number of cases which have occurred in the previous month, or if none, to return the card indicating a nil return. As a guide, only conditions with an estimated incidence of less than one in 2000 births are surveyed, and thus the most common response is a nil return. Nil returns are, however, extremely important as they allow us to confirm the number of women in the denominator birth cohort for each study.

On receiving a case report (return of the monthly card mailing), the UKOSS central team dispatches a data collection form to collect more detailed information about each case. The data collection forms are developed individually for each condition and are designed to be short and easily completed from a woman's case notes without requiring reference to any other sources of information. The data collection forms seek confirmation of the appropriate case definition and additional information on risk factors, management and outcomes according to the protocol relating to each condition. UKOSS does not collect any personally identifiable information, including women's names, addresses, dates of birth or hospital numbers. Reporting clinicians are asked to keep their own record of the names of women they have reported, in order that they can retrieve the woman's case notes to complete the data collection form. The National Information Governance Board (NIGB) and the Confidentiality and Security Advisory Group for Scotland (CSAGS) have judged that collection of information only, for the purpose of studying incidence and identifying means to improve patient care, which is not individually identifiable and does not lead to any change in management for the individual patient is acceptable without requiring individual patient consent^{8,9}. The UKOSS methodology and that of each individual study are approved by Research Ethics Committees.

In order to perform case-control or cohort studies, information is also collected on control or comparison women for some studies. For these studies only, clinicians who report a case are asked to follow specific instructions to identify appropriate comparison women and complete a similar data collection form from their case notes. The process of selecting comparison women is individual to each study.

Examples of questions which can be addressed using UKOSS studies include:

1. Estimating disease incidence; for example UKOSS surveillance of eclampsia demonstrated a 45% reduction in incidence between 1992 and 2005².
2. Describing the prevalence of factors associated with near-miss maternal morbidity; for example a UKOSS study estimated that more than 1 in every 1200 women delivering in the UK is extremely obese (BMI 50kg/m² or greater)¹⁰.
3. Quantifying risk factors for severe morbidity; for example UKOSS surveillance of peripartum hysterectomy for severe haemorrhage showed a significant association with previous delivery by caesarean section⁵.
4. Auditing of national guidelines; for example UKOSS surveillance of antenatal pulmonary embolism showed that very few women were not receiving thromboprophylaxis according to Royal College of Obstetricians and Gynaecologists guidelines^{3,11}.
5. Investigating different management techniques; for example the use of total versus subtotal hysterectomy was examined in the UKOSS study of peripartum hysterectomy for severe haemorrhage but no significant differences in complication rates between the two techniques was found¹.
6. Describing the outcomes of severe morbidity; for example UKOSS surveillance of acute fatty liver of pregnancy showed that both maternal and infant outcomes were better than suggested by previous hospital-based historical studies⁶.

UKOSS can, in addition, be used to conduct studies rapidly in response to emerging public health issues, thus in response to the influenza AH1N1v ('swine flu') pandemic, surveillance of women admitted to hospital with confirmed infection was initiated to inform ongoing clinical guidance during the course of the pandemic¹².

Figure 1: UKOSS Report Card

UKOSS Report Card
United Kingdom Obstetric Surveillance System

March 2011

Nothing to report

Please specify the number of cases seen this month:

Adrenal Tumours - **NEW STUDY** Non-renal Solid Organ Transplant

Amniotic Fluid Embolism Pituitary Tumours

Aortic Dissection Placenta Accreta

Myeloproliferative Disorders Pulmonary Vascular Disease

Severe Obstetric Cholestasis (**bile acids >40 µmol/l**)

Contact details have changed Yes / No

The new details are: _____

email: _____

Telephone no: _____

UKOSS Clinician's Section
Hospital name
March 2011

Condition	Patient's name	Patient's Hospital number

Detach and keep this section.

3. Participation

All 219 units with consultant-led maternity units in the UK contribute to UKOSS. This represents 100% participation of eligible units and effectively means that the denominator for all UKOSS studies is the entire birth cohort in the UK. The mean monthly card return rate during 2010 was 92% (Figure 2), with regional return rates varying between 88% and 99% (Figure 3). These card return rates continue the high rates obtained during the first five years of reporting, and are a testament to the dedication of reporting clinicians throughout the UK.

Figure 2: UKOSS national card return rates January-December 2010

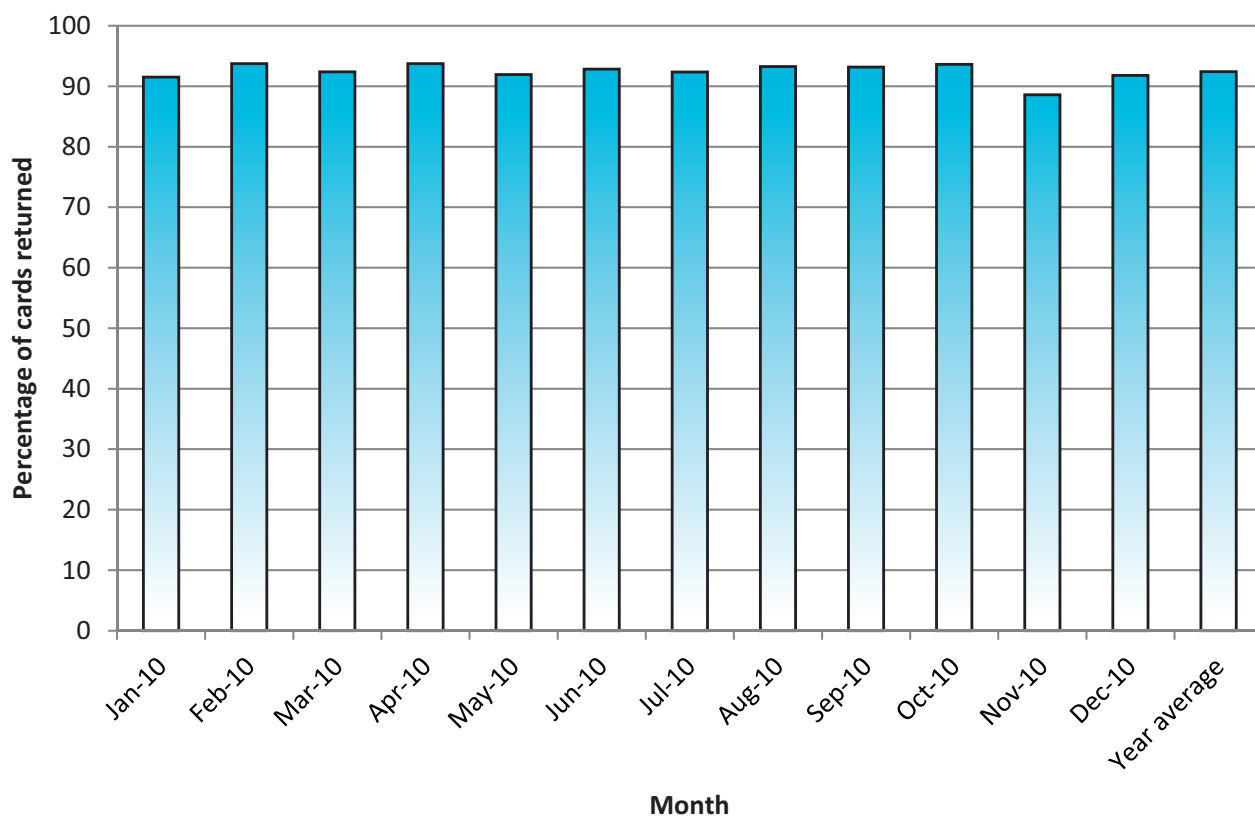


Figure 3: Map showing regional card return rates during 2010



4.2. Studies completed in 2010

4.2.1 Antenatal Stroke

Key points

- Stroke is an important cause of severe maternal morbidity and mortality in the UK.
- The increasing age of women at childbirth, along with other risk factors, may lead to an increase in the incidence of stroke associated with pregnancy.
- This study suggests that currently the incidence of stroke in pregnancy in the UK is similar to that in the non-pregnant population, although we cannot exclude the possibility of under-ascertainment of cases.
- Future approaches to studying the topic may benefit from a joint approach to identifying cases through both maternity and stroke services.

Background

The decreasing incidence of direct causes of maternal death over the past half century has led to a heightened awareness of non-obstetric factors responsible for maternal mortality¹³. While stroke associated with pregnancy is rare (estimates of incidence from retrospective studies vary from 3 to 30 per 100,000 pregnancies), the last eight Confidential Enquiries into Maternal Deaths report a total of 168 deaths from stroke associated with pregnancy. In addition to premature death, stroke associated with pregnancy causes ongoing disability in many survivors, which has a serious impact for mother and infant, and on families, caregivers, and health services. Several population based studies suggest that there is an increase in the rate of all forms of stroke postnatally, but not during pregnancy itself¹⁴, however the estimates of incidence from different studies vary widely. As the age of women childbearing increases, alongside an increase in other vascular risk factors, the incidence of stroke in pregnancy may be increasing.

Case definition

All women in the UK identified as having a stroke during pregnancy. To be included as a case the stroke must:

- EITHER** Be confirmed at postmortem
OR Be confirmed by a consultant neurologist or physician
OR Be confirmed by diagnostic testing (e.g. MRI/CT)

Surveillance Period

October 2007 – March 2010

Results

Seventy-eight cases were reported during the study period and data returned about 65 of them (83%). Thirty-two cases did not meet the case definition and there were three duplicates; of the women whose cases were excluded, one did not meet the case definition, and 19 suffered from their stroke postpartum. There were thus 30 confirmed cases of antepartum stroke in an estimated 1,965,178 maternities, giving an estimated incidence of 1.5 cases per 100,000 maternities (95% CI 1.0-2.1). Eighteen (60%) strokes were non-haemorrhagic, and 12 (40%) were haemorrhagic. The median gestational age at the time of all strokes was 30 weeks (n=29, inter-quartile range 14-38 weeks) and was similar for haemorrhagic and non-haemorrhagic strokes. Preliminary risk factor analysis suggests associations between occurrence of stroke and maternal age, migraine and hypertensive disorders of pregnancy. Six women died (case fatality 20%, 95% CI 8-39%).

Conclusions

These results suggest that the incidence of stroke during pregnancy in the UK is similar to that in the non-pregnant population of reproductive age. However, we cannot exclude the possibility of under-ascertainment of cases, particularly cases which occurred early in pregnancy, when affected women may not have been cared for by maternity services, or more minor strokes. The case fatality rate estimated by this study was higher than reported elsewhere which suggests that we may have identified a subset of more severe strokes. Future approaches to studying the topic may benefit from a joint approach to identifying cases through both maternity and stroke services.

Funding

This study is funded by Wellbeing of Women.

Wellbeing of Women

Charity Registration No: 239281

4.2.2 Congenital Diaphragmatic Hernia Key points

Key points

- Currently we have limited information about the extent to which CDH is diagnosed and managed antenatally across the UK.
- Population-based incidence information and information about the impact of different management strategies, is essential to provide a true picture of the prognosis for infants with CDH in the UK.
- Existing congenital anomaly registers cover only 50% of UK births and cannot be used to study the condition on a national basis.
- Once data collection through paediatric surgical units is also complete, this study will provide a national picture of the incidence of the condition, its management and outcomes.

Background

Congenital diaphragmatic hernia (CDH) is a musculoskeletal defect of the diaphragm which occurs during fetal development. It affects between 1 in 2,000 to 1 in 4,000 births in the UK¹⁵. Based on antenatal ultrasound findings the clinician can provide some, although at present incomplete, information to expectant parents about the likely immediate outcomes for their pregnancy. Available data are limited but indicate that a significant proportion of surviving infants experience substantial problems of respiratory, neurological, skeletal and gastrointestinal function and growth, and consequent disability¹⁶⁻¹⁸. However, CDH is a rare condition and thus this information largely comes from case series collected over long periods of time reported from referral centres rather than population-based data which would give the full up-to-date picture.

The aim of this study is to combine the use of UKOSS, paediatric surgical and congenital anomaly reporting systems to assess the diagnosed and birth incidence of CDH in the UK and to describe the management and outcome of affected pregnancies.

Case definition

Any pregnant woman with a fetus affected by a congenital diaphragmatic hernia.

Surveillance Period

April 2009 – March 2010

Interim Results

Two hundred and fifty six cases were reported up until March 2010 and data have been returned for 234 cases (91%). Three cases did not meet the case definition criteria, there were 38 duplicate reports and 14 cases which were subsequently reported by clinicians as not cases. Thus, there are 179 confirmed cases in an estimated 794,300 total births. This represents an estimated incidence of 2.3 cases per 10,000 total births (95% CI 1.9 to 2.6).

Interim Conclusions

Data collection for this study through paediatric surgical units to determine one-year outcomes of surviving infants is ongoing. At study completion, obstetric and paediatric surgical information will be combined with that obtained from congenital anomaly registers to provide a full picture of outcomes to one year of age.

Investigators

Jennifer Kurinczuk, Marian Knight, Peter Brocklehurst, NPEU

Mr David Howe, University of Southampton

Dr Judith Rankin, University of Newcastle

Professor Elizabeth Draper, University of Leicester

Professor Paul Losty, University of Liverpool

Funding

Action Medical Research.



4.2.3 Failed Intubation

Key points

- Although anaesthetic-related maternal deaths have decreased in number in recent years, hypoxia related to failed intubation remains a consistent cause of mortality.
- The incidence of failed intubation in the obstetric population is thought to be higher than in the non-pregnant population.
- The reasons for this higher incidence in the obstetric population are multiple.
- This study will investigate the incidence, risk factors, management and outcomes of failed intubation in the obstetric population in the UK in order to inform future guidelines for prevention and treatment.

Background

Reports from the Confidential Enquiries into Maternal Deaths have shown a decrease in the number of anaesthetic related deaths over recent years¹³. However, a consistent cause of death is hypoxia relating to a failure to intubate and ventilate. The incidence of failed intubation among the pregnant population is estimated to be up to 8 times that of the non-pregnant population^{19,20}, but as yet, no national data exist.

The reasons for this higher incidence in the obstetric population are several. Anatomical changes in the airway due to physiological changes in pregnancy have been noted²¹. Additionally, the physiological changes of a reduced functional residual capacity and an increased metabolic rate in pregnancy lead to a rapid progression to hypoxia following induction and apnoea. This adds pressure on the anaesthetist to intubate quickly before desaturation occurs. These issues are compounded by the fact that obstetric surgical procedures are now less frequently performed under general anaesthesia, so that training opportunities for junior anaesthetists are increasingly rare²². The procedures are also frequently required "out of hours" when the trainee anaesthetist is likely not to be working under direct supervision. Finally, the amount of time spent in training is reduced overall²³.

Case definition

Any woman of over 20 weeks gestation given a general anaesthetic (whether on delivery suite or another hospital department) where a failed intubation has occurred.

Failed intubation is defined as failure to achieve tracheal intubation during a rapid sequence induction for obstetric anaesthesia, thereby initiating a failed intubation drill.

Surveillance Period

April 2008 – March 2010

Interim Results

79 cases were reported and data returned about 69 of them (87%). Eight cases did not meet the case definition and there were four duplicate reports. There were thus 57 confirmed cases, giving an estimated incidence of failed intubation in obstetrics of 1 in 500 general anaesthetics. This figure assumes an estimated 19,000 obstetric general anaesthetics per year in the UK (data from the Obstetric Anaesthetists Association). There were no maternal deaths.

Interim Conclusions

The investigators, led by Audrey Quinn, are still in the process of undertaking statistical analysis of these data. The results to date suggest an incidence of failed intubation in obstetrics approximately half of that anticipated at the outset of the study.

Investigators

David Milne, Audrey Quinn, Amanda Pinder, Heather Gorton; Leeds General Infirmary.

Funding

This study is funded by the Obstetric Anaesthetists Association (OAA).



4.2.4 Myocardial Infarction

Key points

- Myocardial infarction in pregnancy is known to be associated with significant maternal and fetal mortality.
- Current trends in lifestyle factors and increasing age at childbirth are likely to be leading to an increase in incidence.
- The incidence of pregnancy related MI as estimated by this study is substantially lower than estimates reported by recent retrospective population based studies; this may represent an underestimate of the true underlying burden of non-fatal disease.
- Management of women with MI in pregnancy varied widely, suggesting there is a role for further research to inform clinical guidelines. This work would be facilitated by links between leading national perinatal research groups and cardiologists.

Background

Myocardial infarction in pregnancy is known to be associated with significant maternal and fetal mortality²⁴. The widely quoted incidence estimate of 1 in 10,000 births is based on a study conducted in 1970²⁵. However, with current trends in lifestyle factors associated with cardiovascular disease risk and increasing age at childbirth, the incidence of MI during pregnancy can be expected to have increased. A recent retrospective database analysis from the USA²⁶ provided evidence that this may be the case, identifying an increase in incidence of myocardial infarction in pregnancy from 1 in 73,400 pregnancies in 1991 to 1 in 24,600 in 2000. To date this is the only recent population study of this condition, although there are more than 150 individual case reports in the world literature²⁷. A systematic review of the case reports in 1996 identified a number of features of MI during pregnancy which differed from MI outside of pregnancy, and reported a case fatality rate of 21% and a fetal mortality rate of 13%²⁴. Normal coronary artery morphology was noted in 29% of women; MI in pregnancy may be caused by coronary artery dissection, embolus without atheroma in addition to atherosclerosis^{24,28}. Classic coronary risk factors appear to be the exception rather than the rule: 19% of patients had hypertension, 26% were smokers and only 2% had hyperlipidaemia. The authors of this review acknowledge the possible biases in favour of reporting of cases which are in some way unusual; a systematic prospective study on a population basis is thus needed.

Case definition

All women in the UK identified as having acute myocardial infarction during pregnancy using the joint European Society of Cardiology/American College of Cardiology criteria²⁹:

EITHER A typical rise and gradual fall (troponin) or more rapid rise and fall (CK-MB) of biochemical markers of myocardial necrosis with at least one of the following: (a) ischaemic symptoms, (b) development of pathologic Q waves on the ECG, (c) ECG changes indicative of ischaemia (ST segment elevation or depression), or (d) coronary artery intervention (e.g. coronary angioplasty)

OR Pathological findings of an acute MI.

Surveillance Period

August 2005 – February 2010

Results

Fifty-four cases were reported up to February 2010 and data returned about 51 of them (94%). Eighteen were subsequently reported by clinicians as not being cases, a further 6 cases did not meet the case definition for MI in pregnancy and two were duplicates. There were thus 25 confirmed cases in an estimated 3,339,620 maternities, representing an estimated incidence of 0.7 cases per 100,000 maternities (95% CI 0.4-1.1).

Management of women with MI in pregnancy varied widely. Fifteen of the women with a confirmed MI had angiography; 9 had coronary atheroma, 3 coronary artery dissection, 1 coronary arterial thrombosis and 2 had normal coronary arteries. Eight women underwent coronary artery stenting, six had angioplasty and two women received thrombolysis. The remaining nine women were managed conservatively, defined as medical treatment alone excluding thrombolysis.

There were no deaths amongst women who suffered a pregnancy related MI.

Conclusions

The incidence of pregnancy related MI estimated from this study is substantially lower than estimates reported by recent retrospective population based studies. Although these other studies use routine data sources, which may result in inclusion of false positive cases, and hence an over-estimation of incidence, our results may represent an underestimate of the true underlying burden of non-fatal disease. The small number of cases identified by this study limit the statistical power to investigate risk factors and management, but the variation in treatment suggests there is a role for further development of management guidelines. Further research would be facilitated by links between leading national perinatal research groups and cardiologists to enable an international multicentre prospective study on MI in pregnancy to obtain further information on trends in incidence, important risk factors and the impact of different interventions.

4.2.5 Uterine Rupture

Key points

- Uterine rupture is associated with significant maternal and fetal morbidity.
- A decrease in the number of women attempting vaginal birth after caesarean section may be due to concerns about the risk of uterine rupture.
- There are no systematic data available at a population level to quantify the incidence of uterine rupture and to assess the risks associated with induction and augmentation of labour in women who have had a previous caesarean delivery.
- This study shows that uterine rupture is rare, even amongst women with a previous caesarean delivery, although when it occurs there is significant associated perinatal and maternal morbidity and mortality.
- Further work is underway to quantify additional risk factors for uterine rupture after previous caesarean delivery.

Background

Uterine rupture is a catastrophic event, and in the developed world it most commonly occurs in women who have previously delivered by caesarean section³⁰. This observation has led to debate about the optimal management of labour and delivery in women who have previously delivered by caesarean section. Women with a previous caesarean delivery have generally been encouraged to attempt a trial of labour³¹, but recent reports of an increased risk of morbidity, particularly due to uterine rupture, are thought to have contributed to a marked decrease in the number of women attempting vaginal birth after caesarean section³². Two recent systematic reviews^{30,33} identified only one previous UK population-based study³⁴, which reported 12 ruptures in 48,865 deliveries, a rate of approximately 1 in 4,000 deliveries.

In addition to difficulties in quantifying the incidence of uterine rupture, Guise et al³³ noted that existing observational studies were insufficient to answer additional questions about the risks of rupture associated with induction and augmentation of labour. This case-control study using UKOSS sought to address these questions and quantify the national incidence of uterine rupture in the UK.

Case definition

All women identified as having a uterine rupture using the following definition^{33,35}: a complete separation of the wall of the pregnant uterus, with or without expulsion of the fetus, involving rupture of membranes at the site of the uterine rupture or extension into uterine muscle separate from any previous scar, and endangering the life of the mother or fetus. Any asymptomatic palpable or visualised defect (for example dehiscence noted incidentally at caesarean delivery) was excluded.

Surveillance Period

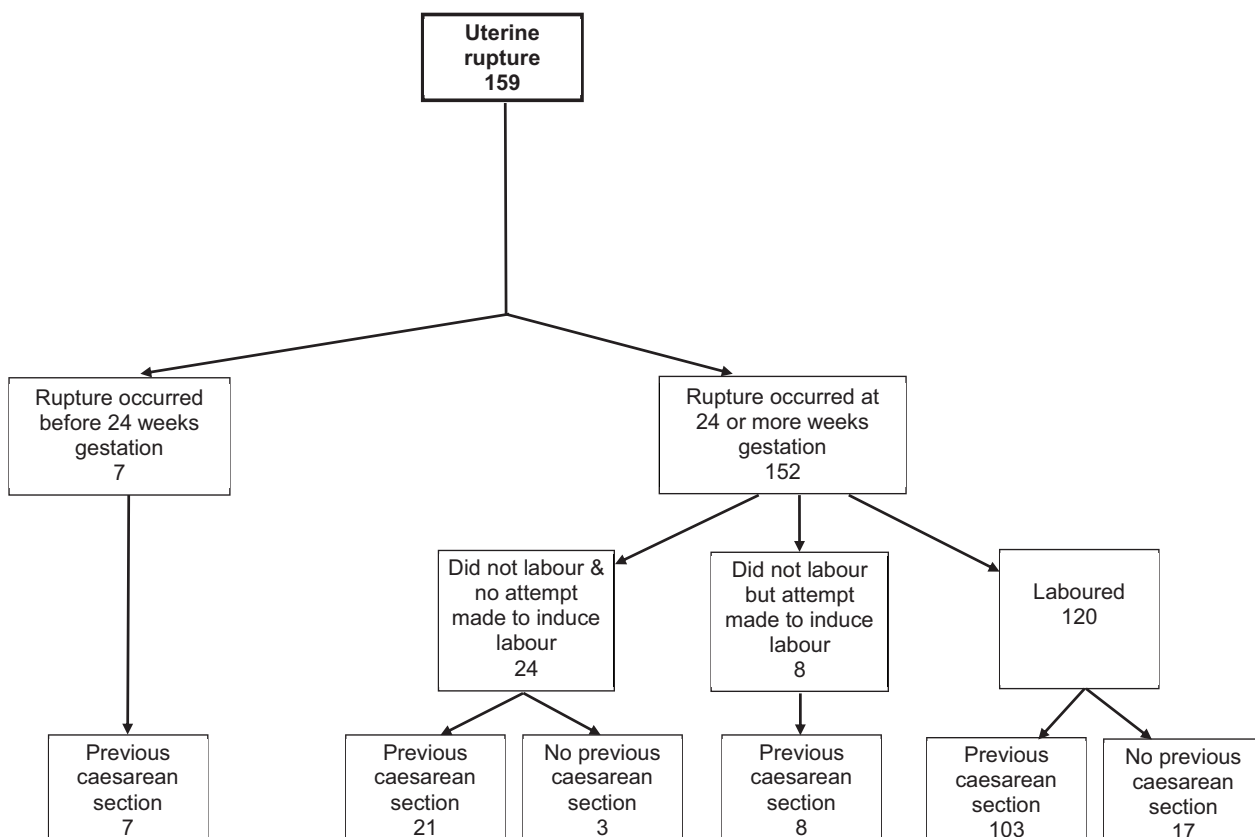
April 2009 – April 2010

Results

Of the 216 notified cases of uterine rupture, data collection was complete for 90%. There were 159 confirmed cases of uterine rupture representing an estimated incidence of 1.9 cases per 10,000 maternities (95% CI 1.6 to 2.2). The median gestational age at diagnosis of uterine rupture was 39 weeks (range 8 to 42 weeks). Of the 152 ruptures diagnosed at 24 or more weeks gestation, the majority (120/152, 79%) occurred in women who laboured (Figure 5). A total of 139 (87%) of the uterine ruptures occurred in women who had previously delivered by caesarean section, estimated incidences being 11 (95% CI 9 to 13) and 0.3 (95% CI 0.2 to 0.4) per 10,000 maternities in women with and without a previous

caesarean delivery, respectively. Two women died (case fatality 1.3%, 95% CI 0.2 to 4.5%) and there were 9 stillbirths and 10 early neonatal deaths associated with uterine rupture among 146 infants (perinatal mortality 130 per 1,000 total births, 95% CI 80 to 196).

Figure 5. Uterine rupture cases by gestational age at rupture, labour and previous caesarean section status



Conclusions

Although uterine rupture is associated with significant maternal and perinatal mortality and morbidity, it is a rare occurrence. Further analysis of these data, including quantification of additional risk factors for uterine rupture after prior caesarean delivery is currently underway.

Investigators

Marian Knight, Kate Fitzpatrick, Jenny Kurinczuk, Peter Brocklehurst, NPEU

Zarko Alfirevic, University of Liverpool

Funding

This study is funded by Wellbeing of Women and by the National Institute for Health Research as part of the UK Maternal Near-miss Surveillance Programme (UKNeS).**



4.3. Studies in progress

4.3.1 Amniotic Fluid Embolism

Key points

- Amniotic fluid embolism (AFE) is a leading cause of maternal mortality in the UK today but estimates of incidence and mortality vary widely.
- The estimated incidence using active surveillance through UKOSS is more than twice that obtained through passive registration.
- AFE is associated with induction of labour and caesarean delivery in the UK population.
- There is no evidence of an increase in incidence over the six years of UKOSS surveillance.

Background

Amniotic fluid embolism (AFE) has been consistently identified by the UK Confidential Enquiry into Maternal Deaths as a leading cause of maternal mortality^{13,36}. Estimates of incidence vary tenfold between 1.3 and 12.5 per 100,000 pregnancies³⁷. Estimates of the mortality rate from this condition also vary widely³⁸, from as much as 86% to more recent estimates of 16-30%. Recent retrospective database analyses suggest possible links with induction of labour and caesarean delivery^{39,40}, and a wide range of treatments have been described in case reports³⁸. A database of voluntary notifications was established in the UK to collect information on epidemiology and management⁴¹; this register was incorporated into UKOSS to improve ascertainment and allow a comprehensive study of the epidemiology and current management. Analysis of UKOSS data on AFE up to February 2009 showed that AFE occurrence was significantly associated with induction of labour and multiple pregnancy, and that an increased risk was also noted in older ethnic minority women. Caesarean delivery was associated with postnatal amniotic fluid embolism⁴².

Case definition

EITHER A clinical diagnosis of AFE (acute hypotension or cardiac arrest, acute hypoxia or coagulopathy in the absence of any other potential explanation for the symptoms and signs observed)

OR A pathological diagnosis (presence of fetal squames or hair in the lungs).

Surveillance Period

February 2005 – ongoing

Interim Results

In the first six years of the study 131 cases of AFE in pregnancy were reported. Information has been received for 120 cases (92%). There were 19 cases which were subsequently reported by clinicians as not cases and six duplicate reports. Thirteen further cases did not meet the case definition criteria. There were thus 82 confirmed cases, in an estimated 4,640,433 maternities. This gives an incidence estimate in the UK of 1.8 cases per 100,000 maternities (95% CI 1.4 to 2.2 per 100,000).

Interim Conclusions

There is no evidence of a significant change in the incidence of AFE over the six years of the study, and mortality, as reported in the latest report of the national Confidential Enquiries into Maternal Deaths³⁶, appears to have decreased since the previous triennium. However, in view of the extreme rarity of this condition and the significant associated mortality, surveillance through UKOSS is ongoing in order to further investigate risk factors and describe outcomes following the use of different management techniques.

Funding

This study has been funded by the National Institute for Health Research as part of the UK National Maternal Near-miss Surveillance Programme (UKNeS).**



4.3.2 Aortic Dissection/aneurysm

Key points

- Aortic dissection in pregnancy is a significant cause of maternal morbidity and mortality.
- Changes in birth patterns, with a rise in older mothers and increased prevalence of obesity may contribute to an increased occurrence of aortic dissection in the UK.
- There have been no prospective studies to estimate the incidence of this disease and its investigation and management during pregnancy.
- This study will determine the national incidence of aortic dissection in the pregnant population in the UK and use this national initiative to characterise and quantify risk factors for aortic dissection in pregnancy.

Background

Aortic dissection in pregnancy is a life-threatening event to both mother and baby and accounts for 14% of maternal cardiac deaths¹³. Although rare, an association between pregnancy and aortic dissection has been reported and anecdotally its incidence in pregnancy appears to be rising. Approximately 50% of cases of aortic dissection in women under the age of 40 occur whilst they are pregnant⁴³. Patients presenting with aortic dissection may do so with a wide array of symptoms and the condition may be missed or symptoms mistaken for other diseases in pregnancy^{44,45}. There is often a cautious approach by clinicians to imaging studies required for diagnosis for fear of radiation effects on the baby and this may hinder prompt diagnosis^{44,45}. Untimely delays in treatment of this disease can lead to potentially catastrophic consequences, since the mortality rate increases by 1% for each hour left untreated⁴⁶. Changes in birth patterns with a rise in older mothers and increased prevalence of obesity may increase the occurrence of aortic dissection, therefore an up to date understanding of the risk factors for aortic dissection in pregnancy is urgently required. This study will determine the national incidence of aortic dissection in pregnancy and will provide information on the current investigation, management and maternal-fetal outcomes of this disease in the UK.

Case definition

Any woman in whom the diagnosis (before or during pregnancy) of (a) aortic dissection was confirmed using suitable imaging (chest X ray, echocardiography, computed tomography, magnetic resonance imaging) or (2) aortic dissection was confirmed at surgery or postmortem.

Surveillance Period

September 2009 – August 2011

Interim Results

Up to February 2011, 12 cases of aortic dissection in pregnancy were reported. Information has been received for 10 of these cases (83%). There was one case which was subsequently reported by clinicians as not a case and 1 duplicate report. 3 cases did not meet the case definition. There were thus 5 confirmed cases in an estimated 1,172,064 maternities. This gives an incidence estimate in the UK of 0.4 cases per 100,000 maternities (95% CI 0.1 to 1.0 per 100,000).

Interim Conclusions

This study has identified very few cases of aortic dissection in pregnancy in the UK. The latest triennial report of the UK Confidential Enquiry into Maternal Deaths reported seven deaths from aortic dissection over three years³⁶, and, although the majority of these women died post-delivery, there remains a significant possibility that cases are being under-ascertained through UKOSS. The investigators are currently investigating other means to improve case ascertainment, but we would be grateful if UKOSS clinicians could check again with their colleagues to retrospectively identify any cases not reported since the study began in September 2009.

Investigators

Sheba Jarvis, Mandish Dhanjal, Queen Charlotte's and Chelsea Hospital, Imperial College Healthcare NHS Trust, Marian Knight, NPEU

Funding

Heart Research UK.



4.3.3 Myeloproliferative Disorders

Key points

- Historical literature suggests myeloproliferative disorders are associated with increased maternal and fetal morbidity and mortality.
- There have been no prospective national studies to estimate the incidence or outcomes of myeloproliferative disorders, persistent thrombocytosis or erythrocytosis in pregnancy.
- This study of myeloproliferative disorders, persistent thrombocytosis or erythrocytosis in pregnancy will investigate the incidence, management and outcomes for mother and infant.

Background

The aim of the proposed study is to use the UK Obstetric Surveillance System to describe the epidemiology of myeloproliferative disorders (MPDs), persistently increased number of platelets or red cells in pregnancy. The Myeloproliferative disorders (MPDs) are clonal haematological malignancies characterised by over production of mature blood cells and a chronic clinical course. They include polycythaemia vera (PV), primary myelofibrosis (PMF) and essential thrombocythaemia (ET).

The most extensive literature for epidemiology and outcome of pregnancy exists for ET with approximately 461 pregnancies reported⁴⁷; for PV and PMF the literature is more limited, reporting mostly single centre studies. MPD especially PV and PMF in pregnancy are thus under-researched, our understanding of them is poor and any interventions used in current clinical practice are rarely based on robust evidence. Prospective data collection on known and occult MPDs in pregnancy using UKOSS will provide valuable information into the epidemiology and complications of MPD in pregnancy.

Case definition

All pregnant women in the UK identified as having:

- EITHER** a myeloproliferative disorder (essential thrombocythaemia, polycythaemia vera, myelofibrosis), diagnosed by a consultant haematologist according to WHO guidelines
- OR** a thrombocytosis (platelet count persistently greater than $600 \times 10^9/l$)
- OR** an erythrocytosis (haemoglobin persistently greater than 16.5g/dl) .

Surveillance Period

January 2010 – December 2011

Interim Results

Up to February 2011, 18 cases of myeloproliferative disorders in pregnancy were reported. Information has been received for 14 of these cases (78%). There were two cases which were subsequently reported by clinicians as not cases and two further cases did not meet the case definition. There were thus 10 confirmed cases in an estimated 911,605 maternities. This gives an incidence estimate in the UK of 1.1 cases per 100,000 maternities (95% CI 0.5 to 2.0 per 100,000). The majority of cases reported (80%) were cases of essential thrombocythemia.

Interim Conclusions

Data collection for this study is still incomplete and it is not possible to draw any definitive conclusions at this stage.

Investigators

Sue Robinson, Claire Harrison, Susan Bewley, Gabriella Gray, Guy's and St Thomas' Hospital

Funding

Guy's and St Thomas' Charity

4.3.4 Pituitary Tumours

Key points

- Pituitary tumours produce hormones that can have a detrimental effect on pregnancy; as the pituitary enlarges in size during pregnancy, tumour may also compress surrounding structures.
- This will be the first national study to evaluate maternal and fetal mortality and morbidity of pituitary tumours in pregnancy.
- This information will be used to develop guidelines for the management of women with pituitary tumours in pregnancy.

Background

Pituitary tumours are rare and complicate approximately 1 in 4,500 pregnancies in the UK. These tumours often secrete hormones, which in excess can have devastating effects on the mother and the unborn baby. In addition, many pituitary tumours require treatment with specific drugs or surgery, and this can also result in adverse outcomes for the fetus or neonate.

Macroprolactinoma is a benign tumour of the pituitary that is 1cm or more in diameter. The risk of enlargement of untreated macroprolactinoma in pregnancy is approximately 26%, compared to 3% in women previously treated with surgery and/ or radiation⁴⁸. Pituitary tumours that secrete excess hormones are associated with a higher incidence of maternal mortality and morbidity. Cushing's disease and acromegaly are both associated with an increased incidence of hypertension (potentially leading to pre-eclampsia), diabetes and cardiac failure⁴⁸. Cushing's disease is associated with high fetal morbidity (spontaneous abortion 5%, stillbirth 6% and prematurity 43%)⁴⁹. There is very little literature on the use of medication in the management of these conditions in pregnancy.

Following this study we will be able to provide comprehensive information on maternal/fetal outcome related to medications used to treat pituitary tumours and this will be used as the basis for the development of clinical management guidelines.

Case definition

All women in the UK with a pituitary tumour in pregnancy **excluding** a microprolactinoma (a prolactin-secreting tumour less than 1.0cm diameter).

This will include women diagnosed in pregnancy and those diagnosed pre pregnancy with a macroprolactinoma, Cushing disease, acromegaly, thyrotrophinomas or non-functioning pituitary tumours.

Surveillance Period

March 2010 – February 2013

Interim Results

Up to February 2011, 35 cases of pituitary tumours in pregnancy were reported. Information has been received for 20 of these cases (57%). There were 8 cases which were subsequently reported by clinicians as not cases and one duplicate report. Two further cases did not meet the case definition. There were thus 9 confirmed cases in an estimated 781,376 maternities. This gives an incidence estimate in the UK of 1.2 cases per 100,000 maternities (95% CI 0.5 to 2.2 per 100,000). The nine confirmed cases included six women with prolactinomas and three women with non-functioning tumours.

Interim Conclusions

Data collection for this study is still incomplete and it is not possible to draw any definitive conclusions at this stage.

Investigators

K Lambert, C Williamson, M Dhanjal, Imperial College Healthcare NHS Trust.

D McCance, Royal Victoria Hospital, Belfast.

Funding

SPARKS



4.3.5 Placenta Accreta

Key points

- Placenta accreta is thought to be becoming more common due to a number of factors including rising maternal age at delivery and an increasing proportion of deliveries by caesarean section.
- There is a debate about the optimal diagnostic and management techniques.
- This study will describe the current management of placenta accreta in the UK and associated outcomes for women and their infants. In addition, this study will estimate the national incidence of placenta accreta in the UK and identify the extent to which previous caesarean section and older maternal age are risk factors in this population.

Background

The presence of placenta accreta/increta/percreta is associated with major pregnancy complications, including life-threatening maternal haemorrhage, uterine rupture⁵⁰, peripartum hysterectomy¹ and maternal death¹³, as well as complications associated with surgical removal including damage to bladder, ureters and other organs⁵⁰. Placenta accreta is thought to be becoming more common^{51,52}, due to a number of factors including rising maternal age at delivery and an increasing proportion of deliveries by caesarean section^{53,54}. There is also a debate about the optimal diagnostic and management techniques. This study will describe the current management of placenta accreta in the UK and associated outcomes for women and their infants. In addition, this study will estimate the national incidence of placenta accreta in the UK and identify the extent to which previous caesarean section and older maternal age are risk factors in this population. This will enable appropriate future service planning, provide accurate information which can be used when counselling women about the risks associated with caesarean section and developing management guidelines, and provide a baseline incidence against which future trends can be monitored.

Case definition

Any pregnant woman in the UK identified as having placenta accreta using the following definition:

- EITHER** Placenta accreta/increta/percreta diagnosed histologically following hysterectomy or post mortem.
- OR** An abnormally adherent placenta, requiring active management, including conservative approaches where the placenta is left in situ.
- EXCLUDED** Women who have had a manual placental removal with minimal or moderate difficulty but required no additional active management.

Surveillance Period

May 2010 – April 2011

Interim Results

Up to February 2011, 128 cases of placenta accreta in pregnancy were reported. Information has been received for 70 of these cases (55%). There were 3 cases which were subsequently reported by clinicians as not cases, two duplicate reports and one case did not meet the case definition. There were thus 64 confirmed cases. Thirty-seven women (58%) went on to have a hysterectomy. The placenta was left intact in situ in 14 women (22%); 7 of these women (50%) subsequently had a hysterectomy.

Interim Conclusions

A significant number of placenta accreta cases have been managed conservatively. However, the data from this study are, as yet, very incomplete and it is not possible to draw any firm conclusions. More definitive conclusions will be drawn at the end of the study.

Investigators

Marian Knight, Jenny Kurinczuk, Peter Brocklehurst, Maria Quigley, NPEU; Sue Sellers, United Bristol Hospitals NHS Trust; Mervi Jokinen, RCM; Shona Golightly, CMACE; Gwyneth Lewis, Department of Health; James Walker, NPSA; Alison Burton, Oxfordshire PCT; Jenny Furniss, Lay representative.

Funding

This study has been funded by the NIHR as part of the UK National Maternal Near-miss Surveillance Programme (UKNeS).**



4.3.6 Pregnancy in Non-renal Solid Organ Transplant Recipients

Key points

- There have been over 14,000 reports of pregnancy in transplant recipients worldwide.
- The UK National Transplantation Pregnancy Register no longer collects information.
- Immunosuppressive regimens are continually developing.
- This study will provide a national picture of the incidence of pregnancy in non-renal solid organ transplant recipients and assess the role of immunosuppressive regimens and other factors in the outcomes of women and their infants.

Background

Despite initial concerns about the advisability of pregnancy in solid-organ transplant recipients, there have now been reports of over 14,000 births to women with transplanted organs⁵⁵. Most studies are centre-based and retrospective⁵⁶. Three voluntary registers have collected data at various times: the US National Transplantation Pregnancy Register (1991-present)⁵⁷, the UK Transplant Pregnancy Register (1994-2001)⁵⁶ and the European Dialysis and Transplant Association Registry (1960-1992)⁵⁸. This UK register, however, no longer collects information. The objective of this project is to collect information about pregnancy outcomes amongst current solid organ transplant recipients in the UK and describe the outcomes for women and their infants. The project is divided into two studies: the first to investigate outcomes in women with renal transplants has now stopped collecting data; this second study to investigate outcomes in women with other solid organ transplants is ongoing.

Case definition

All pregnant women with a transplanted solid organ, including heart, lung, liver, pancreas and small bowel. Isolated renal, corneal and bone marrow transplant recipients are excluded.

Surveillance Period

January 2007 – December 2011

Interim Results

Eighty-three cases of pregnancy in non-renal solid organ transplant recipients were reported and data collection forms were returned for 68 cases (82%). There were six cases which were reported by clinicians as not cases and eight duplicate reports, leaving fifty-four confirmed cases. Forty-five women received liver transplants, of which five women received two transplants each, three women a lung transplant, five a heart transplant and one a heart-lung transplant. One heart transplant recipient died. Four women had a miscarriage, and one woman had a termination. Two infants were stillborn among 51 for whom outcomes are known.

Interim Conclusions

The outcomes for women and their infants appear largely good, but more definitive conclusions will be drawn at the end of the study.

4.3.7 Pulmonary Vascular Disease

Key points

- Pulmonary vascular disease in pregnancy is widely considered to pose an extreme risk of maternal death.
- There have been no recent prospective case series to assess this risk.
- Novel methods of management may impact on case outcomes.
- This study will provide a national picture of the incidence of the disease, its epidemiology and management.

Background

Pre-existing or gestational occurrence of pulmonary vascular disease, including Eisenmenger's syndrome, primary and secondary pulmonary hypertension, is one of the rare conditions widely considered to pose an extreme risk of maternal death⁵⁹. Three of the six maternal deaths in women with congenital heart disease reported in the UK in 2003-5 were associated with pulmonary vascular disease¹³; between 1991 and 2005 there were 25 maternal deaths in the UK associated with this condition. Eisenmenger's syndrome is estimated to carry a maternal mortality rate of 40% per pregnancy⁶⁰, with an infant mortality rate of 10-15%⁵⁹. A systematic review of the literature in 1998 suggested that the maternal mortality rate had remained unchanged over the previous 20 years⁵⁹. However, the authors of this review recognise that there may be inherent biases in published reports of pregnancy in women with pulmonary vascular disease in pregnancy and call for more information from detailed prospective case series in order to differentiate the risks of pregnancy and eventually provide an optimal plan of management. Cases in the UK were collected prospectively on a voluntary basis by the UK Registry of High Risk Obstetric Anaesthesia⁶¹, however, problems with ascertainment caused the register to cease to collect data. The objective of this prospective study through UKOSS is to provide an appropriate national case series with good ascertainment to allow comprehensive study of the epidemiology and current management of Eisenmenger's syndrome and pulmonary hypertension.

Case definition

- EITHER** Pulmonary hypertension: defined as 1) a mean (not systolic) pulmonary artery pressure equal to or greater than 25mmHg at rest or 30 mmHg on exercise in the absence of a left-to-right shunt or 2) a pulmonary artery systolic pressure greater than 36mmHg⁶². Pulmonary hypertension may be primary (no cause identified) or secondary (known cause identified, for example, vasculitis, connective tissue disease, chronic pulmonary thromboembolism, sickle cell disease, drug use),
- OR** Eisenmenger's syndrome: defined as pulmonary hypertension secondary to an uncorrected left-to-right shunt from a ventricular septal defect, atrial septal defect or patent ductus arteriosus⁶³.

Surveillance Period

March 2006 – December 2011

Interim Results

To date, 77 cases of pulmonary vascular disease have been reported, with further information received for 63 cases (82%). There were 23 cases which were subsequently reported by clinicians as not cases, eight cases which did not meet the case definition criteria and four duplicate reports, leaving 28 confirmed cases, an estimated incidence of 0.7 cases in 100,000 maternities (95% CI 0.5 to 1.0 per 100,000). Ten of the cases were attributed to congenital heart disease, two to chronic thromboembolism, one to sleep apnoea, seven to idiopathic pulmonary arterial hypertension, one to connective tissue disease and a further seven had no cause for pulmonary hypertension identified. Sixteen of these cases were known prior to pregnancy and twelve were diagnosed during pregnancy or immediately postnatally. Two women died (case fatality 7% (95% CI 1-24%).

Interim Conclusions

Pulmonary vascular disease in pregnancy is extremely rare in the UK. However, the preliminary results from this study suggest that mortality may not be as high as previously reported. This study will continue for a further year in order to identify a larger population-based series of cases.

4.3.8 Severe Obstetric Cholestasis

Key points

- Obstetric cholestasis is associated with an increased risk of adverse fetal outcomes.
- The risk of adverse fetal outcomes is thought to be increased in women with severe cholestasis.
- There are no prospective national studies to estimate the incidence or outcomes of severe cholestasis in pregnancy.
- This study will investigate the incidence, management and outcomes for mother and infant in pregnancies where the mother has severe obstetric cholestasis.

Background

Obstetric cholestasis (OC) is a pregnancy specific liver disorder that affects about 1 in 200 women in the UK. It typically presents in the third trimester with maternal pruritus and deranged liver function, including raised serum bile acids. The maternal symptoms and biochemical abnormalities resolve rapidly after delivery and OC is therefore considered to be a cause of transient hepatic impairment for the mother. However, OC is associated with an increased incidence of adverse fetal outcomes, including spontaneous preterm labour, fetal distress and sudden intrauterine death⁶⁴.

Several studies have demonstrated a correlation between the maternal serum bile acid level and the risk of adverse fetal events⁶⁵⁻⁶⁸. The most definitive of these studies investigated the incidence and outcomes of OC in a Swedish population of 45,000 women, including 690 with OC⁶⁵. The data from this study demonstrate that the risk of meconium staining of the amniotic fluid, green staining of the placenta and fetal membranes, asphyxial events and preterm delivery is increased by 1-2% for every additional 1 µmol/L of maternal serum bile acids. However, this did not reach statistical significance for women with mild or moderate elevations in maternal fasting serum bile acid levels, but was significant for those with severe cholestasis defined as fasting serum bile acid levels greater than 40 µmol/L. Several small studies have reported the incidences of adverse fetal outcomes in the UK population^{69,70}, but none have been able to demonstrate a correlation with maternal serum bile acid level.

Case definition

Any woman in the UK identified as having severe obstetric cholestasis using the following definition:

Pruritus in the absence of a rash and in association with a single maternal serum bile acid level **greater than or equal to 40 µmol/L** at any time point in the pregnancy

EXCLUDED: Women with obstetric cholestasis but with bile acid levels less than 40 µmol/L.

Surveillance Period

June 2010 – May 2011

Interim Results

Up to February 2011, 541 cases of severe obstetric cholestasis were reported. Information has been received for 344 cases (64%). There were 49 cases which were subsequently reported by clinicians as not cases and 4 duplicate reports. Nineteen cases did not meet the case definition criteria, predominantly because their serum bile acid levels were never greater than 40µmol/L. There are thus 272 confirmed cases to date. One infant was stillborn and one died neonatally among 287 for whom outcomes are known (perinatal mortality 7 per 1,000 total births, 95%CI 1-25).

Interim Conclusions

The data from this study are, as yet, incomplete. However, the outcomes for infants appear to be good. Definitive conclusions will be drawn at the end of the study.

Investigators

Catherine Williamson, Victoria Geenes, Imperial College London

Marian Knight, NPEU

Funding

Wellbeing of Women.

Wellbeing of Women

Charity Registration No: 239281

4.3.9 Sickle Cell Disease

Key points

- Sickle cell disease is the most common genetic disease in the UK and is associated with significant mortality and morbidity during pregnancy.
- There are no prospective national studies to estimate the incidence or outcomes of pregnancy in patients with Sickle Cell Disease.
- This study will investigate the incidence, management and outcomes for mother and infant in pregnancies where the mother has Sickle Cell Disease.

Background

Sickle cell disease (SCD) is the most common genetic disorder worldwide and in the UK, with 12-15,000 affected individuals in the UK. SCD is a multi-organ disorder characterised by intermittent episodes of severe pain which may require hospital admission for treatment, and other complications including chest disease, pulmonary hypertension, stroke, retinopathy, renal failure, avascular necrosis and leg ulcers.

There are some historical data, most from outside the UK, showing a high incidence of maternal and fetal complications in SCD⁷¹, but no contemporary or recent prospective data from the UK. The number of deliveries in women with SCD has increased markedly over recent years, from 25-30 deliveries across the whole UK in the 1970s, to the current situation of approximately 150-250 deliveries per year. There is also a lack of consensus about the best management strategies for optimum care of these women, although it is clear that good committed obstetric care is of vital importance. This lack of knowledge about incidence of pregnancy, makes it difficult to plan services, to plan optimal care, or in the long term to plan further trials into best practice. This study plans to collect data about incidence across the UK and describe current management practice.

Case definition

Any woman in the UK identified as having sickle cell disease using the following definition:

Sickle cell disease including

homozygous sickle cell disease;

compound heterozygous conditions of haemoglobin S with haemoglobin C, D, E,

O-Arab or Beta thalassaemia.

Pregnancies in women with sickle cell trait are **excluded**.

Surveillance Period

February 2010 – January 2011

Interim Results

One hundred and thirteen cases of sickle cell disease in pregnancy have been reported to date, with information received for 56 cases (50%). There were 5 cases which were subsequently reported by clinicians as not cases and 2 duplicate reports. One case did not meet the case definition criteria. There were thus 48 confirmed cases. The expected number of cases is significantly lower than expected, and the investigators are currently in the process of identifying additional cases through their network of haematologists.

Interim Conclusions

Data collection for this study is still incomplete and it is not possible to draw any definitive conclusions at this stage.

Investigators

Jo Howard, Eugene Oteng-Ntim, Guy's and St Thomas' NHS Foundation Trust

Funding

Guy's and St Thomas' Charity

4.4. Future studies

These studies have been approved by the UKOSS Steering Committee to commence in 2011/2012.

4.4.1 Adrenal Tumours

Key points

- Adrenal tumours secrete excessive hormones which adversely affect maternal and fetal health.
- Adrenal tumours are managed with specific drugs or surgery, but it is not known how these affect the mother, the fetus or the neonate.
- This study will investigate the current incidence of rare adrenal tumours including pheochromocytomas, those associated with Conn's Syndrome and Cushing's Syndrome. It will describe their current management and the associated outcomes for women and their infants and develop guidelines for their optimal management.

Background

Tumours of the adrenal glands are very rare⁷² and information in the medical literature on the incidence, their management and maternal, fetal and neonatal outcomes is limited. Pheochromocytomas, tumours associated with Conn's Syndrome, and adrenal or pituitary tumours linked to Cushing's Syndrome produce excess steroid hormones which are associated with major pregnancy complications^{73,74}, including major maternal and fetal morbidity⁴⁹ and mortality^{75,76}. Adrenal tumours are linked to higher rates of hypertension⁷², diabetes⁴⁹ and pre-eclampsia, as well as fetal death, intrauterine growth restriction, fetal hypoxia⁷⁷, fetal distress^{72,78}, spontaneous abortion, stillbirth and prematurity⁴⁹. Currently, there are no data on the incidence of adrenal tumours in pregnancy in the UK and the associated maternal, fetal and neonatal morbidity and mortality. In addition, there are few guidelines on the appropriate pharmacological or surgical management of these tumours. Therefore, this study will examine the effects of the drugs used to treat these in relation to maternal and fetal and neonatal complications and whether the timing of the surgery to remove the tumours is important. This will allow for development of guidelines on the management of adrenal tumours in pregnancy with the ultimate aim of improving maternal and infant outcomes.

Case definition

Any pregnant women in the UK with a functioning adrenal neuroendocrine tumour, including women diagnosed pre-pregnancy who have not undergone surgery to remove the tumour.

INCLUDED:

PHAECHROMOCYTOMA Neuroendocrine adrenal tumour secreting catecholamines (dopamine, nor-adrenaline, adrenaline, metadrenaline and normetadrenaline).

CUSHING'S SYNDROME Adrenal cortex tumour secreting excessive amounts of cortisol.

CONN'S SYNDROME Adrenal cortex adenoma secreting excessive amounts of aldosterone.

EXCLUDED: Women with non-functioning adrenal tumour.

Surveillance Period

March 2011 – February 2012

Main research questions

- What is the current incidence of adrenal tumours in pregnancy in the UK?
- What are the outcomes for women and their babies?
- How is the condition managed in the UK?
- What is the role of the timing of surgery to remove the tumours and what are the complications compared to non-pregnant women in the UK?

Investigators

Catherine Williamson, Kimberly Lambert, Imperial College London

David McCance, Royal Victoria Hospital

Funding

This study is funded by SPARKS



4.4.2 Cardiac Arrest in Pregnancy

Key points

- The risk of death following a cardiac arrest in pregnancy is extremely high for both mother and child, but both can be resuscitated if fast action is taken.
- Cardiac arrest is managed by resuscitation and periarrest/perimortem caesarean section (PMCS).
- There is little information on survivors of cardiac arrest or PMCS.
- This study will investigate the current incidence of cardiac arrest and PMCS in pregnancy. It will describe the current management by resuscitation and PMCS, the associated outcomes for women and their infants and will help to develop guidelines for optimal management.

Background

Cardiac arrest in pregnancy affects around 1:30,000 women⁷⁹; incidence is thought to be rising due to the increasing age and morbidity of the antenatal population in the UK. The risk of death for mother and child is extremely high but some causes of cardiac arrest are reversible. Aggressive resuscitation is required, including caesarean section in most cases over 20 weeks gestation. The importance of rapid delivery after cardiac arrest for maternal benefit is becoming a widely accepted practice and there is evidence to suggest that MOET (Managing Obstetric Emergencies & Trauma) training in obstetric resuscitation is leading to an increase in the use of PMCS in maternal cardiac arrest in the UK⁸⁰ and in Europe⁸¹. In the UK 52 cases of PMCS were recorded between 2003-2005 amongst women who subsequently died¹³.

There is, however, minimal information on survivors of cardiac arrest or PMCS. This study will investigate the incidence, management (including PMCS) and outcomes of maternal cardiac arrest including both women who survive and women who die. This information will be used to establish optimal management guidelines to improve survival of mother and infant.

Case definition

Please report any woman who has received immediate basic life support (BLS) (i.e. chest compressions and, if possible, ventilation breaths) at any point in pregnancy, up to the point of delivery of the baby.

Note that women requiring ventilatory support only, are not included.

Surveillance Period

July 2011 – June 2014

Research questions

- What is the current incidence of cardiac arrest in pregnancy in the UK?
- How often is PMCS used in resuscitation following cardiac arrest in pregnancy?
- What is the outcome for mother and baby following cardiac arrest with or without PMCS?
- What are the characteristics of women who suffer cardiac arrest in pregnancy?
- How is the resuscitation conducted and what interventions make a difference to outcomes?

Investigators

Virginia A. Beckett, Laura McCarthy, Bradford Teaching Hospitals NHS Trust

Paul Sharpe, University Hospitals of Leicester NHS Trust

Marian Knight, NPEU

Funding

This study is funded by Wellbeing of Women.

Wellbeing of Women

Charity Registration No: 239281



4.4.3 HELLP Syndrome

Key points

- There has been no comprehensive study of the risk factors for HELLP syndrome to date.
- There is debate about the optimal management of women who develop the syndrome prior to 34 weeks of gestation when the maternal and fetal status is reassuring and there is some controversy regarding risk factors for adverse outcome.
- This study will estimate the incidence of HELLP syndrome in the UK and will investigate and quantify the associated risk factors, management and outcomes and will also explore whether any factors are associated with poor outcomes.

Background

HELLP syndrome is a serious complication of pregnancy characterised by haemolysis, elevated liver enzymes and a low platelet count⁸². Incidence estimates vary from 0.5 to 7.6 per 1,000 deliveries^{34,83} and between 8% and 24% of cases with severe preeclampsia/eclampsia^{83,84}. Although there have been reports that women with HELLP syndrome are more likely to be older, of white ethnicity and multiparous⁸⁵⁻⁸⁷ and the majority, although not all, have signs of preeclampsia⁸⁸, there has been no comprehensive study of the risk factors for this complication.

There is a consensus that prompt delivery is indicated when HELLP syndrome develops after 34 weeks of gestation or when fetal or maternal conditions deteriorate. However, there is debate about the optimal management of women who develop the syndrome prior to 34 weeks of gestation when the maternal and fetal status is reassuring. There is also some controversy regarding risk factors for adverse outcome. This study aims to estimate the incidence of HELLP syndrome in the UK, to investigate and quantify the associated risk factors, management and outcomes and to explore whether any factors are associated with poor outcomes.

Case definition

All pregnant women identified as having HELLP syndrome defined as **new onset** of the following:

Elevated liver enzymes, defined as:

Serum aspartate aminotransferase (AST) ≥ 70 U/L

OR

Gamma-glutamyltransferase (γ -GT) ≥ 70 U/L

OR

Alanine aminotransferase (ALT) ≥ 70 U/L

AND

Low platelets, defined as platelet count $< 100 \times 10^9/l$.

AND

EITHER

Haemolysis, defined by abnormal peripheral blood smear or serum lactate dehydrogenase (LDH) levels ≥ 600 U/L or total bilirubin ≥ 20.5 $\mu\text{mol/l}$

OR

Hypertension, defined as a systolic blood pressure ≥ 140 mmHg or a diastolic blood pressure ≥ 90 mmHg

OR

Proteinuria, defined as 1+ (0.3 g/l) or more on dipstick testing, a protein:creatinine ratio of 30 mg/mmol or more on a random sample, or a urine protein excretion of 300 mg or more per 24 hours

Surveillance Period

June 2011-May 2012

Research questions

- What is the incidence of HELLP syndrome in the UK?
- What are the risk factors for HELLP syndrome?
- How is HELLP syndrome managed in the UK?
- What are the outcomes for mother and infant?
- Are there any factors that are associated with poor outcomes?

Investigators

Kate Fitzpatrick, Marian Knight, Jenny Kurinczuk, Peter Brocklehurst, Maria Quigley, NPEU;
Sue Sellers, United Bristol Hospitals NHS Trust; Mervi Jokinen, RCM;
Shona Golightly, CMACE; Gwyneth Lewis, Department of Health;
James Walker, NPSA; Alison Burton, Oxfordshire PCT; Jenny Furniss, Lay representative.

Funding

This study has been funded by the National Institute for Health Research as part of the UK National Maternal Near-miss Surveillance Programme (UKNeS).*



4.4.4 Pregnancy after Gastric Band Surgery

Key points

- Laparoscopic Adjustable Gastric Band (LAGB) insertion is the primary surgical method of surgical weight reduction in the UK.
- LAGB insertion is increasing rapidly and the increase in gastric banding in women of reproductive age has resulted in increasing numbers of pregnancies following gastric banding.
- Management of pregnancy following gastric band surgery is not well defined.
- This study will use UKOSS to describe the epidemiology and management of gastric banding in pregnancy in the UK and use this information to develop future guidelines for optimal management.

Background

The impact of obesity on pregnancy is well established; obesity negatively impacts on maternal, fetal and neonatal wellbeing⁸⁹. Laparoscopic Adjustable Gastric Band (LAGB) insertion is the primary surgical method of surgical weight reduction in the UK. It involves application of an adjustable silicone balloon around the upper portion of the stomach, resulting in a small upper stomach pouch and a narrowed outlet, which limits the stomach's capacity to intake food and increases the feeling of fullness. These two effects assist subsequent weight loss. LAGB insertion is increasing rapidly both in the private sector and in the NHS, with an estimated 1,700 bands inserted in women under the age of 40 years in 2007. The increase in gastric banding in women of reproductive age has resulted in increasing numbers of pregnancies following gastric banding.

Nevertheless, management of pregnancy following gastric band surgery has not been well defined. In most reports, women who conceive following LAGB have the band deflated for the duration of the pregnancy⁹⁰ because of concerns regarding hyperemesis and poor nutritional intake. Deflating the gastric band has the adverse effect of excessive weight gain⁹¹ and subsequent pregnancy complications. However, pregnancy following LAGB has been shown to be well tolerated and studies have also demonstrated a reduction in incidence of gestational diabetes⁹²⁻⁹⁴, maternal hypertension⁹²⁻⁹⁵ and caesarean delivery⁹⁵ when compared to obese controls.

Case definition

Any woman with a confirmed ongoing pregnancy following laparoscopic adjustable gastric band surgery.

Surveillance Period

September 2011 – August 2012

Research questions

- What is the incidence of pregnant women with previous gastric band surgery in the UK?
- How are pregnant women who have a gastric band currently managed in the UK?
- What are the medical, obstetric and neonatal outcomes of pregnant women after gastric band surgery?
- What is the weight change in pregnant women who have had gastric band surgery?

Investigators

Elinor Medd, Judith Hyde, Mary Lynch, Andrew Johnson, Tim Draycott, Southmead Hospital, Bristol

Funding

This study is funded by a grant from North Bristol NHS Trust.

4.4.5 Severe Sepsis

Key points

- Mortality due to severe maternal sepsis has increased in the UK and is now the leading cause of direct maternal death in the UK.
- Underlying each maternal death is a much larger number of cases of sepsis-related morbidity; however there has been no national-level study to measure the incidence or risk factors for this condition in the UK.
- This study will describe, on a population level, the incidence of severe maternal sepsis in the UK, associated risk factors, causative organisms, management and outcomes and investigate whether any factors are associated with poor outcomes.

Background

Maternal sepsis can be a severe complication of pregnancy or birth, which if untreated, can rapidly progress along a continuum of severity to septicaemic shock and eventually death. In the UK, the incidence of fatal maternal sepsis has increased over the last two decades. In the late 1980's the maternal mortality rate (MMR) due to sepsis was 0.4/100,000 maternities, while in the period from 2006-2008 the MMR increased to 1.13/100,000³⁶. This places sepsis as the leading cause of direct maternal death, surpassing hypertensive disorders^{36,96}. Underlying each maternal death is a much larger number of cases of morbidity during pregnancy and puerperium⁹⁷. Given the recent increase in maternal deaths and morbidity incidence in the general population due to sepsis⁹⁸, an understanding of the risk factors in the UK of obstetric sepsis morbidity before death occurs is needed to better target potential points of clinical intervention and prevent poor outcomes for mothers and their infants.

While there are several well-established risk factors for maternal sepsis including caesarean section⁹⁹⁻¹⁰¹ and anaemia^{100,102}, there has been no national-level study of the incidence or risk factors for this complication in the UK. The aim of this study, therefore, is to carry out a population-based case-control study using UKOSS to estimate the incidence of severe maternal sepsis in the UK, to investigate and quantify the associated risk factors, causative organisms, management and outcomes and to explore whether any factors are associated with poor outcomes.

Case definition

Any pregnant or recently pregnant woman (up to 6 weeks postpartum) diagnosed with severe sepsis (irrespective of the source of infection).

Report only cases diagnosed as having severe sepsis by a senior clinician.

A severe sepsis case would be expected to include women in one of the following groups:

1. Death related to infection or suspected infection
2. Any women requiring level 2 or level 3 critical care (or obstetric HDU type care) due to severe sepsis or suspected severe sepsis
3. A clinical diagnosis of severe sepsis.

As a guide clinical diagnosis of severe sepsis would usually be associated with 2 or more of the following:

- a) Temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$ measured on two occasions at least 4 hours apart
- b) Heart rate >100 beats/ minute measured on two occasions at least 4 hours apart
- c) Respiratory rate >20 / minute measured on two occasions at least 4 hours apart
- d) White cell count $>17 \times 10^9/\text{L}$ or $<4 \times 10^9/\text{L}$ or with $>10\%$ immature band forms, measured on two occasions.

Surveillance Period

June 2011 – May 2013

Research questions

- What is the incidence of severe maternal sepsis in the UK?
- What are the risk factors for severe maternal sepsis?

- What are the main causative organisms?
- How is severe maternal sepsis managed in the UK?
- What are the outcomes for mother and infant?
- Are there any factors that are associated with poor outcomes?

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5. Publications

5.1. Fetomaternal Alloimmune Thrombocytopenia

Published Article

Knight M, Pierce M, Allen D, Kurinczuk JJ, Spark P, Roberts DJ, Murphy MF.

The incidence and outcomes of fetomaternal alloimmune thrombocytopenia: a UK national study using three data sources. *Br J Haematol.* 2011 Feb;152(4):460-8.

Key points

- Fetomaternal alloimmune thrombocytopenia (FMAIT) is the most common cause of severe neonatal thrombocytopenia in otherwise well, term infants.
- This study identified cases between October 2006 and September 2008 through UKOSS, the British Paediatric Surveillance Unit (BPSU) and the NHS Blood and Transplant Platelet Immunology database, and followed affected infants to one year of age.
- The estimated incidence of clinically detected FMAIT was 12.4 cases per 100,000 total births (95%CI 10.7-14.3).
- Fifty-two cases (30%) were known at the start of pregnancy; 120 (70%) were unknown (n=115) or unrecognised (n=5).
- Cases known at the outset of pregnancy were more likely to be delivered by caesarean section (82% vs 30%, $p<0.001$), had higher platelet counts at birth and were less likely to have a platelet count below $20 \times 10^9/l$ at birth than cases not known at pregnancy outset (2% vs 58%, $p<0.001$).
- Unknown cases were more likely to experience any haemorrhagic complication (67% vs 5%) ($p<0.001$) and more likely to have an intracranial haemorrhage (20% vs 4%) ($p=0.014$) than known cases receiving antenatal management.
- In view of the incidence of severe disease identified, further assessment of the case for antenatal screening is important.
- There were a number of cases in which the significance of a history of FMAIT in a previous sibling was not recognised and there is a need for continuing awareness of the importance of this diagnosis.

5.2. Influenza AH1N1v in Pregnancy

Published Articles

Yates LM, Pierce M, Stephens S, Mill AC, Spark P, Kurinczuk JJ, Valappil M, Brocklehurst P, Thomas SHL and Knight M. Influenza A/H1N1v in pregnancy: An investigation of the characteristics of affected women and the relationship to pregnancy outcomes for mother and infant. *Health Technol Assess.* 2010. 14(34): p. 109-82.

Knight M, Pierce M, Seppelt I, Kurinczuk J, Spark P, Brocklehurst P, McLintock C, Sullivan E, on behalf of the UK Obstetric Surveillance System, the ANZIC Influenza Investigators, and the Australasian Maternity Outcomes Surveillance System. Critical illness with AH1N1v influenza in pregnancy: a comparison of two population-based cohorts. *BJOG* 2010; 118(2): 232-239.

Key points

- AH1N1v is expected to remain the predominant circulating influenza virus strain in the UK in 2011.
- Women hospitalised with AH1N1v in pregnancy in the UK during the 2009 pandemic were significantly at risk of maternal and pregnancy complications: 1.7% of women admitted to hospital with confirmed AH1N1v influenza in pregnancy died (95% CI 0.5-4.2%), an estimated 1.6 deaths per 100,000 maternities (95% CI 0.5-3.7); there was a significant increase in the odds of preterm delivery associated with admission with AH1N1v infection in pregnancy (OR 3.1; 95% CI 2.1, 4.5).

These findings emphasise the importance of ongoing routine immunisation of pregnant women against influenza. Immunisation is particularly important in women with asthma and other co-morbidities who are more likely to be admitted to hospital with AH1N1v in pregnancy.

- Treatment within two days of symptom onset was associated with an 84% reduction in the odds of admission to an intensive care unit (ICU) (OR 0.16, 95%CI 0.08-0.34); in the context of high circulating levels of influenza in the community, early use of antiviral agents (oseltamivir or zanamivir) in pregnant women with influenza symptoms is important.
- Maternal obesity during pregnancy was associated with both admission to hospital with confirmed infection and critical illness from AH1N1v. This highlights the importance of ongoing work to support obesity prevention at a community level.
- Maternal smoking, particularly in younger mothers, was also associated with admission with AH1N1v in pregnancy. Smoking in pregnancy is associated with a number of risks to both mother and fetus and thus prevention programmes continue to be important.
- There was a significantly higher ICU admission risk in Australia and New Zealand than in the UK in 2009 (risk ratio 2.59, 95% CI 1.75–3.85), which may reflect the success of clinical and public health interventions in the UK in the second phase of the pandemic.

5.3. A novel use of a classification system to audit severe maternal morbidity

Published Article

Homer CSE, Kurinczuk JJ, Spark P, Brocklehurst P, Knight M. A novel use of a classification system to audit severe maternal morbidity. *Midwifery* 2010, 26(5): 532-536.

Key points

- The Robson Ten Group Classification System (TGCS) is a tool widely used to audit caesarean section delivery rates.
- The aim of this study was to examine whether the TGCS could be extended in a novel way to classify women who had a peripartum hysterectomy.
- The analysis of data from the UKOSS study conducted in 2005-6 showed that women who underwent a peripartum hysterectomy were predominantly from the more complex classification groups. After adjusting for age, ethnicity and socio-economic status, the groups with an increased odds of peripartum hysterectomy were those who had a previous caesarean section, as revealed in the original analysis of these data.
- This investigation shows that the TGCS can be used in a novel way, that is, to examine an outcome other than caesarean section, and could be part of a new system to monitor patient safety; however, it may not necessarily be a useful way to monitor other events in childbirth.
- Further work is needed to develop other classification systems which could be used as benchmarking tools to monitor patient safety in maternity care.

5.4. Planned vaginal delivery or planned caesarean delivery in women with extreme obesity

Published Article

Homer CSE, Kurinczuk JJ, Spark P, Brocklehurst P, Knight M. Planned vaginal delivery or planned caesarean delivery in women with extreme obesity. *BJOG* 2011. 118(4): 480-487.

Key points

- Evidence suggests that the risk of caesarean delivery is increased by 50% in women with a body mass index (BMI) of 30-35 kg/m² and more than double in women with a BMI >35 kg/m² compared with women with a normal BMI (20-25 kg/m²).

- Factors associated with the higher risk of caesarean delivery in obese women may include medical and pregnancy complications such as diabetes and pre-eclampsia, as well as poor uterine contractility and concerns regarding the challenges of both general and regional anaesthesia in the emergency situation.
- Anecdotally, there appears to be an increasing move to recommend planned caesarean delivery to avoid the perceived risks of emergency caesarean delivery in this group of women.
- The aim of this study was to investigate, using data from the UKOSS national cohort of pregnant women with a BMI 50kg/m² or over, the factors associated with mode of birth, and to compare the outcomes in women planned to deliver vaginally with those planned to deliver by caesarean.
- After adjustment, there were no significant differences in anaesthetic, postnatal or neonatal complications between women with planned vaginal delivery and planned caesarean delivery, with the exception of shoulder dystocia (3% versus 0%, P = 0.019).
- There were no significant differences in any outcomes in the subgroup of women who had no identified medical or antenatal complications.
- This study does not, therefore, provide any evidence to support a routine policy of caesarean delivery for extremely obese women on the basis of concern about higher rates of delivery complications, but does support a policy of individualised decision-making on the mode of delivery based on a thorough assessment of potential risk factors for poor delivery outcomes.

5.5. Saving Mothers' Lives 2006-8

Published Article

Lewis, G. (Ed), R. Cantwell, et al. Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer: 2006-2008. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom. BJOG 2011. 118 Suppl 1: 1-203.

Key points

Information from UKOSS studies has been used to provide denominator morbidity information for the latest report from the UK Confidential Enquiries into Maternal Deaths³⁶. Appendix 2A of the Saving Mothers' Lives 2006-8 report summarises the studies which provided underlying morbidity data:

Haemorrhage and associated conditions:

Peripartum Hysterectomy

Management with specific second-line therapies for postpartum haemorrhage

Uterine Rupture**

Placenta Accreta**

Hypertension and related disorders:

Eclampsia

Acute Fatty Liver of Pregnancy

Antenatal Stroke

Thrombosis and thromboembolism:

Antenatal Pulmonary Embolism

Amniotic Fluid Embolism**

Cardiac disease:

Myocardial Infarction

Pulmonary vascular disease

Aortic dissection

Anaesthetic deaths:

Failed intubation

5.6. Uterine Compression Sutures

Published Article

Kayem G, Kurinczuk JJ, Alfirevic Z, Spark P, Brocklehurst P, Knight M on behalf of UKOSS. Uterine compression sutures for the management of severe postpartum hemorrhage. *Obstet Gynecol.* 2011 Jan;117(1):14-20.

Key points

- Two hundred and eleven women who had a uterine compression suture to treat a postpartum haemorrhage were reported over the 19 months of the study. Thirty-seven percent had a B-Lynch procedure, 23% a modified B-Lynch with two vertical sutures; 15% other specific techniques; and for 25% the technique was not specified.
- The overall rate of failure, leading to hysterectomy, was 25% (95% confidence interval(CI) 19–31%); there were no significant differences in failure rates among B-Lynch sutures, modified B-Lynch sutures, and other suture techniques.
- Women were more likely to have a hysterectomy if they were older (adjusted odds ratio (aOR) 2.77, 95%CI 1.13-6.77), multiparous (aOR 2.83, 95%CI 1.00-8.00), of non-managerial socioeconomic status (aOR 3.54, 95%CI 1.20-10.4) or had a vaginal delivery (aOR 6.08, 95%CI 1.33-27.8).
- A prolonged delay of two to six hours between delivery and uterine compression suture was independently associated with a fourfold increase in the odds of hysterectomy (aOR 4.60, 95%CI 1.62-13.1).
- These data emphasise the need for a careful evaluation of blood loss after delivery to avoid any prolonged delay in recognition of haemorrhage.

5.7. Abstracts

The following abstracts were presented at meetings in 2010 and are available on our website www.npeu.ox.ac.uk/ukoss

Influenza A/H1N1v in pregnancy: an investigation of the characteristics and management of affected women and the relationship to pregnancy outcomes for mother and infant. Presented at the British Maternal Fetal Medicine Society meeting June 2010

Specific therapies for severe postpartum haemorrhage in the UK. Presented at the British Maternal Fetal Medicine Society meeting June 2010

Caesarean section and severe maternal obesity. Presented at the Breathing New Life into Maternity Care conference July 2010

5.8. UKOSS Publications to date

Knight, M., J. J. Kurinczuk, et al. (2005). "The UK Obstetric Surveillance System for rare disorders of pregnancy." *BJOG* 112(3): 263-265.

Knight, M., J. Kurinczuk, et al. (2005). "UK Obstetric Surveillance System uncovered." *RCM Midwives* 8(1): 38-39.

Knight, M. on behalf of UKOSS (2007). "Eclampsia in the United Kingdom 2005." *BJOG* 114(9): 1072-1078.

Knight, M. on behalf of UKOSS (2007). "Peripartum hysterectomy in the UK: management and outcomes of the associated haemorrhage." *BJOG* 114(11): 1380-1387.

Knight, M., J. J. Kurinczuk, et al. (2008). "Caesarean delivery and peripartum hysterectomy." *Obstet Gynecol* 111(1): 97-105.

Knight, M., C. Nelson-Piercy, et al. (2008). "A prospective national study of acute fatty liver of pregnancy in the UK." *Gut* 57(7): 951-956.

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- Homer, C. S., J. J. Kurinczuk, et al. (2011). "Planned vaginal delivery or planned caesarean delivery in women with extreme obesity." *BJOG* 118(4): 480-487.
- Knight, M., M. Pierce, et al. (2011). "The incidence and outcomes of fetomaternal alloimmune thrombocytopenia: a UK national study using three data sources." *Brit J Haematol* 152(4): 460-468.
- Lewis, G. E., R. Cantwell, et al. (2011). "Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer: 2006-2008. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom." *BJOG* 118 Suppl 1: 1-203.

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