Effectiveness of antenatal screening for sickle cell trait: the impact on women's self-report of sickle cell trait status

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Objectives: The sickle gene frequency in the Jamaican population has not changed over a generation. It is unknown whether routine antenatal screening for sickle cell trait (SCT) has affected women's knowledge of their SCT status. The aim of this study was to compare the prevalence of self-reported SCT in parous women to the prevalence in nulliparous women, men and to the observed prevalence of SCT measured in an antenatal clinic.

Methods: All participants in the nationally representative Jamaica Health and Lifestyle Survey 2008 were asked whether they had the SCT. The impact of gender, age, educational attainment, geographical location, and pregnancy on self-reported SCT were assessed. The prevalence of SCT in women attending a large antenatal clinic concurrently was compared to that reported by women of child-bearing age in the lifestyle survey.

Results: Self-report significantly underestimated the prevalence of SCT (2.9% versus 10.1%, $P < 0.001$). Those with secondary education were more likely than those with presecondary education ($P = 0.01$) and women more likely than men (3.2% versus 1.1%, $P = 0.001$) to report having SCT. Women who had been pregnant were no more likely than other women to report having SCT (3.1% versus 4.1%, $P = 0.4$).

Conclusions: Attendance at antenatal clinic where SCT screening is routine, is not associated with increased self-report of SCT. Screening programs must ensure that, as well as technically accurate screening, there is effective communication of the results of screening for SCT to those tested to help reduce the public health burden of sickle cell disease in tropical countries.

Keywords: Sickle cell trait, Self-report, Screening, Effectiveness, Antenatal

Introduction

Sickle cell disease (SCD) is one of the most prevalent inherited diseases worldwide. More than 250 000 children are born annually with SCD worldwide.¹ The World Health Organization estimated that the proportion of infants conceived in 2003 who had SCD was 0.07/1000 infants in the European Region, 0.49/1000 infants in the American Region, 0.68/1000 infants in the South-East Asian Region, 0.84/1000 infants in the Eastern Mediterranean Region, and 10.68/1000 infants in the African Region.¹ Persons born with SCD have significant morbidity and are at risk of premature death.² Treatment options have improved, but some are unavailable in developing countries as are technologies, such as bone marrow transplantation, that could result in a cure.^{3,4}

SCD is a significant public health problem in Jamaica. One in 170 babies born in Jamaica has

SCD.⁵ Newborn screening was first performed on 100 000 consecutive non-operative births at the Victoria Jubilee Hospital, a major obstetric hospital in Jamaica from June 1973 to December 1981. This cohort has provided invaluable understanding into the natural history of SCD.⁶ The screening program was reintroduced in 1995, and has been extended to include other major hospitals such as the University Hospital of the West Indies (UHWI) and Spanish Town Hospital. The results of the screening of the first 150 803 infants have been reported.⁵ The frequencies from the two cohorts have yielded consistent estimates of 10% for the abnormal haemoglobin S allele.^{5,6} The haemoglobin S allele frequency in the Jamaican population has not changed over a generation.⁷ In both cohorts, resources have been insufficient to allow for contacting of trait carriers to inform them of their status.

In addition to the sickle gene, 4% of Jamaican adults carry another significant beta hemoglobin trait and are at risk of having a child with SCD.^{5,6} It is therefore critical that persons are screened before pregnancy and are aware of their risk status.

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Public antenatal clinics carry out the sickle solubility test on blood samples obtained from all women attending the clinic, which identifies the presence of cells that sickle without differentiating between sickle cell trait (SCT) and SCD; confirmatory hemoglobin electrophoresis is conducted on samples with positive sickle solubility tests. The UHWI carries out hemoglobin electrophoresis on blood samples from all ante-natal clinic attendees. Some mothers, attending the Sickle Cell Unit after diagnosis of SCD in their children, were unaware of their SCT status, while others were aware but did not understand the risk of having an affected infant and had not had their partner tested (personal experience). Jamaicans, more so men, who are not routinely screened, may be unaware of their SCT status.

It is important to determine the effectiveness of the current screening program in antenatal clinics to assess how it can be improved if necessary.

In this national health survey of Jamaicans 15–74 years old, the aim of this report was to assess whether women, who have been pregnant and thus would have had an antenatal clinic sickle cell screening test, would be more likely than men to report having the SCT and to determine whether age, union status, educational level and geographical location were associated with self-reporting of SCT. A secondary aim was to compare the prevalence of self-reported SCT in women of child-bearing age in the national survey to the measured prevalence in women attending the antenatal clinic at the UHWI during the time of recruitment for the Jamaica Health and Lifestyle Survey 2008 (JHLS).

Patients and Methods

A representative sample of Jamaican adults, aged 15–74 years, were interviewed on a wide spectrum of health-related practices and issues from November 2007 to April 2008.⁸ This nationally representative sample was selected in collaboration with the Statistical Institute of Jamaica (STATIN) by selection from households in clusters called primary sampling units. These primary sampling units are selected from each parish by probability proportionate to size. The study was approved by the Faculty of Medical Sciences, University of the West Indies, UHWI Ethics Committee.

As part of the questionnaire used in the JHLS, respondents were asked whether they have the SCT. Women were asked whether they had ever been pregnant. Age, gender, union status, educational level, and geographical location were recorded. Union status was categorized as in no current relationship (single, separated, divorced, or widowed) or in a cohabiting relationship (married, in a common law relationship) or in a visiting relationship. Educational level was

defined by highest-level examination passed which was categorized as presecondary (none or primary education) and secondary (secondary or tertiary). Geographical location was defined by whether they lived in the Kingston and St Andrew Metropolitan Area (KSA) or elsewhere. Women were classified by whether they reported at least one pregnancy and also whether they reported having at least one live birth.

The results of all hemoglobin electrophoresis tests performed at the UHWI antenatal clinic from November 2007 to April 2008 were examined and the prevalence of SCT was determined and compared with the results of the JHLS II.

Statistical analysis

Univariate analyses were performed using Chi-square for categorical variable and *t*-tests for continuous variables. All variables of interest were entered into logistic regression analyses to determine whether they had a statistically significant impact on the reporting of SCT. The model examining gender differences did not include pregnancy-related variables. Logistic regression was also undertaken in women with all variables except gender. The proportion of women of child-bearing age (15–49 years old) who lived in the Kingston and St Andrew reporting SCT was compared to the proportion of women who had been screened positive for SCT at the UHWI antenatal clinic using Chi-square analysis. Analysis was performed using SPSS 12.0 for Windows.

Results

Antenatal hemoglobin electrophoresis

From November 2007 to April 2008 inclusive, 1003 samples were submitted for hemoglobin electrophoresis. Of these, 10.1% were compatible with SCT. When compared to 1370 women of child-bearing age in the JHLS of whom 3.4% reported having SCT, there was a statistically significant difference in the proportions ($P < 0.001$).

Jamaica Health and Lifestyle Survey 2008

There were 2848 participants in the JHLS, of whom 2838 (98.0%) responded to the SCT status question. Analysis was restricted to the responders. There were 883 men and 1955 women. Seventy-three persons (2.6%) reported that they had the SCT. A higher proportion of women than men reported having an SCT (3.2% versus 1.1% respectively, $P = 0.001$). Men who reported having SCT were older than those who did not report having SCT (51.7 ± 17.0 years versus 41.2 ± 16.7 years, $P = 0.049$); age was not associated with SCT report in women (37.8 ± 15.8 years versus 41.4 ± 15.5 years, $P = 0.10$). Higher education in women, but not in men, was associated with increased report of SCT (Table 1). Union status and location had no significant association with self-reported SCT (Table 1). Among women, there was no association

Table 1 Relationship between demographic variables with self-reported positive SCT among men and women

Variable	n	All		Male		Female	
		SCT n (%)	P value	SCT n (%)	P value	SCT n (%)	P value
Union status	No current relationship (1285)	31 (2.4)	0.32	3 (0.07)	0.44	28 (3.2)	0.33
	Visiting (375)	14 (3.7)		3 (2.0)		11 (4.8)	
	Cohabiting (1173)	28 (2.4)		4 (1.2)		24 (2.9)	
Educational attainment n (%)	None (1294)	26 (2.0)	0.01	3 (0.7)	0.50	23 (2.6)	0.02
	Primary (910)	18 (2.0)		4 (1.5)		14 (2.2)	
	Secondary (365)	17 (4.7)		1 (0.8)		16 (6.5)	
	Tertiary (240)	9 (3.8)		2 (2.5)		7 (4.4)	
Location	KSA (728)	20 (2.7)	0.79	1 (0.5)	0.47	19 (3.6)	0.56
	Other (2110)	53 (2.5)		9 (1.3)		44 (3.1)	

Note: SCT: sickle cell trait; KSA: Kingston and St Andrew Metropolitan Area.

between SCT self-report and having been pregnant ($P=0.4$) or having delivered a live infant ($P=0.4$).

In a logistic regression model including sex, age, secondary education, union status, and location, significant factors associated with SCT self-report were female gender [odds ratio (OR)= 2.9, $P=0.002$] and higher (secondary/tertiary) education (OR=2.2, $P=0.002$) (Table 2). In men, age (OR=1.1, $P=0.03$) was a significant predictor. In women, when age, educational attainment, location, history of pregnancy, and live birth were entered into a model, higher education was associated with higher self-report of SCT (OR=2.1, $P=0.009$).

Discussion

There was significant underestimation of SCT using self-reported status in a representative sample of Jamaican adults and this is more marked among men. In light of the current 10% prevalence of SCT among pregnant women, the under-reporting of this prevalence among women in the general population is significant. Although women were more likely to report having SCT, this difference could not be attributed to having attended antenatal clinic, which would have provided access to screening and counseling as reporting levels in parous and non-parous women were similar.

The use of the antenatal population to provide an actual prevalence of SCT is reasonable even for

comparison with men as there should be no gender difference in trait rate and trait status does not affect fertility rates. The use of data over 6 months decreases substantially any chance of repeat testing as two pregnancies in the time frame are unlikely. Thus, the assertion that the SCT is significantly under-reported is well supported by this comparison.

The use of the sickle solubility test in the public health service may have been associated with some cases of SCT being missed. This test has been reported to have a sensitivity of 93.8% and specificity of 100% when compared to hemoglobin electrophoresis and high-performance liquid chromatography.⁹ While some authors view the sickle solubility test as being inadequate for screening purposes,¹⁰ others have suggested its use in remote areas where facilities for confirmatory testing are not available.⁹ While protocol dictates that women screened as positive with the solubility test in the public health care system in Jamaica should have a confirmatory hemoglobin electrophoresis performed, these will not identify SCT in persons who have false negative solubility test. Furthermore, the solubility test does not identify other mutations of the beta globin gene, thus missing persons with other traits, such as Hb AC or thalassemia trait, which may, in concert with SCT, give rise to a child with SCD.

SCT prevalence should be equal in men and women as inheritance is by an autosomal recessive

Table 2 Logistical regressions of SCT self-report with demographic and reproductive variables

	All		Men		Women	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Female gender	2.9 (1.5–5.6)	0.002				
Age (per year)	1.00 (0.98–1.02)	1.0	1.1 (1.01–1.10)	0.03	0.99 (0.97–1.01)	0.2
Secondary education	2.2 (1.3–3.8)	0.002	3.0 (0.6–14.1)	0.2	2.1 (1.2–3.8)	0.009
Current relationship	1.2 (0.7–2.0)	0.4	1.3 (0.4–4.9)	0.7	1.2 (0.7–2.1)	0.5
KSA	0.9 (0.5–1.6)	0.8	0.3 (0.04–2.9)	0.3	1.0 (0.6–1.8)	0.9
Pregnancy ever					1.0 (0.2–4.7)	1.0
Live birth ever					1.2 (0.3–5.2)	0.8

Note: SCT: sickle cell trait; KSA: Kingston and St Andrew Metropolitan Area. Age increases in odds per year of age. Secondary education compares no education or primary education to secondary or tertiary education.

gene. Hicks *et al.*¹¹ showed this when they screened 6960 young adult African-Americans. We have demonstrated a difference in awareness of SCT status between men and women that has previously been reported in the literature. Wright *et al.*¹² studied a convenience sample of 147 African-Americans attending Accident and Emergency Department. Only 31% claimed to be aware of their SCT status and women were more likely than men to report that they knew their SCT status. Although not specific to SCT screening, there are data suggesting that men are less likely to have medical checkups and to undertake screening tests as recommended by a physician.^{13,14}

There may be several reasons for the absence of a relationship between child-bearing and awareness of SCT status. These include women's non-attendance at an antenatal clinic during pregnancy, sickle tests not being carried out or non-communication of the results to mothers or mothers may have forgotten their results. The majority of women who were counseled about their HTLV1 status in Jamaica did not retain this knowledge 5 years later.¹⁵ The 2002 Jamaica Reproductive Health Survey reports that 98.1% of women who had pregnancies resulting in live births in previous 5 years had accessed antenatal care,¹⁶ but there are no data available regarding the percentage of women attending clinics who have been tested for SCT and how the results of screening are communicated. Additionally, some of these women may have attended ante-natal clinic late in pregnancy and not benefited from screening.

In general, using self-reported trait status may be a less reliable method of obtaining information on sickle cell status. Persons who have never been tested, may also be asymptomatic. Persons may also have been tested and told that they do not have SCD, and interpreted this to mean that they also do not have SCT. They may not have been informed of test results, or having been informed, not been counseled about the importance of these results.

Knowledge of SCT could be affected by the clinical setting in which antenatal care is delivered. In Kingston and St Andrew, a metropolitan area, more women access antenatal care from private physicians than elsewhere in Jamaica. In 2002, 63.4% of women from Kingston and St Andrew used government clinics, whereas 82.1% of women from rural areas used these clinics.¹⁶ This did not, however, affect self-reported SCT as rural and urban women had similar self-reporting prevalence in the lifestyle survey.

As SCT does not affect survival, there is no reason to suspect that SCT rates change with age. Castro *et al.*¹⁷ found no association between age and SCT prevalence when they screened 30 400 apparently healthy black individuals in the Washington, DC Metropolitan Area, who were participating in a

community-based sickle cell screening program. If, however, women are more likely to be screened when they are of child-bearing age, one may see a difference in self-reported SCT in younger women, who have been screened more recently. These data do not support this premise as age was not a significant predictor of SCT report in women. There are no previous data regarding age and SCT self-report in men. However, as men age and have more chronic diseases, increased encounters with healthcare professionals may lead to increased testing and self knowledge regarding SCT status. This may account for increased self-report of SCT in older men in this study.

The observed increase in self-reported SCT in those who have completed at least secondary education compared with those who have not is not unexpected. Functional health literacy and health-promoting behavior is more common in those who are well educated.¹⁴ Persons with more formal education may be more actively involved in their own health care.¹⁸ Low literacy is associated with several poor health outcomes and decreased use of available health information and services.¹⁹

These data demonstrate that the lack of awareness of one's SCT status in the Jamaican population would hamper attempts to decrease the incidence of SCD through preconception methods. In resource poor situations, the effect of screening programs for SCD must be maximized so that they not only identify cases of SCD, but also lead to the decrease in new cases. People with SCT must have the power of choice with regards to pregnancies. There should be careful analysis of the current process of screening to ensure that those screened are aware of their status and the implications thereof, as well as attempts to make screening accessible to the entire population, including men and women who do not attend antenatal clinics. The implications of SCT status among women should be reinforced at each pregnancy so that this knowledge is retained. Standardized procedures such as a checklist to be completed by health personnel which states the counseling done and a card with screening results distributed to all those screened may improve the program but would be an additional cost.

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