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Pregnancy in sickle cell-haemoglobin C (SC) disease. A retrospective study of birth size and maternal weight gain

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ABSTRACT

Objective: To assess pregnancy and fetal outcomes in Jamaican subjects with sickle cell-haemoglobin C (SC) disease.
Study design: A retrospective chart review over 21 years (1992–2012) of all pregnancies in SC disease and a comparison group matched by gender and date of delivery in mothers with a normal haemoglobin (AA) phenotype at the University Hospital of the West Indies, Jamaica. There were 118 pregnancies in 81 patients with SC disease and 110 pregnancies in 110 in the normal comparison group. Corrections were made for repeat pregnancies from the same mother. Outcome measures included maternal weight at 20, 25, 30, 35 and 38 weeks gestation, maternal pregnancy complications, birth weight, head circumference and crown heel length and were used to analyse possible predictors of birth weight.
Results: First antenatal visits occurred later in women with SC disease, who also had lower haemoglobin level and lower systolic blood pressure. The prevalence of pregnancy-induced hypertension, pre-eclampsia, ante-partum or postpartum haemorrhage did not differ between genotypes. Maternal weight gain was significantly lower in SC disease and there was a significantly lower birth weight, head circumference, and gestational age.
Conclusions: Pregnancy in SC disease is generally benign but mothers had lower weight gain and lower birth weight babies, the difference persisting after correction for gestational age.

Introduction

The term sickle cell disease covers a group of conditions in which pathology results from the presence of sickle haemoglobin (HbS) [1]. Inheriting the sickle cell gene from both parents results in homozygous sickle cell (SS) disease which is generally severe, whereas double heterozygotes with sickle cell-haemoglobin C (SC) disease are usually mildly affected.

In SS disease, pregnancy was associated with increased bone pain crises, acute chest syndrome, urinary tract infections and maternal mortality, increased fetal loss at every stage, and a low birth weight baby [2,3]. In the Jamaican Cohort Study [4], which followed 150 females with SS disease from birth, 36% of pregnancies ended in spontaneous abortion, and completed pregnancies showed a lower gestational age and birth weight [5]. Four deaths occurred, two published in an earlier report [5] giving a mortality rate of 2.1% but two further deaths occurred later (unpublished observations). Although pregnancy outcome in SS disease is variable and unpredictable, there is often a severe clinical course for both fetus and mother.

Sickle cell-haemoglobin C (SC) disease is the second most common form of sickle cell disease among mothers of West African ancestry and results from the inheritance of HbS and HbC genes. Early reports, certainly influenced by symptomatic selection, suggested that pregnancy in SC patients ran a more severe clinical course than in SS disease [6,7] but it is now clear that SC patients have a more benign outcome [2,8,9]. These reports have tended to focus on maternal performance and complications, and the data on fetal outcome and birth weight are conflicting. To clarify this issue, the present study has addressed the birth outcome and infant size in a retrospective study of patients and an appropriate comparison group over 21 years at a single institution. This group has also

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provided an opportunity to examine some of the potential determinants of birth weight.

Materials and methods

Patients

Retrospective chart review of patients with SC disease delivering at the University Hospital of the West Indies (UHWI), Kingston, Jamaica over 21 years (January 1, 1992 and December 31, 2012) found 118 singleton pregnancies in 81 women (57 single pregnancies, 13 with two, 9 with three and 2 with four pregnancies). A comparison group of singleton pregnancies in 110 females with a normal haemoglobin (AA) phenotype was derived from the same source, matching maternal age within 1 year and delivery date within 1 day. Maternal measurements at the first antenatal visit included weight, height, haemoglobin level, systolic and diastolic blood pressure and serial measurements of weight were performed at 20, 25, 30, 35 and 38 weeks gestation. Indices of birth outcome included gestational age, birth weight, head circumference, crown-heel length and APGAR scores. Placental weight and estimated blood loss were also recorded. Postpartum haemorrhage was defined as blood loss greater than 500 ml in a spontaneous vaginal delivery or exceeding 1000 ml at Caesarean section. The study was approved by the University of the West Indies/UHWI Ethics Committee.

Statistical analysis

Since observations of weight gain required knowledge of the pre-pregnancy weight, analysis was limited to a subset of 88 SC pregnancies where mothers attended antenatal clinics before 16 weeks gestation when weight still reflected pre-pregnancy levels [10]. Maternal weight gain (overall and rate of weight gain), hospital admissions and the outcome variables were compared between the SC and comparison groups using a regression model. Adjusting for differences within, and between, mothers with more than one pregnancy was performed by a mixed linear random effects model for continuous outcomes and a mixed logistic regression random effects model for binary outcomes. Body mass index (BMI) was calculated as weight (kg)/height (m) squared. Statistical Package for the Social Sciences (SPSS) Version 22 was used.

Results

First antenatal clinic visit

Patients with SC disease presented later at first visit, had lower haemoglobin levels, and lower systolic blood pressure but maternal weight, height, body mass index, age or diastolic blood pressure did not differ (Table 1).

Maternal outcome

Prior to delivery-related admissions, there were 44 admissions among SC patients (23 bone pain crisis, 11 pre-eclampsia, 5 pregnancy induced hypertension, 4 urinary tract infection, 2 acute chest syndrome, 2 gestational diabetes), and 15 admissions in controls (5 pregnancy induced hypertension, 4 pre-eclampsia, 3 urinary tract infection, 2 vomiting, one gestational diabetes). There was no maternal mortality in either group. Pre-eclampsia was more common in SC mothers (11/118 [9.3%]) than comparison group (4/110 [3.6%]), although the difference was no longer significant ($p = 0.098$) after correction for repeat pregnancies and there were no significant genotype differences in the prevalence of pregnancy induced hypertension (SC 5/118 [4.2%]; comparison group 5/109 [4.6%]), urinary tract infections (4/118 [3.4%]; 3/110 [2.7%]), mean duration of labour (8.64 h; 8.02 h), mode of delivery (Caesarean section 31/118 [26.2%]; 22/110 [20.0%]), or postpartum haemorrhage (6/115 [5.2%]; 7/109 [6.4%]). Maternal weight gain was consistently lower in SC disease throughout pregnancy and the total weight gain in mothers with SC disease completing 38 weeks gestation was 2.42 kg (Table 2) less than in the comparison group ($p < 0.0001$).

Infant outcome

Infants of SC mothers had lower gestational age and birth weight (Table 3), despite similar rates of induction of labour (SC 5; comparison group 6) and of Caesarean sections. Infants of SC mothers weighed 443 g less (95% CI 266–620) after controlling for repeat pregnancies. The difference was reduced to 299 g (CI 156–441) after controlling for gestational age but remained highly significant (300 g, CI 157–442 g) after controlling for both gestational age and induction/operative deliveries ($p < 0.001$). Focusing on the 51 pregnancies derived from the Cohort Study, the birth weight was 414 g lower (CI 177–651, $p = 0.001$) than the AA controls, after correction for individuals contributing more than one pregnancy. Low birth weight babies (<2500 g) were more frequent in SC pregnancies (SC 22.9%, AA 5.5%, $p < 0.0001$) and head circumference and placental weight were also significantly lower than controls. Apgar scores of 7 at 1 min (SC 21/110 [18.8%], comparison group 17/110 [15.5%]) and 5 min (SC 7/118 [5.9%] versus 4/110 [3.6%]) did not differ between the groups, χ^2 0.6 and 0.2 respectively.

Possible determinants of lower birth weight

In mothers with SC disease, birth weight was not influenced by admissions for bone pain crisis ($p = 0.755$), acute chest syndrome

Table 1
Maternal characteristics at first antenatal clinic visit.

Characteristic	SC disease		AA phenotype		*p*-Value
	n	Mean (SD)	*n*	Mean (SD)	
Maternal age (years)	118	24.7 (5.3)	110	25.2 (5.5)	0.49
Gestational age (weeks)	115	15.7 (6.0)	110	12.7 (2.9)	<0.0001
Weight (kg)	114	65.2 (14.8)	109	68.0 (17.4)	0.20
Height (cm)	83	162.7 (6.6)	75	164.4 (6.1)	0.10
Body mass index (kg/m^2)	83	24.9 (5.1)	75	24.6 (6.5)	0.75
Age at menarche (years)	115	13.4 (1.7)	109	12.7 (1.9)	0.002
Parity	118	1.0 (1.1)	110	0.7 (0.9)	0.02
Systolic blood pressure (mmHg)	115	106.5 (12.1)	110	111.2 (14.3)	0.01
Diastolic blood pressure (mmHg)	115	67.1 (7.9)	110	69.0 (9.4)	0.11
Haemoglobin (g/dl)	108	10.5 (1.0)	104	12.2 (1.0)	<0.0001