Pregnancy outcomes in sickle cell disease: a retrospective cohort study from two tertiary centres in the UK

A R Chase*, M Sohal†, J Howard‡, R Laher§, A McCarthy**, D M Layton† and E Oteng-Ntim*

*Women's Health Department, Guy's and St Thomas' Hospital NHS Foundation Trust; †Department of Haematology, Imperial College Healthcare NHS Trust; ‡Department of Haematology, Guy's and St Thomas' Hospital NHS Foundation Trust (GSTFT); §King's College London School of Medicine; **Department of Obstetrics, Queen Charlotte's and Chelsea Hospital (QCCH), London, UK

Summary: The objective of this retrospective cohort study from two tertiary centres in the UK was to describe the pregnancy outcomes of women with sickle cell disease (SCD) who booked at these centres between 2004 and 2008, and to compare this with historical data. The study population comprised 122 singleton pregnancies in women with SCD: homozygous sickle cell disease 64, sickle cell haemoglobin C disease 45, sickle b plus thalassaemia 11, sickle cell haemoglobin E disease 1 and sickle cell delta disease 1 from 2004 to 2008 managed in the joint haematology/obstetric antenatal clinics in two tertiary teaching hospitals. The main outcome measures were the frequency of sickle cell crises and obstetric complications. Age and gestation at booking were 18–43 years (mean 29.7) and 9–36 weeks gestation (mean 17.3), respectively. Complications of SCD occurred in 25% of pregnancies. Fifty-four percent of women had induction of labour and 39% were delivered by emergency caesarean section. Thirty-three percent had a postpartum haemorrhage. Nineteen percent of women delivered before 37 completed weeks. Birth weight below 2500 g occurred in 20% of singleton pregnancies. Three neonates developed transient complications related to maternal opiate exposure postnatally. Three intrauterine deaths occurred at 24, 29 and 34 weeks. Two of these had congenital defects, and the other severe intrauterine growth restriction. No maternal deaths occurred. Successful pregnancy outcomes can be achieved in SCD. There has been an improvement in fetal and maternal morbidity and mortality compared with historical data. Pregnancy in women with SCD remains high risk. Early access to antenatal care and to expertise in SCD is essential. A matched control population from the same time period and prospective data collection is needed to address confounders such as ethnicity and deprivation.

Keywords: sickle cell disease, obstetric complications, pregnancy

INTRODUCTION

Sickle cell disease (SCD) is a heterogeneous disorder of increasing national importance in the UK.¹ There are approximately 12,000 people affected by SCD in the UK and it has a prevalence of almost one in 2000 live births.¹ It is well established that SCD in pregnancy is associated with an increase in maternal and fetal complications.^{2,3} Maternal complications include pre-eclampsia, increased vaso-occlusive crises, thromboembolism and maternal death.⁴ Fetal complications include increased rates of preterm delivery, intrauterine growth restriction (IUGR) and perinatal mortality.⁴ While there have been recent cohort studies from Jamaica⁵ and the USA,^{6,4} there has been little work on pregnancy outcome in patients with SCD in the UK, and there have been considerable changes in this time in both obstetric and sickle care. This study aims to assess pregnancy outcome of SCD in two tertiary referral centres in the UK and compares the outcome with previous published studies.

SUBJECTS AND METHODS

We conducted a retrospective study of women who booked antenatally with SCD at Guy's and St Thomas' NHS Foundation Trust (GSTFT), Queen Charlotte's and Chelsea Hospital (QCCH) and Hammersmith Hospital between 2004 and 2008. Both GSTFT and QCCH/Hammersmith are tertiary obstetric centres in London, who have large sickle obstetric practices based on their local populations and referral patterns. The patients were identified using the joint obstetric/haematology antenatal clinic appointment lists. The study population comprised 122 singleton pregnancies (two twin pregnancies were excluded) in women with SCD: homozygous sickle cell (SS) disease 64, sickle cell haemoglobin C disease (SC) 45, sickle b plus thalassaemia (Sb⁺) 11, sickle cell haemoglobin E disease (SE) 1 and sickle cell delta disease (SD) 1.

All patients received care as per our local protocol, which included low-dose aspirin (75 mg daily) because of the associated risk of pre-eclampsia,^{7,8} and, if there was a personal or family history of thrombosis, prophylactic low molecular weight heparin.

The information about each pregnancy was collected from paper hospital records and electronic patient records including Terranova Healthcare and the Haemoglobinopathy database.

Correspondence to: Eugene Oteng-Ntim
Email: Eugene.Oteng-Ntim@gstt.nhs.uk

The information in this database is completed by midwives after formal training and security access. Accuracy is maintained by daily quality and data checks. The woman's identification, gestation at booking, age at delivery, haemoglobinopathy, gestational age at delivery, mode of delivery, delivery outcome, birth weight, blood loss at delivery, coexisting medical conditions and complications during pregnancy and labour were recorded. Gestational age of the fetus was calculated from the last menstrual period and/or ultrasound dating. An intrauterine death or stillbirth was defined as at or after 24 weeks gestation. Neonatal death refers to the death of a live born baby within 28 days. Pregnancy induced hypertension (PIH) was defined as a blood pressure >140/90 mmHg after the 20th week gestation. Preeclampsia was defined in the same way but with significant proteinuria (>0.3 g in 24 hours). Postpartum haemorrhage was an estimated loss of 500 mL or more of blood following delivery of baby. The incidence of birth weight <2500 g was recorded.

All pregnancies in women with SCD in these hospitals are managed in the joint obstetric/haematology clinics, so it was possible to identify all SCD pregnancies during the study period. Women who attended the antenatal clinic during this time but delivered elsewhere were excluded.

RESULTS

Mean age at booking was 29.7 years (range 18–43 years) and mean gestation at booking was 17.3 weeks (range 9–36 weeks). The obstetric complications are outlined in Table 1. The majority of women underwent induction of labour (54%) and 39% were delivered by emergency caesarean section (EMCS; see Figures 1 and 2). Nineteen percent of women delivered before 37 completed weeks of gestation. Birth weight <2500 g occurred in 20% of singleton pregnancies. Three neonates developed transient complications related to maternal opiate exposure postnatally. Three intrauterine deaths occurred at 24, 29 and 34 weeks. Two of these had congenital defects, and the other severe IUGR. No maternal deaths occurred. Sickie crisis requiring admission occurred in 25% of pregnancies.

DISCUSSION

Women with SCD have increased risk of both medical and obstetric complications in pregnancy.⁹ The UK experience of pregnancy outcome in these women has been documented in three previous studies. In 1983 Tuck *et al.*¹⁰ reported a series of 125 pregnancies over the six-year period of 1975–1981. The main complications were sickle crises (38%), anaemia (65%), infections (61%) and severe PIH (5%). The incidence of

Figure 1 Mode of delivery. SVD = spontaneous vaginal delivery; EMCS = emergency lower segment caesarean section; ELCS = elective lower segment caesarean section

miscarriage, preterm delivery and both emergency and elective caesarean section were greater than background. Mean infant birth weight was significantly lower and there was a perinatal mortality rate of 48 per 1000 live births. There were no features identified that would be of predictive value in determining those pregnancies that would later develop severe complications. There were no maternal deaths in this current series.

More recently Howard *et al.*¹¹ (see Table 2) reported the findings of his multicentre study, which included 81 pregnancies complicated by SCD over the period 1991–1993. At the time the main therapeutic tool in the management of women with SCD during pregnancy was prophylactic blood transfusion, although its benefit is yet to be established. There were increased rates of preterm delivery and EMCS. The perinatal mortality rate was 60 per 1000 live births. There were two maternal deaths in this series.

The high rate of caesarean section in our series is due to fetal compromise. Improved fetal monitoring has led to increased

Figure 2 Mode of delivery by haemoglobinopathy. SVD = spontaneous vaginal delivery; EMCS = emergency lower segment caesarean section; ELCS = elective lower segment caesarean section; SS = homozygous sickle cell disease; SC = sickle cell haemoglobin C disease; SD = sickle cell delta disease; SE = sickle cell haemoglobin E disease; SBThal = sickle b plus thalassaemia

Table 1 Frequency of obstetric complications and sickle-related complications in 122 pregnancies complicated by sickle cell disease

Obstetric complication	Cases (%)
Preeclampsia	13 (11)
Preterm delivery	23 (19)
Ante-partum haemorrhage	5 (4)
Postpartum haemorrhage	40 (33)
Sickle-related complications	31 (25)

Table 2 Comparison with the literature (Howard *et al.*, 1995;¹¹ Sun *et al.*, 2001;⁶ Sergeant *et al.*, 2004⁵)

Parameter	STT/QCCH/HH	Howard	Sun	Sergeant (HbSS)
Number of pregnancies	122	78	127	94
Preterm delivery (%)	19	23	67	44
Caesarean section (%)	60	38	64	17
IUGR (%)	20	18	66	42
Preeclampsia (%)	11	9	13	

IUGR = intrauterine growth restriction

likelihood of intervention. Close ultrasound monitoring to assess for fetal wellbeing has also been a valuable tool.¹²

The HbSS phenotype has a higher rate of sickle-related complications compared with other phenotypes.⁵ This finding was confirmed in our study even though the numbers were small. The main sickle complication identified was an increase in vaso-occlusive crises usually occurring after 20 weeks gestation. Other complications were recurrent urinary tract infections, chest infection, papillary necrosis, pulmonary embolus and hyperhaemolysis. There were no maternal deaths in this series. Previous series have shown thromboembolism is a major cause of death in this group of women.¹³ Our local guidelines advocate low-dose aspirin as primary prophylaxis against preeclampsia, and low molecular weight heparin in those with a personal or family history of thrombosis. If the delivery is operative, we suggest continuation for six weeks postpartum. The uptake of this is variable.

Maternal opiate use during pregnancy is a problem if women are seen at multiple units. This is reflected in three neonates developing transient complications postnatally related to maternal opiate use.

Although improvements have been made compared with historical data, pregnancy in women with SCD remains high risk. Early access to antenatal care, close fetal monitoring and expert maternal supervision in SCD is essential.

This series is limited due to its retrospective, observational nature. In addition, findings of studies from one country^{5,6} cannot always be generalized to other countries. There must be consistency of findings between cohorts in different geographical locations, by different investigators and in different

time periods. Thus, our study from a UK cohort adds to the evidence that a dedicated team caring for pregnant women with SCD may result in improved outcome. In addition, there should be consistent evidence from other types of studies such as case control and prospective studies to corroborate these findings. We are currently undertaking a UK-wide prospective case control study through United Kingdom Obstetric Surveillance System.¹⁴

REFERENCES

- 1 Streetly A, Latinovic A, Hall K, Henthorn J. Implementation of universal newborn bloodspot screening for sickle cell disease and other clinically significant haemoglobinopathies in England: screening results for 2005–7. *J Clin Pathol* 2009;**62**:26–30
- 2 Why Mothers Die 2000–2002. *The Sixth Report of Confidential Enquiries into Maternal Deaths in the United Kingdom*. Gwyneth Lewis and CEMACH. London: RCOG Press, 2004
- 3 Oteng-Ntim E, Chase AR, Howard J, Khazaezadeh N, Anionwu E. Sickle cell disease in pregnancy. *Obstet Gynaecol Reprod Med* 2008;**18**:272–8
- 4 Villers M, Jamison M, De Castro L, James A. Morbidity associated with sickle cell disease in pregnancy. *Am J Obstet Gynaecol* 2008;**199**:125e1–5
- 5 Serjeant GR, Loy LL, Crowther M, Hambleton IR, Thame M. Outcome of pregnancy in homozygous sickle cell disease. *Am J Obstet Gynecol* 2004;**190**:1278–85
- 6 Sun PM, Wilburn W, Raynor BD. Sickle cell disease in pregnancy: 20 years of experience at Grady Memorial Hospital. *Am J Obstet Gynecol* 2001;**184**:1127–30
- 7 CLASP (Collaborative Low-dose Aspirin Study in Pregnancy) Collaborative Group. CLASP: a randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 women. *Lancet* 1992;**343**:619–29
- 8 Hypertension (CG34) Guideline. Management of Hypertension in Adults in Primary Care. NICE 2004
- 9 Hassell K. Pregnancy and sickle cell disease. *Haematol Oncol Clin North Am* 2005;**19**:903–16
- 10 Tuck SM, Studd JWW, White JM. Pregnancy in sickle cell disease in the UK. *Br J Obstet Gynecol* 1983;**90**:112–17
- 11 Howard RJ, Tuck SM, Pearson TC. Pregnancy in sickle cell disease in the UK: results of a multicentre survey of the effect of prophylactic blood transfusion on maternal and fetal outcome. *Br J Obstet Gynecol* 1995;**102**:947–51
- 12 Anyaegbunam A, Langer O, Brutsman L, Witty J, Merkatz IR. Third trimester prediction of small for gestational age infants in pregnant women with sickle cell disease. *J Reprod Med* 1991;**36**:577–80
- 13 Rajab KE, Skerman JH. Sickle cell disease in pregnancy. Obstetric and anaesthetic management perspectives. *Saudi Med J* 2004;**25**:265–76
- 14 Knight M, Spark P, Pierce M, *et al.* on behalf of UKOSS. *United Kingdom Obstetric Surveillance System (UKOSS) Annual Report 2010*. National Perinatal Epidemiology Unit, Oxford, 2010

(Accepted 16 August 2010)