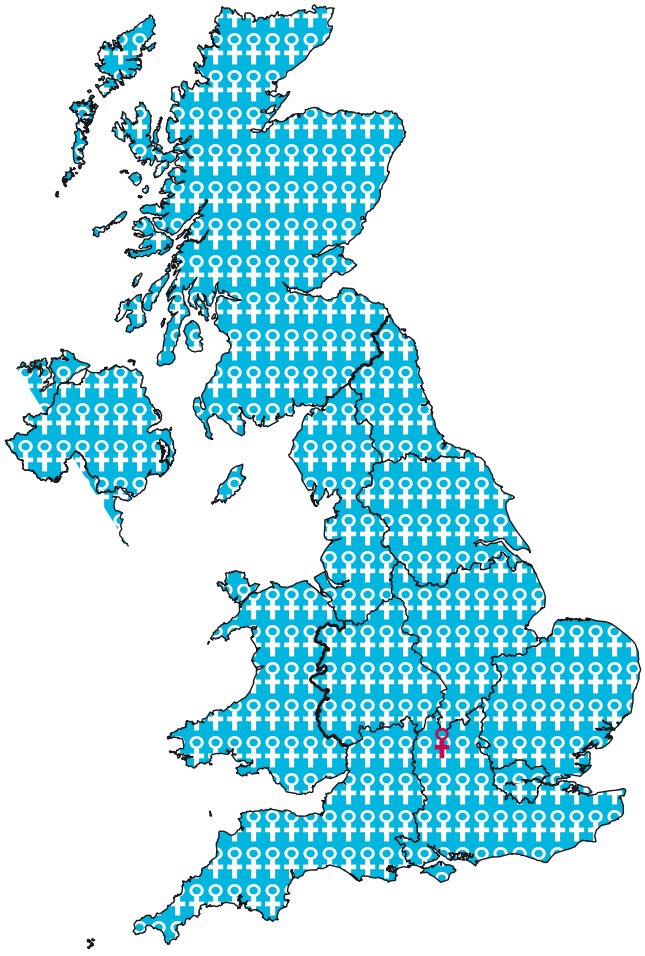
UKOSS

UK Obstetric Surveillance System

Fourth Annual Report 2010

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

npeu National Perinatal Epidemiology Unit

This report should be cited as:

Knight M, Spark P, Pierce M, Kayem G, Kurinczuk JJ, and Brocklehurst P on behalf of UKOSS. United Kingdom Obstetric Surveillance System (UKOSS) Annual Report 2010. National Perinatal Epidemiology Unit, Oxford 2010.

Table of Contents

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 Centre for Maternal and Child Enquiries (CMACE), the Department of Health, the Health Protection Agency and the National Patient Safety Agency (NPSA).

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 information.[1-6]

Studies using UKOSS may be undertaken by any investigator who identifies a suitable topic.[7] 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 which can be suitably addressed using the UKOSS methodology (prospective descriptive, cohort or case-control studies). This report outlines the studies undertaken during the fifth 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 fewer 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.

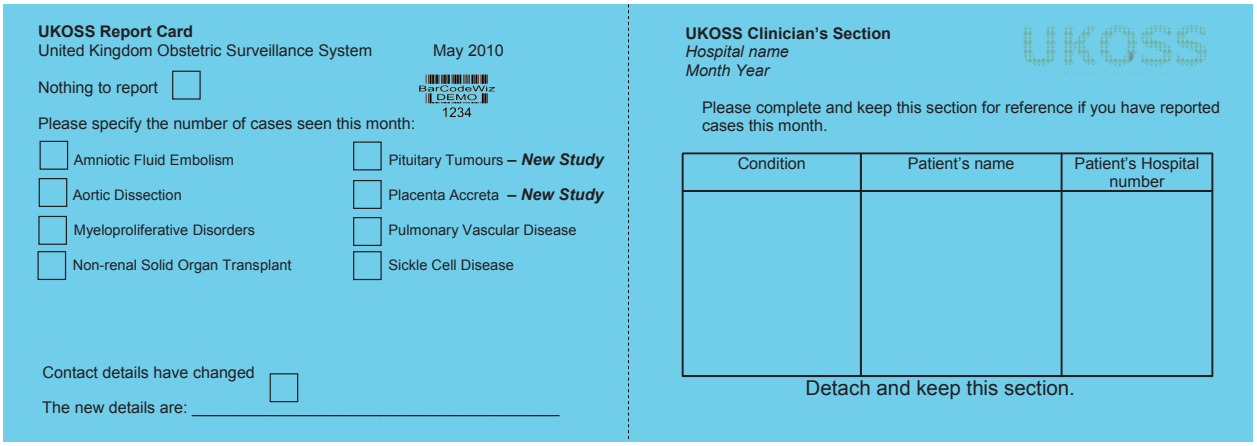
In order to perform case-control or cohort studies, information is also collected on control or comparison women for some studies. For these studies only, clinicians who report a case are asked to follow specific instructions to identify appropriate comparison women and complete a similar data collection 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 2005.[2]
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/m^2 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 section.[5]
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 found.[1]
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 studies.[6]

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 pandemic[12] (further information about this study can be found in section 4.2.1).

Figure 1: UKOSS Report Card



3. Participation

All 223 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 2009 was 93% (Figure 2), with regional return rates varying between 90% and 98% (Figure 3). These card return rates continue the high rates obtained during the first four 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 2009

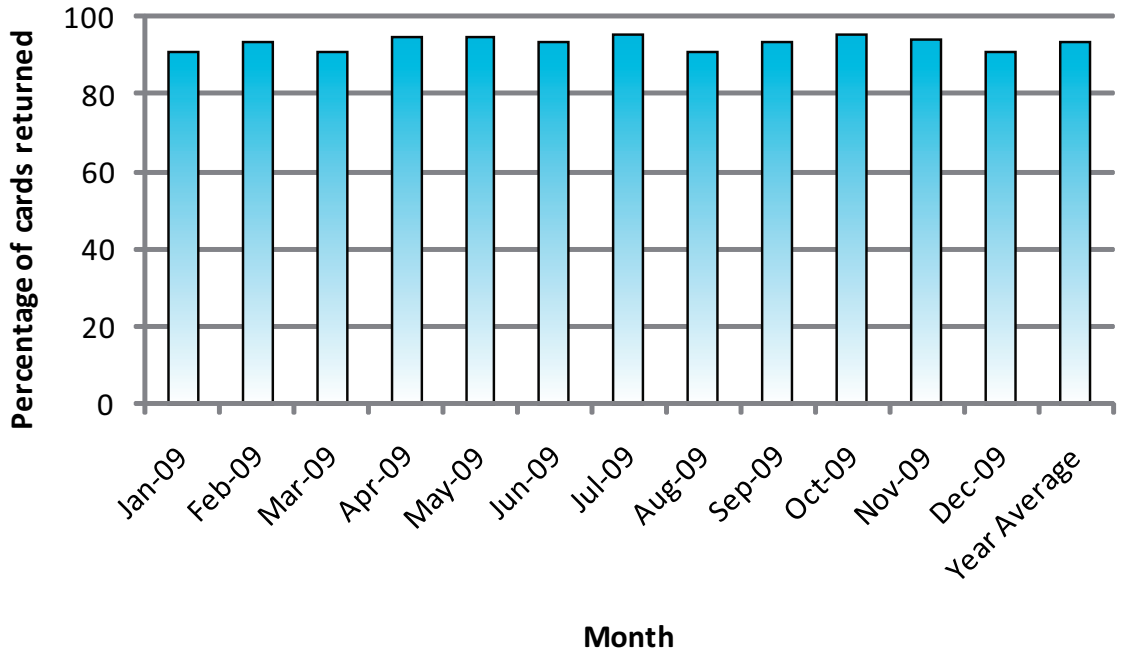
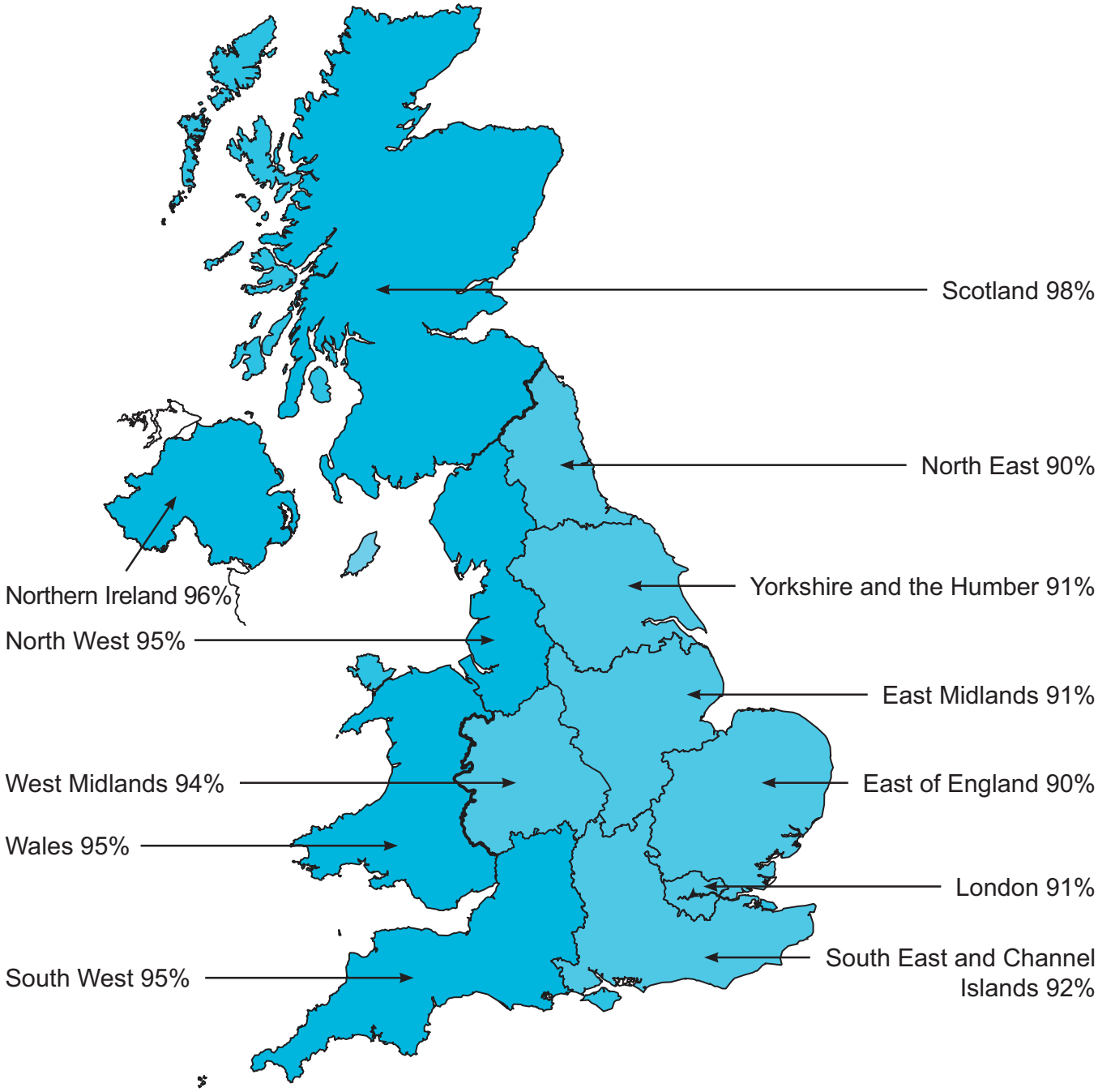


Figure 3: Map showing regional card return rates during 2009

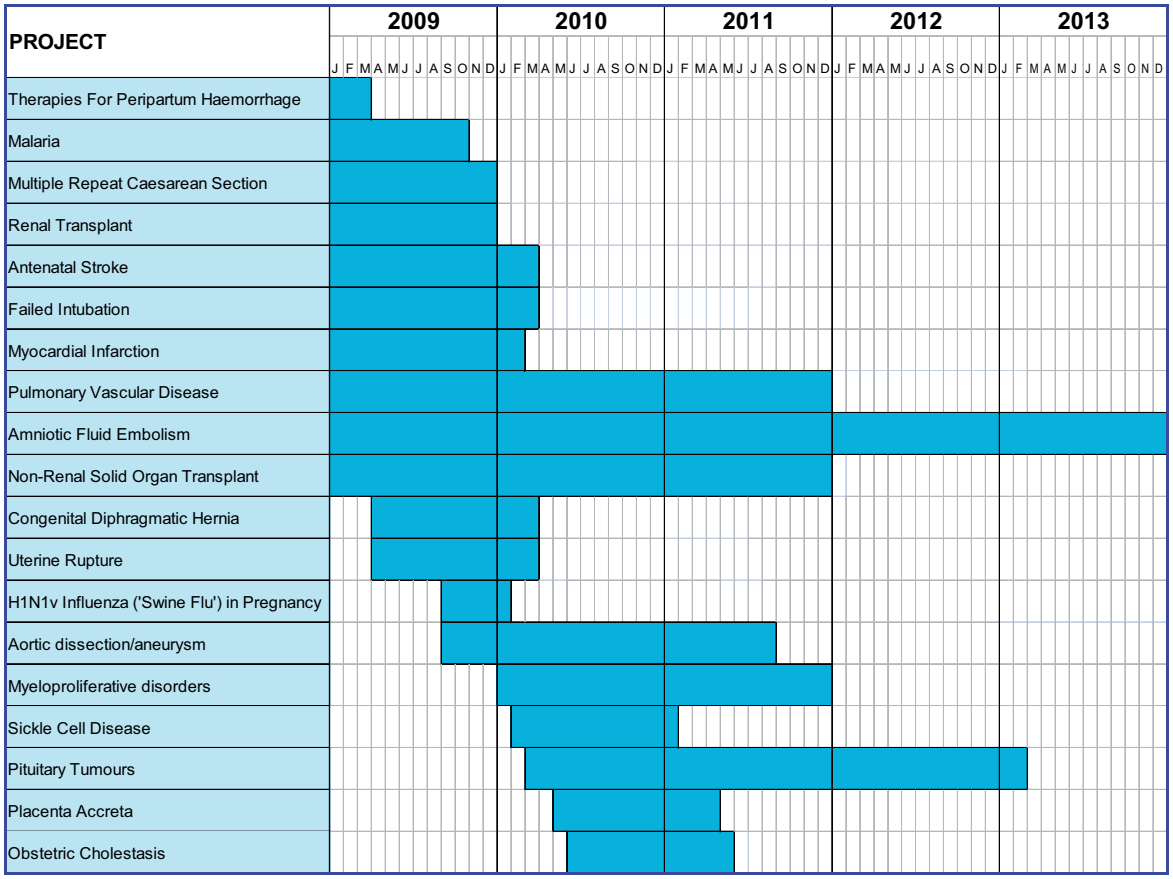


4. Studies

Unless otherwise specified, the results included in this report represent analysis of cases reported and data available up to February 2010. All studies have been funded through a grant to the NPEU from the Department of Health except where indicated. Please note the data presented are provisional, not peer reviewed and definitive conclusions should not be drawn from them.

4.1. Study Timetable

Figure 4: Provisional UKOSS Study Data Collection Timetable 2009-2013



4.2. Studies completed in 2009

4.2.1 AH1N1v influenza ('swine flu') in pregnancy

Key points

- At the onset of the pandemic there was very limited information about the complications of AH1N1v infection ('swine flu') in pregnancy in the UK.
- This study provided national information about women hospitalised with AH1N1v in pregnancy and rapid analysis of these data to produce updated monthly guidance for clinicians.
- Women with asthma, obesity and other co-morbidities are more likely to be admitted to hospital with AH1N1v in pregnancy and to suffer critical illness.
- Earlier treatment with antiviral agents is associated with improved outcomes for women, yet few women were treated with antivirals prior to admission to hospital. Further actions may be needed in future pandemics to ensure that antiviral agents are provided promptly to pregnant women.

Background

Preliminary data, particularly from the United States and Mexico,[13] suggested that pregnant women were more susceptible to complications of influenza AH1N1v infection, and worldwide data suggested that younger people, including women of reproductive age were at increased risk of infection. However, detailed epidemiological studies investigating risks in subgroups of pregnant women and the impact of pregnancy management strategies on outcomes were lacking. The collection of information on the severe end of the disease spectrum has been recommended as an appropriate method in the pandemic situation when surveillance of all cases becomes impractical,[14] thus this project identified, through UKOSS collaborating clinicians, all pregnant women hospitalised with confirmed influenza AH1N1v in the UK. This information was used to investigate the relationship between demographic, pregnancy characteristics, management and outcomes in order to generate immediate recommendations for changes in practice to improve outcomes for women and their infants during the course of the pandemic.

Case definition

Any woman admitted to hospital with confirmed or suspected AH1N1v influenza infection in pregnancy.

Surveillance Period

September 2009 – January 2010

Interim Results

241 pregnant women were admitted to hospital with laboratory confirmed AH1N1v infection (Figure 5). Eighty-three percent of women hospitalised with AH1N1v influenza were treated with antiviral agents, but only 6% received antiviral treatment before hospital admission. Women hospitalised with AH1N1v in pregnancy were more likely to be overweight (aOR 1.7, 95% CI 1.2-2.4) or obese (aOR 2.0, 95% CI 1.3-3.0) than the comparison cohort. They were also more likely to have asthma requiring inhaled or oral steroids (aOR 2.3, 95% CI 1.4-3.9), to be multiparous (aOR 1.6, 95% CI 1.1-2.2), to have a multiple pregnancy (aOR 5.2, 95% CI 1.9-13.8) and to be from a black or other minority ethnic group (aOR 1.6, 95% CI 1.1-2.3). Younger smokers had a raised odds of admission with confirmed H1N1v influenza (aOR 4.2, 95%CI 2.0-8.9) when compared with older non-smokers.

Treatment within two days of symptom onset was associated with an 84% reduction in the odds of admission to ITU (OR 0.16, 95%CI 0.08-0.34); women admitted to ITU were three times more likely to be obese (aOR 3.4, 95%CI 1.2-9.2) than women not admitted to an ITU.

Sixty-three percent of women had completed their pregnancies at the time of reporting. Women admitted to hospital with AH1N1v infection are more likely to deliver preterm; a conservative estimate accounting for the high proportion of women who are undelivered suggests a three times increased risk compared to an uninfected population cohort (OR 3.1; 95% CI 2.1, 4.5).

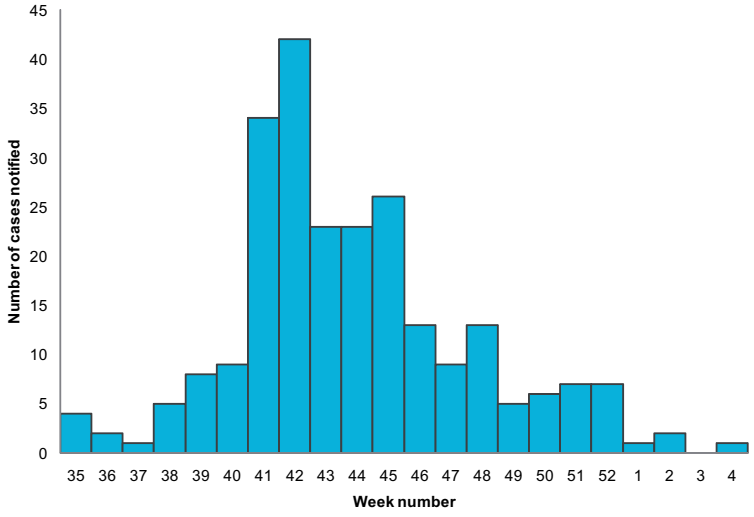


Figure 5: Hospital admissions with AH1N1v in pregnant women by week of hospital admission or start of symptoms (2009-2010, n=241)

Conclusions

Earlier treatment with antiviral agents is associated with improved outcomes for women, yet few women were treated with antivirals prior to admission to hospital. Further actions may be needed in future pandemics to ensure that antiviral agents are provided promptly to pregnant women, particularly in the primary care setting.

Maternal obesity is associated with both admission to hospital with confirmed AH1N1v in pregnancy and critical illness from AH1N1v in pregnancy. This highlights the importance of ongoing work to support obesity prevention at a community level.

Maternal smoking, particularly in younger mothers, is 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 are important.

Women with asthma and other co-morbidities are more likely to be admitted to hospital with AH1N1v in pregnancy. Clinicians should be aware of this association and work to ensure particularly that women with influenza and co-existing illnesses are treated appropriately.

Data on outcomes of pregnancy in women admitted to hospital with confirmed AH1N1v influenza are, as yet, incomplete. However, there appears to be a significantly increased risk of preterm delivery which may impact on service provision in a future pandemic. Further research on longer-term outcomes for infants exposed to AH1N1v influenza in the perinatal period may be warranted.

Funding

This study was funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme.

4.2.2 Malaria

Key points

- Malaria is an important cause of maternal and perinatal morbidity and mortality worldwide
- Travel-associated cases in the UK occur most commonly in the 15-44 age group
- There is no national information about the incidence of malaria in pregnancy in the UK, how these women are treated and the outcomes of pregnancy
- This study sought to describe the epidemiology of malaria in pregnancy in the UK and use the information to inform development and implementation of guidelines for both prevention and management. However, in view of the very low number of cases reported, we have stopped actively collecting cases and are seeking alternative means to address this question.

Background

Worldwide, malaria is the cause of severe maternal and perinatal morbidity and mortality. It is estimated that the population attributable fraction of maternal deaths due to malaria in sub-Saharan Africa is up to 23% and of neonatal deaths 18%.[15] Research in African and Asian populations shows that pregnant women are at higher risk both of acquiring disease and of suffering from more severe disease than non-pregnant women.[15] Malaria can cause severe anaemia, and in semi-immune populations may be associated with few other symptoms prior to the onset of severe complications such as adult respiratory distress syndrome or death, due to the sequestration of malarial parasites within the placenta.[16] In non-immune pregnant women, infection with falciparum malaria is more likely to lead to severe complications such as cerebral malaria than in the non-pregnant population. Infants are similarly severely affected; maternal malaria may lead to stillbirth and also preterm birth or intrauterine growth retardation, with a consequent increase in neonatal mortality.

The majority of information about malaria in pregnancy comes from populations in which malaria is endemic or epidemic. About 1500-2000 travel-associated cases of malaria are reported in the UK annually, with the peak occurring in the population aged 15-44.[17] However, no information exists about the number of women with malaria in the UK who are pregnant, the populations in the UK in which malaria in pregnancy occurs, how these pregnant women with malaria are treated or the consequences of the disease in these women and their infants. This information is important to develop and implement guidelines for both prevention and management.

Case definition

Any woman with a positive blood film for malaria parasites (or confirmed placental malaria) at any time during pregnancy or immediately postpartum (before discharge from hospital after delivery).

Surveillance Period

October 2008 - October 2009

Interim Results

Only six cases were reported over the course of one year. Full details were available for five women. All cases were travel-associated (travel to Africa in all cases) and all were in women from ethnic minority groups. Four of the five women had taken no antimalarial prophylaxis, emphasising the importance of taking prophylaxis on all visits to malaria affected areas, even during pregnancy.

Conclusions

In view of the very low rate of reporting, this study was unlikely to achieve its objectives without a very extended data collection period. The study was therefore stopped and we are seeking alternative means to assess the research questions.

Investigators

Marian Knight, Jennifer Kurinczuk, Peter Brocklehurst, National Perinatal Epidemiology Unit

Richard Pebody, Jane Jones, Health Protection Agency

Christopher Whitty, London School of Hygiene and Tropical Medicine

Peter Chiodini, Hospital for Tropical Diseases

4.2.3 Multiple Repeat Caesarean Section

Key points

- Repeat caesarean section is an important cause of maternal morbidity and mortality.
- The increasing incidence of primary caesarean section in the UK may lead to an increase in the incidence of multiple repeat caesarean section.
- There have been no prospective national studies to estimate the incidence or outcomes of multiple repeat caesarean section.
- This study will investigate the incidence, management and outcomes for mother and infant of multiple repeat caesarean section. It will allow comparison between the risks associated with multiple repeat caesarean and those described in fewer repeat procedures.

Background

The incidence of primary caesarean section is rising throughout the world and the UK also demonstrates this trend.[18] This is thought to be due to the introduction of fetal monitoring in labour, maternal preference, maternal obesity, and possibly defensive obstetric practice. After having three lower segment caesareans women are advised to undergo repeated elective caesarean in any subsequent pregnancies, rather than attempt a vaginal delivery.[19] This practice is thought to reduce the risk of uterine rupture which can be life-threatening for both mother and baby. All caesarean procedures however, have associated risks; venous thromboembolism and haemorrhage - which are leading causes of maternal mortality, infection, and damage to the viscera. Repeated caesareans are also associated with placental invasion into the myometrium and peripartum hysterectomy. Babies born via caesarean are more likely to experience breathing difficulties and require admission to a specialist unit.

Current knowledge concerning the maternal-fetal outcomes and management of multiple repeat caesarean is limited and mainly derived from hospital-based retrospective case analysis outside the UK.[20-23] Complication rates are variously reported as not significantly different to lower order caesareans, or increased. A large cohort study of elective caesareans in North American tertiary centres described an increase in maternal morbidity with higher order procedures.[24] No population-wide studies of incidence or complications have been undertaken. This study will determine the national incidence of multiple repeat caesarean section in the UK and identify the accompanying complications and their respective rates. It will allow comparison between the risks associated with multiple repeat caesarean and those described in fewer repeat procedures. It will also ascertain the current UK practice in such cases with regards to timing of elective caesarean and postnatal counselling for future pregnancies.

Case definition

Any woman giving birth to an infant via her **5th or more** elective or emergency caesarean section (ie who has previously undergone four or more other caesarean procedures).

Surveillance Period

January 2009 – December 2009

Interim Results

One hundred and twenty cases were reported over one year and data has been returned for 97 of them (81%). Five did not meet the case definition and there were 4 duplicate cases; there were thus 88 confirmed cases.

Interim Conclusions

Final data collection for the outstanding cases is currently underway. The investigators, led by Joanna Cook, plan to complete the analysis and presentation of the data by the end of 2010.

Investigators

Joanna Cook, St. Mary's Hospital, Imperial College Healthcare NHS Trust

Mandish Dhanjal, Sheba Jarvis, Floria Cheng, Queen Charlotte's & Chelsea Hospital, Imperial College Healthcare NHS Trust

Funding

RCOG/UKOSS Award from the Edgar Research Fellowship Fund.

Royal College of Obstetricians and Gynaecologists

Setting standards to improve women's health

4.2.4 Pregnancy in Renal Transplant Recipients

Key points

- There have been over 14,000 reports of pregnancy in transplant recipients worldwide.
- The UK National Transplantation Pregnancy Register identified high rates of preterm and caesarean section delivery in renal transplant recipients, but it no longer collects information.
- Immunosuppressive regimens are continually developing.
- This study will provide a national picture of the incidence of pregnancy in 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 organs.[25] Most studies are centre-based and retrospective.[26] Three voluntary registers have collected data at various times: the US National Transplantation Pregnancy Register (1991-present),[27] the UK Transplant Pregnancy Register (1994-2001)[26] and the European Dialysis and Transplant Association Registry (1960-1992).[28] Recent analysis of data from the UK Transplant Pregnancy Register identified high rates of preterm delivery (50%) and delivery by caesarean section (72%) in pregnant renal transplant recipients. Worse outcomes were associated with poorer pre-pregnancy graft function and drug-treated hypertension during pregnancy. 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 and the second to investigate outcomes in women with other solid organ transplants.

Case definition

All pregnant women with a transplanted kidney, with or without other transplanted organs.

Surveillance Period

January 2007 – December 2009

Interim Results

One hundred and thirty-one cases of pregnancy in renal transplant recipients were reported, and data collection forms returned for 113 (86%). There were four duplicate cases, three which did not meet the case definition and two women with lost notes, leaving 104 confirmed cases. There have been no maternal deaths. Nine pregnancies miscarried and there was one termination of pregnancy. There were two perinatal deaths among 96 infants (including three sets of twins), giving a perinatal mortality rate of 21 per 1000 total births (95% CI 3-73 per 1000).

Interim Conclusions

The outcomes for women and their infants appear largely good, but more definitive conclusions will be drawn once full analysis of the data has been undertaken. Final data collection for those cases for whom we have not received data collection forms is currently underway and the data will be fully analysed by the end of 2010.

4.2.5 Therapies for Peripartum Haemorrhage

Key points

- Haemorrhage remains an important cause of maternal mortality in the UK.
- Uterine compression sutures are the most commonly used of these specific second-line therapies for postpartum haemorrhage (PPH) in the UK.
- All techniques examined were associated with significant failure rates.
- Women whose haemorrhage was not successfully controlled with a uterine compression suture were more likely to have had a later placement of the suture than women whose haemorrhage was controlled, highlighting the importance of early recognition and treatment of postpartum haemorrhage to improve outcomes for women.

Background

Haemorrhage is the second most common cause of direct maternal death in the UK as identified in the most recent report of the Confidential Enquiry into Maternal Deaths[29]. However, deaths from haemorrhage represent only the tip of the iceberg of disease; severe haemorrhage has been included in the definition of 'near-miss' maternal morbidity in several studies.[30,31]

The basic treatment of major peripartum haemorrhage consists of surgery and/or medical management with transfusion and uterotonic drugs. However, there are now a number of reports of the use of other therapies, including recombinant factor VIIa[32], uterine compression sutures,[33] ligation[34] and embolisation[35] of major pelvic vessels (internal iliac/uterine arteries) in cases with continued bleeding. None of these therapies have been evaluated in large randomised controlled trials, but all are used widely throughout the UK. This descriptive study collected information on the timing of use of these therapies, subsequent haemorrhage and requirement for additional management strategies such as hysterectomy with the aim of informing future guidelines for prevention and management of PPH.

Case definition

All women in the UK treated for peripartum haemorrhage with:

EITHER Activated factor VIIa

OR B-Lynch or other brace suture

OR Arterial ligation or embolisation.

Surveillance Period

October 2007- March 2009

Interim Results

Twenty-eight women had a specific second line therapy to prevent and 286 to treat a PPH. An estimated 2.6 women per 10,000 maternities were managed with these therapies. Almost a quarter of women subsequently underwent a hysterectomy following failure of control of the haemorrhage. Uterine compression sutures were the most frequently used of these specific second line therapies; the compression sutures failed to control the haemorrhage in 29% of cases (95% CI 26-36%). Treatment with uterine artery embolisation failed to control haemorrhage in 21% of cases (95% CI 6-46%), surgical ligation of pelvic vessels was performed in a very small number of cases and was associated with a failure rate of 68% (95% CI 43-87%) and factor VIIa, used in 12% of cases, unsuccessfully controlled haemorrhage for 71% of women (95%CI 52-85%). Women whose haemorrhage was not successfully controlled with a uterine compression suture were significantly more likely to have had a later placement of the suture (more than two hours following delivery) than women whose haemorrhage was controlled (aOR 3.86, 95% CI 1.65-8.99).

Interim Conclusions

When first line therapies have failed, uterine compression sutures are the most common additional treatment used in cases of severe PPH in the UK. All techniques examined were associated with significant failure rates.

Funding

This study is funded by Wellbeing of Women.

Wellbeing of Women

Charity Registration No: 239281

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.
- Preliminary analysis shows 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 an increased risk of fatality in ethnic minority women but with high quality supportive care outcomes for women are good.

Background

Amniotic fluid embolism (AFE) has been identified by the UK Confidential Enquiry into Maternal Deaths as a leading cause of maternal mortality;[29] the most recent report noted a three-fold increase in the number of deaths from this condition since the previous report. Estimates of incidence vary tenfold between 1.3 and 12.5 per 100,000 pregnancies.[36] Estimates of the mortality rate from this condition also vary widely,[37] 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.[38,39] A wide range of treatments have been described in case reports,[37] but there has been no comprehensive study of the epidemiology and management of this condition in the UK. A database of voluntary notifications was established in the UK to collect information on epidemiology and management;[40] this register was incorporated into UKOSS to improve ascertainment and allow a comprehensive study of the epidemiology and current management.

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 five years of the study 111 cases of AFE were reported. Information has been received for 104 of these cases (94%). There were 18 cases which were subsequently reported by clinicians as not cases and five duplicate reports. Thirteen further cases did not meet the case definition. There were thus 68 confirmed cases in an estimated 3,278,000 maternities. This gives an incidence estimate in the UK of 2.1 cases per 100,000 maternities (95% CI 1.6 to 2.6 per 100,000).

Detailed analysis of the 60 cases identified between February 2005 and February 2009 shows no evidence of change in incidence over the four years, although the study has limited power to detect any difference due to small annual case numbers. AFE occurrence was significantly associated with induction of labour (aOR 3.86, 95%CI 2.04-7.31) and multiple pregnancy (aOR 10.9, 95%CI 2.81-42.7); an increased risk was also noted in older ethnic minority women (aOR 9.85, 95%CI 3.57-27.2). Caesarean delivery was associated with postnatal amniotic fluid embolism (aOR 8.84, 95%CI 3.70-21.1). Twelve women died (case fatality 20%, 95%CI 11-32%); five of 37 infants of women with antenatal AFE died (perinatal mortality 135/1000 total births, 95%CI 45-288). Women who died were significantly more likely to be from ethnic minority groups (aOR 11.8, 95%CI 1.40-99.5).

Interim Conclusions

These data show that high-quality supportive care can result in good maternal outcomes after amniotic-fluid embolism. The observed increased risk of fatality in ethnic minority women may be associated with differences in underlying medical conditions or access to care, and appropriate services should be provided to minimize this risk.

4.3.2 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.
- There have been no prospective national studies to estimate the incidence or outcomes of this condition.
- This study will investigate the incidence, risk factors, management and outcomes of stroke in pregnancy in the UK in order to inform future guidelines for prevention and treatment.

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 mortality.[29] While stroke associated with pregnancy is rare (estimates of incidence from retrospective studies vary from 3 to 30 per 100,000 pregnancies), the last seven Confidential Enquiries into Maternal Deaths report 144 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 itself,[41] 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. By prospectively collecting data on maternal stroke this study will provide valuable information into the epidemiology of stroke associated with pregnancy.

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

Interim Results

75 cases were reported up to February 2010 and data returned about 59 of them (79%). Twenty-five did not meet the case definition and there were 3 duplicates. There were thus 31 confirmed cases in an estimated 988,000 maternities. This represents an estimated incidence of 1.6 cases per 100,000 maternities (95% CI 1.1-2.3 per 100,000).

Interim Conclusions

These interim results suggest that the incidence of antenatal stroke in the UK is similar or lower than that estimated from the literature. The data collection for this study will be completed shortly, having been extended to March 2010 due to a smaller number of cases than expected being reported. We will then undertake confirmation of case numbers, following which detailed analysis of risk factor and outcome information will be undertaken.

Investigators

Cathy Scott, NHS Oxford Deanery

Susan Bewley, Anthony Rudd, Beverley Hunt, Charles Wolfe, Guys and St Thomas' NHS Foundation Trust

Marian Knight, NPEU

Funding

This study is funded by Wellbeing of Women.

Wellbeing of Women

Charity Registration No: 239281

4.3.3 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 deaths.[29] Although rare, an association between pregnancy and aortic dissection has been reported and its incidence in pregnancy is rising. Approximately 50% of cases of aortic dissection in women under the age of 40 occur whilst they are pregnant.[42] 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.[43,44] 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.[43,44] Untimely delays in treatment of this disease can lead to potentially catastrophic consequences, since the mortality rate increases by 1% each hour if left untreated.[45] Current understanding of aortic dissection and its management in pregnancy is limited. Published data is mainly in the form of case reports with no clear management guidelines for this disease. Risk factors for aortic dissection within the pregnant population are equally not well-defined. 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 (1) 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

Main Research Questions

- What is the current incidence of aortic dissection in the UK?
- What are the risk factors for aortic dissection in pregnancy?
- How is aortic dissection currently diagnosed in pregnancy in the UK?
- How are the various aortic dissection subtypes in pregnancy managed in the UK?
- What are the maternal-fetal outcomes in patients diagnosed with aortic dissection?

Interim Results and Conclusions

To date only two cases have been reported and it is therefore too early to draw any conclusions.

Investigators

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

Funding

Heart Research UK.

4.3.4 Congenital Diaphragmatic Hernia

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.
- 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 UK.[46] 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 disability.[47-49] 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 twenty-three cases were reported up to February 2009 and data has been returned about 150 of them (67%). Eight cases did not meet the case definition, there were 20 duplicate reports and four women are yet to deliver. There are thus 118 confirmed cases to date.

Interim Conclusions

Data collection for this study 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

David Howe, University of Southampton

Judith Rankin, University of Newcastle

Elizabeth Draper, University of Leicester

Paul Losty, University of Liverpool

Funding

Action Medical Research.

4.3.5 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 years.[29] 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,[50,51] 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 noted.[52] 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 rare.[53] 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 overall.[54]

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

75 cases were reported up to February 2010 and data returned about 63 of them (84%). Eight cases did not meet the case definition and there were four duplicate reports. There were thus 51 confirmed cases in an estimated 1,401,000 maternities representing an estimated incidence of 3.6 cases per 100,000 maternities (95% CI 2.7-4.8 per 100,000).

Interim Conclusions

Data collection will shortly cease for this study. The investigators, led by Audrey Quinn, plan to complete the analysis and presentation of the data by the end of 2010.

Investigators

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

Funding

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

4.3.6 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 current 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 reported;[55] 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 definitions

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 $x10^9$/l)

OR an erythrocytosis (haemoglobin persistently greater than 16.5g/dl) .

Surveillance Period

January 2010 - December 2011

Main Research Questions

- What is the current number of pregnant women with a diagnosis of a myeloproliferative disorder, persistently increased number of platelets (thrombocytosis) or red cells (erythrocytosis) in pregnancy in the UK per 10,000 pregnant women per year?
- How are pregnant women with a diagnosis of a myeloproliferative disorder, persistently increased number of platelets or red cells managed in pregnancy?
- What is the outcome of pregnancies in women with a diagnosis of a myeloproliferative disorder, persistently increased number of platelets or red cells for the mother and infant?
- Interim Results and Conclusions

Data collection for this study has only just commenced and no results or conclusions are available yet.

Investigators

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

Funding

Guy's and St Thomas' Charity

4.3.7 Myocardial Infarction

Key points

- Myocardial infarction in pregnancy is known to be associated with significant maternal and fetal mortality.
- The current incidence estimate is based on a study from 1970.
- Current trends in lifestyle factors and increasing age at childbirth are likely to be leading to an increase in incidence.
- This study will provide a national picture of the incidence of the disease, its epidemiology and management.

Background

Myocardial infarction in pregnancy is known to be associated with significant maternal and fetal mortality.[56] The widely quoted incidence estimate of 1 in 10,000 births is based on a study conducted in 1970.[57] 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 USA[58] 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 literature.[59] 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%.[56] 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.[56,60] 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 criteria:[61]

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

Interim Results

54 cases were reported up to February 2010 and data returned about 50 of them (93%). 25 did not meet the case definition and 2 were duplicates. There were thus 23 confirmed cases, representing an estimated incidence of 7 cases per million maternities (95% CI 4-10). Fourteen of the women with a confirmed MI had angiography; 7 had coronary atheroma, 3 coronary artery dissection, 2 coronary arterial thrombosis and 2 had normal coronary arteries.

Interim Conclusions

In view of the increasing prevalence of risk factors for ischaemic heart disease among women delivering in the UK, this is likely to represent an underestimate of the true underlying burden of non-fatal disease. Note that an additional 25 cases were reported which did not meet the criteria for MI during pregnancy, including four women with a postnatal MI, one case which occurred pre-pregnancy, two cases of severe angina and a further 5 cases of cardiomyopathy. Full analysis of these data and comparison with fatal cases reported to CMACE will be undertaken once data collection is complete.

4.3.8 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 4500 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 radiation.[62] 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 failure.[62] Cushing's disease is associated with high fetal morbidity (spontaneous abortion 5%, stillbirth 6% and prematurity 43%).[63] 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 - March 2013

Main Research questions

- What proportion of women with pituitary tumours have significant tumour expansion during pregnancy?
- What are the current monitoring and management strategies for women with pituitary tumours during pregnancy?
- What are the outcomes of pregnancy for mother and infant?

Interim Results and Conclusions

Data collection for this study has only just commenced and no results or conclusions are available yet.

Investigators

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

D McCance, Royal Victoria Hospital, Belfast.

Funding

SPARKS

4.3.9 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 organs.[25] Most studies are centre-based and retrospective.[26] Three voluntary registers have collected data at various times: the US National Transplantation Pregnancy Register (1991-present),[27] the UK Transplant Pregnancy Register (1994-2001)[26] and the European Dialysis and Transplant Association Registry (1960-1992).[28] 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

Sixty-seven cases of pregnancy in non-renal solid organ transplant recipients were reported, and data collection forms returned for 59 (88%). There were four cases which were reported in error and eight duplicates, leaving 47 confirmed cases. Thirty-nine women had received liver transplants, three lung transplants, four a heart transplant and one a heart-lung transplant. One of the heart transplant recipients died; there were no other maternal deaths. Three women had a miscarriage, one had a termination. Two infants were still-born among 43 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.

4.3.10 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 death.[64] Three of the six maternal deaths in women with congenital heart disease reported in the UK in the last triennium were associated with pulmonary vascular disease;[29] since 1991 there have been 25 maternal deaths in the UK associated with this condition. Eisenmenger's syndrome is estimated to carry a maternal mortality rate of 40% per pregnancy,[65] with an infant mortality rate of 10-15%.[64] A systematic review of the literature in 1998 suggested that the maternal mortality rate had remained unchanged over the previous 20 years.[64] However, the authors of this review recognise that there may be inherent biases in published reports of pregnancy in women with pulmonary vascular disease 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 Anaesthesia,[66] 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 36mmHg.[67] 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 arteriosus.[68]

Surveillance Period

March 2006 – February 2012

Interim Results

To date 68 cases of pulmonary vascular disease have been reported, with further information available for 55 (81%). Three duplicate cases were reported and there were 28 reported cases which did not meet the case definition (the majority being cases of pulmonary embolism), leaving 24 confirmed cases; an estimated incidence of 8 cases per million maternities (95% CI 5-12 per million). Nine of the cases were attributed to congenital heart disease, two to chronic thromboembolism, one to sleep apnoea, eleven to idiopathic pulmonary arterial hypertension and one to connective tissue disease. Fourteen of these cases were known prior to pregnancy and ten were diagnosed during pregnancy or immediately postnatally.

Interim Conclusions

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

4.3.11 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 is some historical data, most from outside the UK, showing a high incidence of maternal and fetal complications in SCD, but no contemporary or recent prospective data from the UK. [69] 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 and

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

Main Research questions

- What is the current incidence of pregnancy in women with sickle cell disease in the UK?
- What management strategies are used for women with sickle cell disease during pregnancy; in particular what is the incidence of blood transfusion and anticoagulation therapy?
- What complications are seen during pregnancy in women with sickle cell disease compared to controls with out sickle cell disease?
- What are the outcomes for mother and infant compared to controls?

Interim Results and Conclusions

Data collection for this study has only just commenced and no results or conclusions are available yet.

Investigators

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

Funding

Guy's and St Thomas' Charity

4.3.12 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 will investigate the incidence, risk factors and outcomes of uterine rupture in the UK.

Background

True uterine rupture is a catastrophic event, and in the developed world it most commonly occurs in women who have previously delivered by caesarean section.[70] 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 labour,[71] 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 section.[72] Two recent systematic reviews[70,73] identified only one previous UK population-based study,[31] which reported 12 ruptures in 48,865 deliveries, a rate of approximately 1 in 4000 deliveries.

In addition to difficulties in quantifying the incidence of uterine rupture, Guise et al[73] noted that existing observational studies were insufficient to answer additional questions about the risks of rupture associated with induction and augmentation of labour. The planned case-control study using UKOSS will 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:[73,74] 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) will be excluded.

Surveillance Period

April 2009 - March 2010

Interim Results

One hundred and eighty-three cases of uterine rupture were reported over ten months, and data collection forms returned to date for 134 (73%). There were eight cases which were reported in error, nine which did not meet the case definition and four duplicates, leaving 113 confirmed cases representing an estimated incidence of 1.8 cases per 10,000 maternities (95%CI 1.5-2.1 per 10,000).

Interim Conclusions

The results of this study to date suggest that uterine rupture is uncommon. Once data collection is complete full analysis including quantification of risk factors for uterine rupture in the UK population will be undertaken.

Investigators

Marian Knight, Jenny Kurinczuk, Peter Brocklehurst, NPEU

Zarko Alfirevic, University of Liverpool

Funding

This study is funded by Wellbeing of Women.

Wellbeing of Women

Charity Registration No: 239281

4.4. Future studies

These studies have been approved by the UKOSS Steering Committee to commence in 2010/2011.

4.4.1 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 rupture,[75] peripartum hysterectomy[1] and maternal death,[29] as well as complications associated with surgical removal including damage to bladder, ureters and other organs.[75] Placenta accreta is thought to be becoming more common,[76,77] due to a number of factors including rising maternal age at delivery and an increasing proportion of deliveries by caesarean section.[78,79] However, the risk associated with these factors has not been quantified on a population basis in the UK.

There is also a debate about the optimal diagnostic and management techniques for placenta accreta. 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 if caesarean delivery rates continue to rise nationally.

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 postmortem
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

Main Research questions

- What is the current incidence of placenta accreta/increta/percreta in the UK?
- How is the condition managed in the UK?
- What proportion of cases are diagnosed antenatally by ultrasound or MRI? What ultrasonographic features are most commonly present and do any of these predict poor outcome?
- What is the role of previous caesarean section delivery (and number of previous caesarean deliveries) in relation to a) risk of the condition and b) outcome from the condition?
- What are the outcomes of the condition for women and their babies?
- Do any factors, including antenatal diagnosis, timing of diagnosis and seniority of operator impact on outcomes?

Investigators

Marian Knight, Jenny Kurinczuk, Peter Brocklehurst, Maria Quigley, NPEU;

Sue Sellers, United Bristol Hospitals NHS Trust; Mervi Jokinnen, 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 new UK National Maternal Near-miss Surveillance Programme (UKNeS)

4.4.2 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), also called intrahepatic cholestasis of pregnancy, 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 (both antenatally and during labour) and sudden intrauterine death.[80]

The aetiologies of the maternal disease and the fetal complications associated with the condition are incompletely understood. Despite this, there are several lines of evidence suggesting that the adverse outcomes may be due to the toxic effects of bile acids, and several studies have demonstrated a correlation between the maternal serum bile acid level and the risk of adverse fetal events.[81-84] The most definitive of these studies investigated the incidence of OC and of the adverse fetal outcomes in a Swedish population of 45,000 women, of whom 690 women were diagnosed with OC.[81] 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,[85,86] 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 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

Research questions

- What is the current incidence of severe obstetric cholestasis in the UK?
- What management strategies are used for women with severe obstetric cholestasis; in particular the incidence of elective preterm delivery and the use of ursodeoxycholic acid treatment?
- What complications are seen during pregnancy in women with severe obstetric cholestasis?
- What are the outcomes for mother and infant?

Investigators

Catherine Williamson, Victoria Geenes, Imperial College London

Marian Knight, NPEU

Funding

This study is funded by Wellbeing of Women.

Wellbeing of Women

Charity Registration No:239281

5. Publications

5.1. Amniotic fluid embolism

Published Article

Knight M, Tuffnell D, Brocklehurst P, Spark P, Kurinczuk JJ. Incidence and Risk Factors for Amniotic-Fluid Embolism. Obstet Gynecol 2010;115(5):910-7.[87]

Key points

- Analysis of data reported over four years to UKOSS shows an estimated incidence of amniotic fluid embolism (AFE) of 2.0 cases per 100,000 maternities (95% CI 1.5-2.5/100,000).
- AFE occurrence was significantly associated with induction of labour (aOR 3.86, 95%CI 2.04-7.31) and multiple pregnancy (aOR 10.9, 95%CI 2.81-42.7).
- An increased risk was also noted in older ethnic minority women (aOR 9.85, 95%CI 3.57-27.2).
- Caesarean delivery was associated with postnatal amniotic fluid embolism (aOR 8.84, 95%CI 3.70-21.1). Twelve women died (case fatality 20%, 95%CI 11-32%); women who died were significantly more likely to be from ethnic minority groups (aOR 11.8, 95%CI 1.40-99.5).
- 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.

5.2. Ethnic inequalities in severe maternal morbidity

Published Article

Knight M, Kurinczuk JJ, Spark P, Brocklehurst P on behalf of UKOSS. Inequalities in maternal health: national cohort study of ethnic variation in severe maternal morbidities. BMJ 2009;338:b542[88]

Key points

- Black Caribbean and black African women have twice as much risk of experiencing severe 'near-miss' maternal morbidity compared to white women. Pakistani women have a one and a half times increased risk.
- This pattern is very similar to reported ethnic differences in maternal death rates.
- For white women the estimated risk of severe complications is around 80 cases per 100,000 maternities (95% CI 73-87), 119 cases per 100,000 maternities (95% CI 83-165) for Pakistani women, 188 cases per 100,000 maternities (95% CI 110-301) for black African woman and 196 cases per 100,000 maternities (95% CI 143-261) for black Caribbean women.
- These differences may be due to the presence of pre-existing maternal medical factors, or to factors related to care during pregnancy, labour and birth, but are unlikely to be due to differences in age, socioeconomic or smoking status, body mass index or parity.
- This highlights to clinicians and policy-makers the importance of tailored maternity services and improved access to care for ethnic minority women.

5.3. Extreme Obesity

Published Article

Knight M, Kurinczuk JJ, Spark P, Brocklehurst P. Extreme obesity in pregnancy in the United Kingdon. Obstet Gynecol 2010;115(5):989-97.[89]

Key points

- Nearly one in every thousand women giving birth in the UK is extremely obese.
- These women are at risk of a number of severe morbidities, including pre-eclampsia (adjusted OR 4.46, 95%CI 2.43-8.16), gestational diabetes (aOR 7.01, 95%CI 3.56-13.8), and intensive care unit admission (aOR 3.86, 95%CI 1.41-10.6).
- Obese women were also more likely to have interventions which put them at risk of severe morbidity, including caesarean delivery (aOR 3.50, 95%CI 2.72-4.51) and general anaesthesia (aOR 6.35, 95%CI 2.63-15.3).
- Basic equipment was not universally available for the care of these women, and this, together with the increase in prevalence of obesity, has important implications for maternity service provision.
- There is an urgent need to address pre-pregnancy care and weight management programs to prevent this increase in prevalence as well as to ensure appropriate services are in place to reduce the inequalities in pregnancy outcomes for these women.

5.4. Trends in post-partum haemorrhage in high resource countries

Published Article

Knight M, Callaghan WM, Berg C, Alexander S, Bouvier-Colle MH, Ford JB, et al. Trends in postpartum hemorrhage in high resource countries: a review and recommendations from the International Postpartum Hemorrhage Collaborative Group. BMC Pregnancy Childbirth 2009;9:55.[90]

Key points

- Additional improvement in the collection of data concerning PPH is required, specifically including a measure of severity.
- Further research is required to determine whether an increased rate of reported PPH is also observed in other countries, and to further investigate potential risk factors including increased duration of labor, obesity and changes in second and third stage management practice.
- Training should be provided to all staff involved in maternity care concerning assessment of blood loss and the monitoring of women after childbirth. This is key to reducing the severity of PPH and preventing any adverse outcomes.
- Clinicians should be more vigilant given the possibility that the frequency and severity of PPH has in fact increased. This applies particularly to small hospitals with relatively few deliveries where management protocols may not be defined adequately and drugs or equipment may not be on hand to deal with unexpected severe PPH.

5.5. TB in pregnancy

Published Article

Knight M, Kurinczuk JJ, Nelson-Piercy C, Spark P, Brocklehurst P. Tuberculosis in pregnancy in the UK. BJOG 2009;116(4):584-8[4]

Key points

- TB in pregnancy is rare in the UK but appears to be limited to ethnic minority women, most commonly recent immigrants.
- Extrapulmonary disease is as common as pulmonary disease and may present a diagnostic challenge.
- The prognosis for both women and infants is good.
- Primary care, obstetric and midwifery staff, particularly in areas of high TB prevalence, should be aware of the potential for nonspecific presentation of TB in pregnancy and consider the diagnosis in women, especially recently arrived immigrants, presenting with nonspecific symptoms.

5.6. Abstracts

The following abstract was presented at a meeting in 2009 and is available on our website www.npeu.ox.ac.uk/ukoss:

Extreme obesity in pregnancy in the UK: Prevalence, pregnancy complications and outcomes. Presented at the British Maternal Fetal Medicine Society Meeting June 2009.

5.7. UKOSS Publications to date

Knight, M., J. Kurinczuk and P. Brocklehurst (2005). “UK Obstetric Surveillance System uncovered.” *RCM Midwives* **8**(1): 38-39.

Knight, M., J. J. Kurinczuk, D. Tuffnell and P. Brocklehurst (2005). “The UK Obstetric Surveillance System for rare disorders of pregnancy.” *BJOG* **112**(3): 263-265.

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

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

Knight, M., J. J. Kurinczuk, P. Spark and P. Brocklehurst (2008) on behalf of UKOSS. “Cesarean delivery and peripartum hysterectomy.” *Obstet Gynecol* **111**(1): 97-105.

Knight, M. (2008) on behalf of UKOSS. “Antenatal pulmonary embolism: risk factors, management and outcomes.” *BJOG* **115**(4): 453-461.

Knight, M., C. Nelson-Piercy, J. J. Kurinczuk, P. Spark and P. Brocklehurst (2008) on behalf of UKOSS. “A prospective national study of acute fatty liver of pregnancy in the UK.” *Gut* **57**(7): 951-956.

Knight, M., W. Callaghan, et al. (2009). “Trends in post-partum haemorrhage in high resource countries.” *BMC Pregnancy and Childbirth* **9**: 55.

Knight, M., J. J. Kurinczuk, P. Spark and P. Brocklehurst (2009). “Inequalities in maternal health: national cohort study of ethnic variation in severe maternal morbidities.” *BMJ* **338**: b542.

Knight, M., J. J. Kurinczuk, C. Nelson-Piercy, P. Spark and P. Brocklehurst (2009) on behalf of UKOSS. “Tuberculosis in pregnancy in the UK.” *BJOG* **116**(4): 584-588.

Knight, M., J. J. Kurinczuk, P. Spark and P. Brocklehurst (2010) on behalf of UKOSS. “Extreme obesity in pregnancy in the United kingdom.” *Obstet Gynecol* **115**(5): 989-997.

Knight, M., D. Tuffnell, P. Brocklehurst, P. Spark and J. J. Kurinczuk (2010) on behalf of UKOSS. “Incidence and risk factors for amniotic-fluid embolism.” *Obstet Gynecol* **115**(5): 910-917.

6. Acknowledgements

These studies would not have been possible without the contribution and enthusiasm of the UKOSS reporting clinicians who notified cases and completed the data collection forms. We would also particularly like to thank Carole Harris, Jane Forrester-Barker and Patsy Spark for ensuring the smooth running of the data collection systems.

Funding

MK is funded by the National Coordinating Centre for Research Capacity Development of the Department of Health. This is an independent report from a study which is part-funded by the Policy Research programme in the Department of Health. The views expressed are not necessarily those of the Department.

UKOSS Management Group, National Perinatal Epidemiology Unit

Alex Bellenger, Data Manager

Peter Brocklehurst, NPEU Director

Jane Forrester-Barker, UKOSS Assistant Administrator

Carole Harris, UKOSS Administrator

Marian Knight, UKOSS Clinical Coordinator

Jenny Kurinczuk, NPEU Deputy Director

Patsy Spark, UKOSS Programmer

UKOSS Steering Committee

Catherine Nelson-Piercy (Chair), Guys and St Thomas' Hospital;

Mervi Jokinen (Member 2005-2008) (Vice-chair 2008-), Royal College of Midwives;

Maggie Blott, Royal College of Obstetricians and Gynaecologists;

Peter Brocklehurst, National Perinatal Epidemiology Unit;

Jean Chapple, Faculty of Public Health;

Cynthia Clarkson, National Childbirth Trust;

Andrew Dawson, Nevill Hall Hospital, Abergavenny;

Jenny Furniss (Vice-chair 2005-2008) (Member 2008-), Lay Member;

Shona Golightly, Confidential Enquiry into Maternal and Child Health;

Ian Greer, Hull York Medical School;

Marian Knight, National Perinatal Epidemiology Unit;

Jenny Kurinczuk, National Perinatal Epidemiology Unit;

Christopher Lennox, NHS QIS;

Gwyneth Lewis, Department of Health;

Nuala Lucas, Obstetric Anaesthetists Association;

Leslie Marr, NHS QIS;

Tim Overton, St Michael's Hospital, Bristol;

Richard Pebody, Health Protection Agency;

Felicity Plaat, Queen Charlotte's and Chelsea Hospitals;

Derek Tuffnell, Bradford Hospitals NHS Trust;

James Walker, National Patient Safety Agency;

References

1. Knight, M., *Peripartum hysterectomy in the UK: management and outcomes of the associated haemorrhage*. BJOG, 2007. **114**(11): p. 1380-7.
2. Knight, M., *Eclampsia in the United Kingdom 2005*. BJOG, 2007. **114**(9): p. 1072-8.
3. Knight, M., *Antenatal pulmonary embolism: risk factors, management and outcomes*. BJOG, 2008. **115**(4): p. 453-61.
4. Knight, M., et al., *Tuberculosis in pregnancy in the UK*. BJOG, 2009. **116**(4): p. 584-8.
5. Knight, M., et al., *Cesarean delivery and peripartum hysterectomy*. Obstet Gynecol, 2008. **111**(1): p. 97-105.
6. Knight, M., et al., *A prospective national study of acute fatty liver of pregnancy in the UK*. Gut, 2008. **57**(7): p. 951-6.
7. UKOSS. *Applications for new surveys*. 2009 [Accessed March 2009]; Available from: *http://www.npeu.ox.ac.uk/UKOSS/index.php?content=survey_applications.inc*.
8. Confidentiality and Security Advisory Group for Scotland. 2001, The Scottish Executive: Edinburgh.
9. Department of Health. *Guidance Notes: Section 60 of the Health and Social Care Act 2001*. [Accessed April 2004]; Available from: *http://www.dh.gov.uk/assetRoot/04/06/63/84/04066384.pdf*.
10. Knight, M., et al., *Extreme obesity in pregnancy in the UK*. Obstet Gynecol, 2010. **In press**.
11. Nelson-Piercy, C. *Thromboprophylaxis during Pregnancy, Labour and after Vaginal Delivery (RCOG Green-top guideline no. 37)*. [Accessed July 2007]; Available from: *http://www.rcog.org.uk/index.asp?PageID=535*.
12. Yates, L.M., et al., *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. **In press.**
13. Jamieson, D.J., et al., *H1N1 2009 influenza virus infection during pregnancy in the USA*. Lancet, 2009. **374**(9688): p. 451-8.
14. Garske, T., et al., *Assessing the severity of the novel influenza A/H1N1 pandemic*. BMJ, 2009. **339**: p. b2840.
15. Desai, M., et al., *Epidemiology and burden of malaria in pregnancy*. Lancet Infect Dis, 2007. **7**(2): p. 93-104.
16. Whitty, C.J., S. Edmonds, and T.K. Mutabingwa, *Malaria in pregnancy*. BJOG, 2005. **112**(9): p. 1189-95.
17. Health Protection Agency. *HPA Malaria Reference Laboratory*. [Accessed March 2007]; Available from: *http://www.malaria-reference.co.uk*.
18. Office for National Statistics. *Caesarean Deliveries in NHS Hospitals*. [Accessed Oct 2004]; Available from: *http://www.statistics.gov.uk/StatBase/Expodata/Spreadsheets/D7412.xls*.
19. Varma, R., J.K. Gupta, and G.C.S. Smith, *Birth after previous caesarean birth*. 2007, RCOG: London.
20. Juntunen, K., L. Makarainen, and P. Kirkinen, *Outcome after a high number (4-10) of repeated caesarean sections*. BJOG, 2004. **111**(6): p. 561-3.
21. Khashoggi, T.Y., *Higher order multiple repeat cesarean sections: maternal and fetal outcome*. Ann Saudi Med, 2003. **23**(5): p. 278-82.
22. Kirkinen, P., *Multiple caesarean sections: outcomes and complications*. Br J Obstet Gynaecol, 1988. **95**(8): p. 778-82.
23. Rashid, M. and R.S. Rashid, *Higher order repeat caesarean sections: how safe are five or more?* BJOG, 2004. **111**(10): p. 1090-4.

24. Silver, R.M., et al., *Maternal morbidity associated with multiple repeat cesarean deliveries*. Obstet Gynecol, 2006. **107**(6): p. 1226-32.

25. McKay, D.B. and M.A. Josephson, *Pregnancy in recipients of solid organs--effects on mother and child*. N Engl J Med, 2006. **354**(12): p. 1281-93.

26. Sibanda, N., et al., *Pregnancy after organ transplantation: a report from the UK Transplant pregnancy registry*. Transplantation, 2007. **83**(10): p. 1301-7.

27. Armenti, V.T., et al., *Report from the national transplantation pregnancy registry (NTPR): outcomes of pregnancy after transplantation*. Clin Transpl, 2004: p. 103-14.

28. Rizzoni, G., et al., *Successful pregnancies in women on renal replacement therapy: report from the EDTA Registry*. Nephrol Dial Transplant, 1992. **7**(4): p. 279-87.

29. Lewis, G.E., ed. *The Confidential Enquiry into Maternal and Child Health (CEMACH). Saving Mothers Lives: reviewing maternal deaths to make childhood safer - 2003-2005*. The Confidential Enquiry into Maternal and Child Health (CEMACH). Saving Mothers Lives: reviewing maternal deaths to make childhood safer - 2003-2005, ed. L.G. (Ed). 2007, CEMACH: London.

30. Brace, V., G. Penney, and M. Hall, *Quantifying severe maternal morbidity: a Scottish population study*. BJOG, 2004. **111**(5): p. 481-4.

31. Waterstone, M., S. Bewley, and C. Wolfe, *Incidence and predictors of severe obstetric morbidity: case-control study*. BMJ, 2001. **322**(7294): p. 1089-93; discussion 1093-4.

32. Ahonen, J. and R. Jokela, *Recombinant factor VIIa for life-threatening post-partum haemorrhage*. Br J Anaesth, 2005. **94**(5): p. 592-5.

33. Allam, M.S. and C. B-Lynch, *The B-Lynch and other uterine compression suture techniques*. Int J Gynaecol Obstet, 2005. **89**(3): p. 236-41.

34. Mousa, H.A. and Z. Alfirevic, *Treatment for primary postpartum haemorrhage*. Cochrane Database Syst Rev, 2003(1): p. CD003249.

35. Badawy, S.Z., et al., *Uterine artery embolization: the role in obstetrics and gynecology*. Clin Imaging, 2001. **25**(4): p. 288-95.

36. Gilbert, W.M. and B. Danielsen, *Amniotic fluid embolism: decreased mortality in a population-based study*. Obstet Gynecol, 1999. **93**(6): p. 973-7.

37. Tuffnell, D.J., *Amniotic Fluid Embolism*. Current Opinion in Obstetrics and Gynaecology, 2003. **15**: p. 119-122.

38. Abenhaim, H.A., et al., *Incidence and risk factors of amniotic fluid embolisms: a population-based study on 3 million births in the United States*. Am J Obstet Gynecol, 2008. **199**: p. 49.e1-49.e8.

39. Kramer, M.S., et al., *Amniotic-fluid embolism and medical induction of labour: a retrospective, population-based cohort study*. Lancet, 2006. **368**: p. 1444-1448.

40. Tuffnell, D.J., *United kingdom amniotic fluid embolism register*. BJOG, 2005. **112**(12): p. 1625-9.

41. Kittner, S.J., et al., *Pregnancy and the risk of stroke*. N Engl J Med, 1996. **335**(11): p. 768-74.

42. Katz, N.M., et al., *Aortic dissection during pregnancy: treatment by emergency cesarean section immediately followed by operative repair of the aortic dissection*. Am J Cardiol, 1984. **54**(6): p. 699-701.

43. Lewis, S., I. Ryder, and A.T. Lovell, *Peripartum presentation of an acute aortic dissection*. Br J Anaesth, 2005. **94**(4): p. 496-9.

44. Wahlers, T., et al., *Repair of acute type A aortic dissection after cesarean section in the thirty-ninth week of pregnancy*. J Thorac Cardiovasc Surg, 1994. **107**(1): p. 314-5.

45. Meszaros, I., et al., *Epidemiology and clinicopathology of aortic dissection*. Chest, 2000. **117**(5): p. 1271-8.

46. EUROCAT. *Welcome to EUROCAT*. [Accessed Aug 2005]; Available from: *http://www.eurocat.ulster.ac.uk/index.html*.

47. Davis, P.J., et al., *Long-term outcome following extracorporeal membrane oxygenation for congenital diaphragmatic hernia: the UK experience*. J Pediatr, 2004. **144**(3): p. 309-15.

48. Lally, K.P. and W. Engle, *Postdischarge follow-up of infants with congenital diaphragmatic hernia.* Pediatrics, 2008. **121**(3): p. 627-32.

49. Smith, N.P., et al., *Recent advances in congenital diaphragmatic hernia*. Arch Dis Child, 2005. **90**(4): p. 426-8.

50. Hawthorne, L., et al., *Failed intubation revisited: 17-yr experience in a teaching maternity unit*. Br J Anaesth, 1996. **76**(5): p. 680-4.

51. Rahman, K. and J.G. Jenkins, *Failed tracheal intubation in obstetrics: no more frequent but still managed badly*. Anaesthesia, 2005. **60**(2): p. 168-71.

52. Pilkington, S., et al., *Increase in Mallampati score during pregnancy*. Br J Anaesth, 1995. **74**(6): p. 638-42.

53. Johnson, R.V., et al., *Training in obstetric general anaesthesia: a vanishing art?* Anaesthesia, 2000. **55**(2): p. 179-83.

54. Sim, D.J., S.R. Wrigley, and S. Harris, *Effects of the European Working Time Directive on anaesthetic training in the United Kingdom*. Anaesthesia, 2004. **59**(8): p. 781-4.

55. Barbui, T. and G. Finazzi, *Myeloproliferative disease in pregnancy and other management issues*. Hematology Am Soc Hematol Educ Program, 2006: p. 246-52.

56. Roth, A. and U. Elkayam, *Acute myocardial infarction associated with pregnancy*. Ann Intern Med, 1996. **125**(9): p. 751-62.

57. Ginz, B., *Myocardial infarction in pregnancy*. J Obstet Gynaecol Br Commonw, 1970. **77**(7): p. 610-5.

58. Ladner, H.E., B. Danielsen, and W.M. Gilbert, *Acute myocardial infarction in pregnancy and the puerperium: a population-based study.* Obstet Gynecol, 2005. **105**(3): p. 480-4.

59. Lange, S.S. and M. Jenner, *Myocardial infarction in the obstetric patient*. Crit Care Nurs Clin North Am, 2004. **16**(2): p. 211-9.

60. de Swiet, M. and C. Nelson-Piercy, *Cardiac Disease*. In: Why Mothers die p137-150. 2004, RCOG: London.

61. Joint European Society of Cardiology/American College of Cardiology Committee, *Myocardial infarction redefined--a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction*. Eur Heart J, 2000. **21**(18): p. 1502-13.

62. Molitch, M.E., *Pituitary tumors and pregnancy*. Growth Horm IGF Res, 2003. **13 Suppl A**: p. S38-44.

63. Lindsay, J.R., et al., *Cushing's syndrome during pregnancy: personal experience and review of the literature*. J Clin Endocrinol Metab, 2005. **90**(5): p. 3077-83.

64. Weiss, B.M., et al., *Outcome of pulmonary vascular disease in pregnancy: a systematic overview from 1978 through 1996*. J Am Coll Cardiol, 1998. **31**(7): p. 1650-7.

65. Lewis, G., ed. *Why mothers die 2000-2002*. Why mothers die 2000-2002, ed. Confidential Enquiry into Maternal and Child Health. 2004, Royal College of Obstetricians and Gynaecologists: London.

66. Dob, D.P. and S.M. Yentis, *UK registry of high-risk obstetric anaesthesia: report on cardiorespiratory disease.* Int J Obstet Anesth, 2001. **10**(4): p. 267-72.

67. Thorne, S., et al., *Pregnancy and contraception in heart disease and pulmonary arterial hypertension*. J Fam Plann Reprod Health Care, 2006. **32**(2): p. 75-81.

68. Yentis, S.M., P.J. Steer, and F. Plaat, *Eisenmenger's syndrome in pregnancy: maternal and fetal mortality in the 1990s*. Br J Obstet Gynaecol, 1998. **105**(8): p. 921-2.

69. Tuck, S.M., J.W. Studd, and J.M. White, *Pregnancy in sickle cell disease in the UK*. Br J Obstet Gynaecol, 1983. **90**(2): p. 112-7.

70. Hofmeyr, G.J., L. Say, and A.M. Gulmezoglu, *WHO systematic review of maternal mortality and morbidity: the prevalence of uterine rupture*. BJOG, 2005. **112**(9): p. 1221-8.

71. 71. National Collaborating Centre for Women's and Children's Health, *Caesarean Section*. 2004, RCOG: London.

72. Dodd, J.M., et al., *Planned elective repeat caesarean section versus planned vaginal birth for women with a previous caesarean birth*. Cochrane Database Syst Rev, 2004(4): p. CD004224.

73. Guise, J.M., et al., *Systematic review of the incidence and consequences of uterine rupture in women with previous caesarean section*. BMJ, 2004. **329**(7456): p. 19-25.

74. Cowan, R.K., et al., *Trial of labor following cesarean delivery*. Obstet Gynecol, 1994. **83**(6): p. 933-6.

75. Oyelese, Y. and J.C. Smulian, *Placenta previa, placenta accreta, and vasa previa*. Obstet Gynecol, 2006. **107**(4): p. 927-41.

76. Khong, T.Y., *The pathology of placenta accreta, a worldwide epidemic*. J Clin Pathol, 2008. **61**(12): p. 1243-6

77. Timmermans, S., A.C. van Hof, and J.J. Duvekot, *Conservative management of abnormally invasive placentation*. Obstet Gynecol Surv, 2007. **62**(8): p. 529-39.

78. Usta, I.M., et al., *Placenta previa-accreta: risk factors and complications*. Am J Obstet Gynecol, 2005. **193**(3 Pt 2): p. 1045-9.

79. Angstmann, T., et al., *Surgical management of placenta accreta: a cohort series and suggested approach*. Am J Obstet Gynecol, 2009.

80. Geenes, V. and C. Williamson, *Intrahepatic cholestasis of pregnancy*. World J Gastroenterol, 2009. **15**(17): p. 2049-66.

81. Glantz, A., H.U. Marschall, and L.A. Mattsson, *Intrahepatic cholestasis of pregnancy: Relationships between bile acid levels and fetal complication rates*. Hepatology, 2004. **40**(2): p. 467-74.

82. Laatikainen, T. and E. Ikonen, *Serum bile acids in cholestasis of pregnancy*. Obstet Gynecol, 1977. **50**(3): p. 313-8.

83. Laatikainen, T. and A. Tulenheimo, *Maternal serum bile acid levels and fetal distress in cholestasis of pregnancy*. Int J Gynaecol Obstet, 1984. **22**(2): p. 91-4.

84. Lee, R.H., et al., *Pregnancy outcomes during an era of aggressive management for intrahepatic cholestasis of pregnancy*. Am J Perinatol, 2008. **25**(6): p. 341-5.

85. Kenyon, A.P., et al., *Obstetric cholestasis, outcome with active management: a series of 70 cases*. BJOG, 2002. **109**(3): p. 282-8.

86. Williamson, C., et al., *Clinical outcome in a series of cases of obstetric cholestasis identified via a patient support group*. BJOG, 2004. **111**(7): p. 676-81.

87. Knight, M., et al., *Amniotic Fluid Embolism in the UK*. Obstet Gynecol, 2010. **In press**.

88. 88. Knight, M., et al., *Inequalities in maternal health: national cohort study of ethnic variation in severe maternal morbidities*. BMJ, 2009. **338**: p. b542.

89. Knight, M., et al., *Extreme obesity in pregnancy in the United Kingdom*. Obstet Gynecol, 2010. **115**(5).

90. Knight, M., et al., *Trends in postpartum hemorrhage in high resource countries: a review and recommendations from the International Postpartum Hemorrhage Collaborative Group*. BMC Pregnancy Childbirth, 2009. **9**: p. 55.

www.npeu.ox.ac.uk/ukoss