ORIGINAL ARTICLES

Iron Deficiency among Jamaican Adolescents

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ABSTRACT

Objectives: *To raise awareness of significant iron deficiency anaemia occurring in Jamaican secondary school students.*

Methods: *Haematological screening of 15 592 students in the fifth and sixth forms of 14 secondary schools in the parishes of Manchester and Clarendon, Jamaica, was done. Samples were subject to haemoglobin electrophoresis, examination of haematological indices, and haemoglobin, alpha 2 (HbA_2) levels where indicated.*

Results: *Of 13 172 students with normal haemoglobin (AA) genotype aged 15–19 years, haemoglobin levels below 10 g/dL occurred in 0.36% of males and in 3.79% females. These subjects had low mean red cell volumes, low mean cell haemoglobin and high red cell distribution width, characteristic of iron deficiency, which was confirmed by dramatic increases in haemoglobin level following iron supplementation. Most revealed classic symptoms, histories of poor diets and pica, which generally resolved on iron supplementation.*

Conclusions: *Iron deficiency, even in the absence of anaemia, is known to limit physical and mental functions and may impair intellectual performance in these high school students. Significant anaemia could be detected by incorporating a blood test into the school medical assessments performed on entry to secondary schools. There is a need for simple oral iron medications to be available at health centres.*

Keywords: AA genotype, iron deficiency anaemia, school screening

Deficiencia de Hierro entre Adolescentes Jamaicanos

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RESUMEN

Objetivos: *Crear conciencia sobre el nivel significativo de anemia ferropénica entre estudiantes de secundaria en Jamaica.*

Métodos: *Se realizó un tamizaje hematológico a 15592 estudiantes de quinto y sexto grado de 14 escuelas secundarias en las parroquias de Manchester y Clarendon, Jamaica. Las muestras fueron sometidas a electroforesis de hemoglobina, examen de índices hematológicos, y niveles de hemoglobina alfa 2 (HbA_2) donde se indicara.*

Resultados: *De 13172 estudiantes en edades de 15–19 años con genotipo de hemoglobina normal (AA), se produjeron niveles de hemoglobina por debajo de 10 g/dL en 0.36% de los varones, y 3.79% en las hembras Estos sujetos tenían volúmenes de bajo promedio de glóbulos rojos, hemoglobina celular media baja, y alta amplitud de distribución eritrocitaria, característica de la deficiencia de hierro, confirmada por el aumento dramático de los niveles de hemoglobina tras la suplementación de hierro. La mayoría reveló síntomas clásicos, historias de dietas pobres y pica, que generalmente se resolvieron con los suplementos de hierro.*

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Conclusiones: *Se sabe que la deficiencia de hierro, incluso en la ausencia de anemia, limita las funciones físicas y mentales, y puede afectar el rendimiento intelectual en estos estudiantes de secundaria. Un grado significativo de anemia podría ser detectado mediante la incorporación de una prueba de sangre en las evaluaciones médicas realizadas al ingreso en las escuelas secundarias. Hay necesidad de que los medicamentos de hierro por vía oral simple estén disponibles en los centros de salud.*

Palabras claves: Genotipo AA, anemia ferropénica, tamizaje de la escuela

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INTRODUCTION

Iron deficiency during childhood is common in all countries but especially in the tropics where limited dietary availability of iron may be combined with the effects of iron loss through intestinal infestations. Estimates have varied widely depending on the diagnostic criteria, age group, socio-economic status and geographical area. Studies in the Caribbean found iron deficiency anaemia, defined as haemoglobin levels below 11 g/dL, to occur in 30–60% of preschool children, aged six months to six years (1). In children aged 6–15 years, using the World Health Organization (WHO) criteria of a haemoglobin level below 12.0 g/dL (2), the prevalence of anaemia was 10–50% and there was a tendency for evidence of iron deficiency to decline with advancing age (3).

The Manchester Project seeks to determine whether identification of the haemoglobin genotype of senior school children, aged 16–19 years, attending secondary schools in the parish would influence reproductive decisions and reduce the frequency of births affected by sickle cell disease. Sickle haemoglobin and haemoglobin C (HbC) were detected by haemoglobin electrophoresis, but detection of the beta thalassaemia trait required assessment of haematological indices in electronic analysers, so virtually all subjects had complete haematology. These data indicated that potentially serious levels of anaemia occurred at this age especially among girls. Although peripheral to the main objectives of the Manchester Project, the relatively high prevalence of haemoglobin levels below 10 g/dL was unexpected and some data among this group are therefore presented in order to raise awareness of the need for haematological monitoring and therapy in these students.

SUBJECTS AND METHODS

Manchester is a parish in south central Jamaica with an area of 830 km^2, stretching from the coast in the south to an altitude of approximately 3000 feet in the north; it had a population of 191 000 in 2012 (Statistical Institute of Jamaica), and the parish capital, Mandeville, is 100 km west of the country's capital, Kingston. As part of a programme to assess whether knowledge of haemoglobin genotype would influence reproductive decisions, haematological screening was offered to the fifth and sixth forms (grades 11–13; mostly aged 15–19 years) of 14 secondary schools over six academic years (2007/8 to 2012/13). Twelve of these schools were in Manchester and two were just across the parish border in the adjacent parish of Clarendon. Compliance with screening, assessed annually, improved from 56% to 92% over the study period. After sensitization of the school staff and parents and illustrated lectures on the features and genetics of sickle cell disease, a team consisting of a physician, clerical assistants, and three to four experienced phlebotomists visited a site at the school selected by the school staff (usually the sick bay, wellness centre or guidance counsellor's office). The students completed a data form of basic demography (school class, date of birth, address, family and contact details) and one 5 ml EDTA sample was taken from each student by venepuncture; depending on local factors, 150–250 students could be screened within a two to two and a half hour period. After identification of the haemoglobin genotype, permanent laminated cards were produced and counselling offered to carriers of abnormal genotypes. Most schools required at least two visits and larger schools received four to five visits to offer the opportunities of screening.

Laboratory procedures

Haematological indices were measured by electronic cell counters (Abbott CellDyn 1700, Sysmex XS-1000*i*) and haemoglobin electrophoresis detected abnormal haemoglobins such as haemoglobin S (HbS) and HbC. Beta thalassaemia genes were detected by estimation of haemoglobin, alpha 2 (HbA_2) levels on all cases with a mean cell haemoglobin (MCH) equal to, or below, 26 pg and subjects with a red cell distribution width (RDW-CV) of 18 and above were excluded as probable iron deficiency. All samples with HbA_2 levels $\geq$ 3.5% were referred to collaborating laboratories elsewhere for DNA sequencing to confirm the presence and identity of beta thalassaemia mutations.

Clinical follow-up

On detection of haemoglobin levels below 10 g/dL, arbitrarily defined as severe anaemia, students were given the results, diet sheets and counselled regarding diet. All students were advised to take anti-helminth treatment and were given six weeks treatment of a proprietary oral iron medicine and offered repeat blood tests after intervals of five to eight weeks. Subgroups of 30 students from each of the academic years 2009/10 and 2010/11 were interviewed in greater detail on symptoms and dietary practices.

Statistical methods

For all students, the distribution of haemoglobin levels were depicted using kernel density estimation and formally compared using a linear regression including predictive terms for gender, age and an interaction term representing gender/age. The model was pre-adjusted for year of screening. For girls with haemoglobin levels below 10 g/dL, the distribution of red cell indices across haemoglobin groups was expressed as the median, the interquartile range (IQR) and the numerical range. Due to the smaller participant numbers in this low haemoglobin subgroup, a normal distribution cannot be assumed and the median absolute deviation (MAD) was used as a robust indicator of variability. Analyses were performed using Stata statistical software (Release 13. College Station, TX: StataCorp LP).

RESULTS

A total of 15 592 students (8763 or 56.2% females) were screened but complete haematology was unavailable in 31 (one male) and a further 68 (45 males) were outside the age range chosen for the analysis (15–19 years), leaving a total study group of 15 493 subjects. The distribution of haemoglobin genotypes (Table 1) shows that the three common genotypes (AA, AS, AC) accounted for 15205 (98.1%) students. Total haemoglobin levels below 10 g/dL occurred in 21/5776 (0.36%) males and in 280/7396 (3.79%) females in the AA genotype (Table 2, Fig. 1); corresponding figures for the AS genotype (males 1/651 [0.15%], females 24/846 [2.84%]) and for the AC genotype (males 0, females 11/309 [3.56%]) showed no significant difference. Further analysis was confined to 13 172 students (5776 males, 7396 females) with an AA haemoglobin genotype, complete haematology and aged 15–19 years.

Table 1: Distribution of haemoglobin genotypes among 15 493 school students aged 15–19 years with complete haematology

Genotype	Males (%)	Females (%)	Total (%)
AA	5776 (85.17)	7396 (84.90)	13172 (85.02)
AS	651 (9.60)	846 (9.71)	1497 (9.66)
AC	227 (3.35)	309 (3.55)	536 (3.46)
Aβ thal trait	65 (0.97)	68 (0.78)	133 (0.86)
SS	8 (0.12)	16 (0.18)	24
$S\beta^+$ thalassaemia	2	7 (0.08)	9 (0.06)
$S\beta^\circ$ thalassaemia	1	1	2
S-HPFH	2	1	3
A-HPFH	24 (0.35)	33 (0.38)	57 (0.37)
SC	14 (0.21)	19 (0.22)	33 (0.21)
CC	4	4	8
$C\beta^\circ$ thalassaemia	1	0	1
S-variant	0	1	1
A-variant	7 (0.10)	10 (0.11)	17 (0.11)
Total	**6782**	**8711**	**15 493**

HPFH – the gene for hereditary persistence of fetal haemoglobin; variants – rare variants other than haemoglobin S (HbS) and haemoglobin C (HbC)

Table 2: Distribution of total haemoglobin levels by gender in 13172 subjects with an AA haemoglobin genotype. Percentage expressed among those with complete haematology

Haemoglobin level (g/dL)	Males (%)	Females (%)	Total
4.0 – 4.9	0	3 (0.04)	3
5.0 – 5.9	0	4 (0.05)	4
6.0 – 6.9	0	18 (0.24)	18
7.0 – 7.9	4 (0.07)	37 (0.50)	41
8.0 – 8.9	2 (0.03)	65 (0.88)	67
9.0 – 9.9	15 (0.26)	153 (2.07)	168
10.0 – 10.9	29 (0.50)	391 (5.29)	420
11.0 – 11.9	75 (1.30)	1369 (18.51)	1444
12.0 – 12.9	344 (5.96)	2745 (37.11)	3089
13.0 – 13.9	1215 (21.04)	2019 (27.30)	3234
14.0 – 14.9	2115 (36.62)	540 (7.30)	2655
15.0 – 15.9	1483 (25.68)	44 (0.59)	1527
16.0 – 16.9	439 (7.60)	6 (0.08)	445
17.0 – 17.9	48 (0.83)	1	49
18.0 –	7 (0.12)	1†	8
Total	**5776**	**7396**	**13172**

NB: Blood sample inadequate for haematology in 28 subjects (1 male, 27 female)
†Subject subsequently found to have congenital heart disease

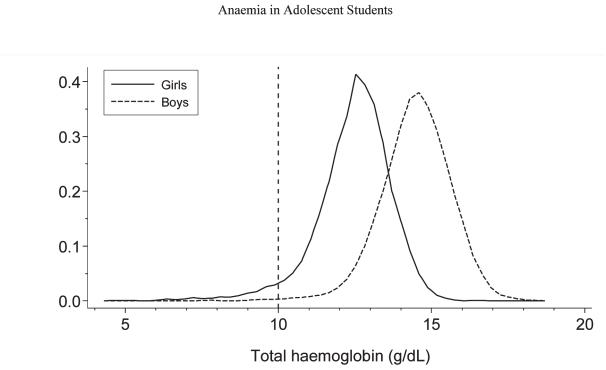

Fig. 1: Distribution of total haemoglobin levels in 13 172 subjects (5776 males, 7396 females) aged 15–19 years with an AA haemoglobin genotype.

Red cell indices, mean cell volume (MCV), MCH and RDW-CV, an indication of anisocytosis, were consistent with iron deficiency, and the abnormalities were most marked in those with the lowest haemoglobin levels (Table 3). The prevalence of severe anaemia among females with an AA genotype was not influenced by age within the age group studied, anaemic subjects (n, mean, SD, median: 280, 16.88, 0.74, 16.8) being similar to non-anaemic subjects (7116, 16.86, 0.79, 16.7), nor was there any age trend with the severity of anaemia. Both gender and age were strong predictors of total haemoglobin; levels in males being 1.79 g/dL higher than in females (gender effect, $p < 0.001$) and levels rising with age (age effect, $p < 0.001$), an effect more marked in males than females (age×gender interaction effect, $p = 0.005$; Fig. 2). After adjusting for the effects of age and

Table 3: Distribution of indices within haemoglobin bands in 280 anaemic women (Hb < 10 g/dL) with an AA genotype

Hb level (g/dL)	n	MCV median (MAD), IQR (range)	MCH median (MAD), IQR (range)	RDW-CV median (MAD), IQR (range)
< 5	3	57.9 (1.9), 11.5 (56–68)	18.0 (0), 2.8 (15–18)	30.1 (4.1), 9.7 (24.5–34.2)
5.0 – 5.9	4	59.8 (5.3), 12.6 (54–70)	17.5 (0.4), 0.8 (17–18)	28.0 (1.7), 7.7 (17.4–29.8)
6.0 – 6.9	18	57.2 (3.2), 8.0 (51.2–65)	17.0 (1.0), 2.0 (13–19)	22.5 (0.9), 1.5 (20.2–32.6)
7.0 – 7.9	37	61.0 (4.4), 9.1 (50.0–79)	18.0 (1.6), 2.8 (15–25)	22.0 (1.3), 2.6 (14.0–29.8)
8.0 – 8.9	65	64.0 (4.0), 7.0 (54–83)	20.0 (2.0), 3.8 (16–28)	19.6 (1.0), 2.1 (15.4–27.3)
9.0 – 9.9	153	70.0 (5.0), 10.0 (52–92)	22.0 (1.7), 3.0 (17–33)	18.6 (1.4), 2.7 (12.7–26.8)

Hb – haemoglobin; MCV – mean cell volume; MCH – mean cell haemoglobin; RDW-CV – red cell distribution width; MAD – median absolute deviation; IQR – interquartile range; (range) – numerical range

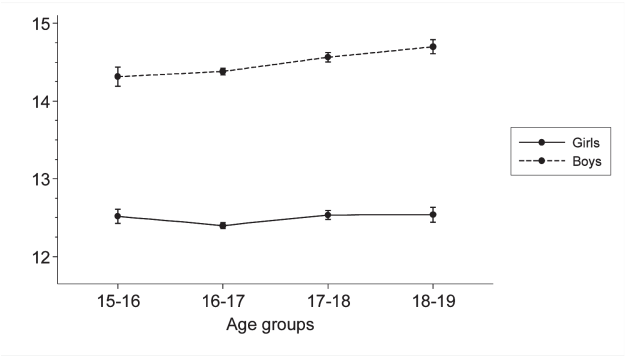

Fig. 2: Total haemoglobin for males and females. Model predictions depicting mean and 95% confidence intervals.

gender, there was a secular change in total haemoglobin, but this was accounted for by a slightly higher average haemoglobin among the participants screened in 2013, year-effect including 2013 ($p = 0.001$), excluding 2013 ($p = 0.12$).

There was no secular trend over the six-year sampling period in the proportion of anaemic cases, logistic regression for haemoglobin below 10 g/dL as the outcome and sampling year as a categorical term ($p = 0.32$). There was also no clear trend with school attended, although the highest prevalence – exceeding 6% – occurred in predominantly rural schools in Porus in the east central part of the parish and in Pratville in the south of the parish.

Subgroup analysis

Sixty students were interviewed in greater detail; 53 (88%) admitted to a history of pica, eating ice, ashes, dusting powder, marl, cement, chalk, coal and small stones. Nearly all students complained of tiring easily and 30% had noticed heavy periods over the preceding six months. Diet was often poor, vegetables being consumed only once weekly in half the group and two students from poor socio-economic backgrounds who had been admitted to the Programme of Advancement through Health and Education (PATH), which provided free vouchers for a cooked lunch, admitted swapping their lunches for pastries and sodas. Following iron therapy, pica resolved completely in 60% and improved in a further 24%, and 60% said that they felt more energetic. Repeat blood tests in 231 (68%) noted a mean haemoglobin increase of 2.3 g/dL (8.6 to 10.9 g/dL) over a mean interval of five weeks. Dramatic increases occurred in some students; two students increased from 4.5 to 11.1 g/dL and another from 5.0 to 12.1 g/dL over seven-month periods. Both noted greater energy, were enjoying school more and one of them stated that she was getting rid of her boyfriend and becoming 'celibate'.

DISCUSSION

Many of the haematological observations in this study are typical of adolescent haematology elsewhere (4–8). These include the higher haemoglobin levels characteristic of males and the tendency for haemoglobin levels to rise with age during adolescence, especially in males, which is believed to be secondary to hormonal changes at puberty. To some extent, these changes may have masked the prevalence of significant iron deficiency in males, haemoglobin levels below 10 g/dL occurring in only 0.4% of males compared with 3.8% among females. It is difficult to compare these frequencies of iron deficiency with those previously published because of the variable definitions of deficiency which are frequently based on erythrocyte protoporphyrin (EPP) levels or serum ferritin. No direct measurements of iron status were available in the present study which was not designed to address this issue and only anticoagulated blood was taken, but the low mean cell volume and cell mean haemoglobin and high values for red cell distribution width are classical for iron deficiency, and the substantial response to oral iron therapy leave little doubt that the great majority of these cases were anaemic from shortage of iron. Iron deficiency anaemia limits physical activity and may also impair short-term memory (9), exercise tolerance (10), and a sense of well-being (11), so it should be avoided, if at all possible, in these intelligent, motivated students in the senior classes of secondary schools.

Two practical recommendations emerge from the present observations. One is the need to increase awareness of severe anaemia among these school students and an argument could be made for incorporating blood tests into the school medicals prior to entry into secondary schools.

Currently, there seems to be no clear format for these school medicals and no clear directives on the use of blood tests and what should be measured. Blood tests prior to school entry would detect many in whom anaemia is likely to impair their learning capacity and also offer options of other important tests such as haemoglobin electrophoresis to detect carriers of abnormal genes and future risk of having a child with sickle cell disease. The other practical recommendation is to make oral iron preparations available through the system of health centres. None of the health centres in Manchester could provide supplies for iron deficient students and supplies for this study had to be funded by the Sickle Cell Trust (Jamaica).

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AUTHORS' NOTE

K Mason, F Gibson, B Serjeant and G Serjeant were involved in developing the concept of school screening and in coordinating blood collection and analysis. I Hambleton assisted in the data analysis. No potential conflicts of interest have been disclosed.

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