

Maternal medicine symposium 2005

R Akolekar

Specialist Registrar, The Simpson Centre for Reproductive Health, Edinburgh Royal Infirmary, Edinburgh, Scotland

ABSTRACT A reflection of the recent trends in medicine is the development of the sub-specialty of obstetric medicine. Advances in healthcare have made it possible for patients with high-risk medical disorders to survive into adulthood. These women need highly specialised multidisciplinary care during pregnancy and labour. Recognising these recent trends in medical practice, a maternal medicine symposium was organised by the Royal College of Physicians of Edinburgh.

KEYWORDS Maternal morbidity, medical disorders, pregnancy

LIST OF ABBREVIATIONS Anti-cardiolipin antibodies (aCL), anti-phospholipid syndrome (APLS), confidential enquiry into maternal and child health (CEMACH), low molecular weight heparin (LMWH), lupus anticoagulant (LA), microchimerism (Mc), thromboembolic disease (TED), unfractionated heparin (UFH)

DECLARATION OF INTERESTS No conflict of interests declared.

Correspondence to Dr R Akolekar,
72 Carnbee Park, Edinburgh EH16
6GH, Scotland

tel. +44(0)131 661 4056

fax. +44 (0)131 661 4056

e-mail ranjit@fastmail.co.uk

Obstetric medicine is one of the newer sub-specialities in the UK and the development of this sub-speciality is a reflection of the trend for more patients with high-risk medical disorders to conceive and to require individualised management during pregnancy and labour.

The first session addressed the important causes of maternal mortality in the UK with a focus on the lessons learnt from the recent report, CEMACH. The second session was an update on the immunological aspects of pregnancy with a detailed discussion of the APLS. The third session was an interactive discussion of the management of diabetes, epilepsy and cancer during pregnancy. The final session of the day was about the management of substance misuse and the therapeutic use of drugs in pregnancy. The day ended with a lively interactive discussion of the management of controversial cases in clinical practice.

Professor J Drife (Consultant Obstetrician, Leeds General Infirmary, England) began the first session with lessons learnt from the recent CEMACH reports.¹ Care during pregnancy and labour has significantly improved over the last few decades and this is reflected in the maternal mortality statistics. The risk of a pregnant woman dying from obstetric complications related to her pregnant state is less than 1 in 19,020. The major causes of direct maternal deaths remain thromboembolic disease, hypertension and haemorrhage. The other causes are early pregnancy deaths, including ectopic pregnancies, sepsis, deaths due to anaesthetic complications and amniotic fluid embolism. 155 deaths were due to indirect causes, of which 44 deaths were due to cardiac disease. Other important causes include suicidal deaths in the post

partum period. He highlighted the higher mortality risk associated with increasing maternal age, obesity, social class and ethnicity.¹

Professor I Greer (Consultant in Obstetrics and Gynaecology, Glasgow Royal Infirmary, Scotland) spoke about TED in pregnancy. Although deaths from thromboembolism have decreased over the decades due to significant improvements in care, thromboembolism was still responsible for the majority of direct maternal deaths. Substandard care was an important factor and symptoms and signs were often ignored or overlooked. Around 50% of venous thromboembolism in pregnancy is associated with a heritable thrombophilia.² The available treatments for thromboprophylaxis in patients at high risk include coumarins, UFH, LMWH, low dose aspirin and physical methods such as elastic stockings.

The final speaker in the first session was Dr S Thorne (Consultant Cardiologist, Queen Elizabeth Medical Centre, Birmingham, England), who outlined the management of pregnant women with congenital cardiac disease. She reiterated that cardiac disease is the most common cause of indirect maternal deaths in the UK.¹ Substandard care was identified as a factor in 40% of cardiac maternal deaths and risk assessment in patients with cardiac disease in pre- and early pregnancy is of paramount importance. Risk assessment involves the stratification of women with congenital cardiac disease into three basic categories: low risk, significant risk and a group in whom pregnancy is contraindicated.³ The latter group carries a significant mortality risk of 10–50% and includes such conditions as pulmonary hypertension, severe left sided obstruction, aortic aneurysm and decreased ventricular

function. She spoke about the need for patients with valvular heart conditions and valve replacements to be anticoagulated.

The second session of the symposium was on immunological aspects of pregnancy and began with a detailed discussion on APLS by Professor Lesley Regan (Head of Department, Obstetrics and Gynaecology, Imperial College at St. Mary's Hospital, London, England). APLS results in a state of acquired thrombophilia and is associated with an exaggerated haemostatic response during pregnancy resulting in adverse outcomes, e.g. recurrent miscarriage, pre-eclampsia and intrauterine growth restriction. A recent study quoted that 15% of patients with recurrent miscarriage have antiphospholipid antibodies, which are responsible for the pregnancy loss.⁴ Screening should be directed towards the most common anti-phospholipid antibodies associated with adverse pregnancy outcomes, aCL and LA. She highlighted the importance of early treatment with aspirin and LMWH.⁵ The late pregnancy morbidity associated with APLS, which occurs despite treatment, includes pre-eclampsia, intrauterine growth restriction, preterm delivery and placental abruption.⁶ The potential mechanisms of pregnancy loss in APLS include thrombosis in placental vasculature, endothelial cell activation, a direct effect on endometrial receptivity and trophoblast function, hormone production and invasion. Interestingly, the non-anticoagulant actions of heparin may be beneficial, e.g. restoration of trophoblast invasive properties, prevention of trophoblast apoptosis and immunomodulation.

In his Davidson Lecture, Professor J Lee Nelson (Department of Rheumatology, University of Washington, Seattle, USA) provided interesting and unique insights into autoimmunity and alloimmunity based on Mc. Microchimerism refers to the low levels of cells, originating from fetal-maternal cell transfer during pregnancy, found in the respective hosts years later.⁷ She explained that her group had developed a panel of real-time quantitative PCR assays targeting specific HLA sequences that can be used even when the source of the Mc is of the same sex. The main interest of the group was the role of Mc in systemic sclerosis, polymorphic eruption of pregnancy, Sjögren's syndrome, thyroiditis and neonatal lupus.

The third session was an interactive discussion of controversial areas in the management of pregnancy in cases of diabetes, epilepsy and cancer. The workshop on diabetes was chaired by Dr J Walker (Consultant Physician, St. John's Hospital, Livingston, Scotland) and Dr H MacPherson (Consultant Obstetrician, Stirling Royal Infirmary, Scotland). It was agreed that good periconceptional glycaemic control with monitoring of HbA1c levels can minimise the risk of congenital abnormalities and that type II diabetes is just as

challenging as type I. The importance of pre-pregnancy care should be explained to all patients with a known history of a type II diabetes. The workshop on epilepsy in pregnancy was chaired by Dr R Davenport (Consultant Neurologist, Western General Hospital, Edinburgh, Scotland) and Ms Fiona Mackinnon (Epilepsy Nurse specialist, Western General Hospital, Edinburgh, Scotland). It was agreed that patients should be reassured that most will have a good outcome, especially if seizure control has been good in the 12–18 months preceding pregnancy. The third workshop, on cancer during pregnancy, was chaired by Dr N Reed (Consultant Clinical Oncologist, Beatson Oncology centre, Western Infirmary, Glasgow, Scotland) and Dr A Jones (Medical Oncologist, Royal Free Hospital, London, England). Fortunately, the UK incidence of pregnancy with cancer is about 1 in 1,000, with the common malignancies being that of ovary, breast, cervix, thyroid and skin.

The final session in the symposium was on uses and abuses of drugs in pregnancy. Dr M Hepburn (Consultant Obstetrician, Princess Royal Maternity Hospital, Glasgow, Scotland) explained that substance misuse is closely associated with socio-economic deprivation and exacerbates the adverse effects of poverty on access to healthcare services and on the medical and social outcomes of pregnancy⁸ and is associated with prematurity, low birth weight, sudden infant death syndrome, and neonatal withdrawal. Pregnant women with drug and/or alcohol problems, and their babies, are, therefore, at a higher risk of maternal and perinatal morbidity and mortality. Women using opioids should be prescribed appropriate substitution therapy during pregnancy and aggressive detoxification should preferably not be attempted.

Dr S Thomas (Reader in Therapeutics, University of Newcastle upon Tyne, Newcastle, England) discussed therapeutic drug use in pregnancy. Of all the congenital malformations, only a small fraction are associated with a drug or chemical exposure. Identification of a teratogenic risk with a drug is limited by several confounding factors in addition to incomplete data collection regarding the occurrence of a malformation due to drug use. Fetal effects of drugs are determined by dose, duration and timing of exposure of the drug. The majority of teratogens cause fetal effects when they are used during the critical period of organogenesis. Definite risk of teratogenesis is associated with only a few drugs e.g. Thalidomide, anti-convulsants drugs, diethylstilboestrol, lithium, retinoids etc.

The symposium ended with a lively interactive session on controversial cases which was chaired by Dr A M Pirie (Consultant Obstetrician and Hon. Senior Lecturer, Birmingham Women's Hospital and University of Birmingham, England) and expert opinions were given by

Professor M de Swiet (Consultant in Obstetrics, Imperial College School of Medicine, London, England). Dr Pirie discussed perplexing case scenarios in maternal medicine,

and Prof De Swiet then went about helping the audience to arrive at a diagnosis in a simple but systematic way, even for the most mystifying clinical situations.

REFERENCES

- 1 In: *Why mothers die 2000–2002*. The sixth report of the confidential enquiries into maternal deaths in the United Kingdom. London: RCOG Press; November 2004.
- 2 McColl MD, Ramsay JE, Tait RC *et al*. Risk factors for pregnancy associated venous thromboembolism. *Thromb Haemost* 1997; **78**: 1183–88.
- 3 Siu SC. Prospective multicentric study of pregnancy outcomes in women with heart disease. *Circulation* 2001; **104**:515–21.
- 4 Rai RS, Regan L, Clifford K, *et al*. Antiphospholipid antibodies and Beta2-glycoprotein-I in 500 women with recurrent miscarriage: Results of a comprehensive screening approach. *Hum Reprod* 1995; **10**:2001–05.
- 5 Rai R, Cohen H, Dave M, Regan L. Randomised controlled trial of aspirin and aspirin plus heparin in pregnant women with recurrent miscarriage associated with phospholipid antibodies (or antiphospholipid antibodies). *BMJ* 1997; **314**:253–7.
- 6 Backos M, Rai R, Baxter N, *et al*. Pregnancy complications in women with recurrent miscarriage associated with antiphospholipid antibodies treated with low dose aspirin and heparin. *Br J Obstet Gynaecol* 1999; **106**:102–7.
- 7 Nelson JL. Maternal-fetal immunology and autoimmune disease. Is some autoimmune disease auto-alloimmune or allo-autoimmune? *Arthritis Rheum* 1996; **39**:191–4.
- 8 Hepburn M (on behalf of the Editorial Board). Drug and alcohol related deaths. In: *Why mothers die 2000–2002*. The sixth report of the confidential enquiries into maternal deaths in the United Kingdom. London: RCOG Press; **Ch. 11B**:174–182.