ORIGINAL ARTICLE

Prevalence and pattern of sickle cell disease in premarital couples in Southeastern Nigeria

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Abstract

Context: Premarital haemoglobin screening is an important strategy for the control of Sickle Cell Disease.

Aims: To determine the prevalence and pattern of sickle cell disease among premarital couples and to assess their attitude to the risk of sickle cell anaemia in their offspring.

Settings and Design: A cross sectional descriptive study using interviewer administered questionnaire and haemoglobin screening to collect data.

Materials and Methods: Systematic sampling of every third premarital couples attending the General outpatient Clinic of Nnamdi Azikiwe University Teaching Hospital, Nnewi, between November 2010 and October 2011 was used to select the subjects for the study.

Statistical Analysis Used: SPSS version 16 was used for statistical analysis of data from 212 premarital couples or 424 subjects.

Results: The prevalence of HbAA and HbAS were 72.64% or 308/424 and 26.4% or 112/424, respectively, while HbSS was 0.94% or 4/424. In 95.3% of the couples there was no risk of offspring inheriting sickle cell anaemia. An equal percentage of males ($\chi^2 = 24.704$; df = 6; $P = 0.000$) and females ($\chi^2 = 12.\ 684$; df 6; $P = 0.048$) (67.9% or 144/212) would call-off their marriage if there was risk of their offspring being HbSS.

Conclusions: Three quarters of the premarital couples had HbAA, while one quarter had Sickle cell trait. A very low percentage of the couples (2.8%) had 1:4 risk of their offspring inheriting SCA (HbSS). About 2/3 of the subjects would call-off the marriage if there was risk of their offspring inheriting SCA.

Key words: Haemoglobin screening, premarital, prevalence, sickle cell disease

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Introduction

Sickle Cell Disease (SCD) is the commonest genetic disease worldwide and includes disorders affecting the structure, function or production of haemoglobin.[1] There is a substitution of glutamate with valine in position 6 of the beta globin (β 6Glu→Val).[2] The disease is expressed when Haemoglobin S (HbSS) is inherited from both parents, the homozygous child or haemoglobin SS (HbSS) suffers from sickle cell anaemia (SCA), while the heterozygous child or Haemoglobin AS (HbAS) is a carrier of a sickle cell trait (SCT).

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HbSS is the most common pathological haemoglobin variant worldwide[3] and majority of children born with SCA die before reaching five years of age.[3] Premarital screening for SCD is an important strategy for the control of SCD.

Alao *et al*. found poor knowledge of SCD among the undergraduates.[4] Furthermore, formal professional genetic counselling is rare especially for families without affected proband.[5]

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Altay *et al*., in Turkey found a frequency rate of 4.6% for carrier (HbAS in one partner) and 2.3% for both partners with HbAS each.[6] Guler *et al*.[7] in Turkey found 0.05% rate of SCT, while Alhamdan *et al*. working in Saudi Arabia found a SCT prevalence rate of 4.27% and 0.26% in one and in both partners respectively.[8] Similarly, in Bahrain, the figures found where 4.2% and 0.26% respectively.[9] In western Nigeria, normal haemoglobin HbAA was found in 73% of the subjects, and HbSS in about 2.4%.[10]

The church has become involved in creating awareness and encouraging their faithful on prevention and control of SCD by demanding for premarital screening for haemoglobin genotype. Premarital haemoglobin screening should be voluntary to enhance sustainability of the progress made in SCD control.

This study is aimed at determining the prevalence of HbSS, and HbAS, among the premarital couples attending General Outpatient Clinics of a federal government owned teaching hospital in south eastern Nigeria and at assessing their attitude to the risk of sickle cell anaemia in their offspring.

Materials and Methods

Study design

A cross sectional descriptive study design with well structured interviewer administered research questionnaire developed for this purpose was used to collect data.

Study location

This study was conducted at the General out Patient Clinic of Nnamdi Azikiwe University Teaching Hospital, a Federal Government owned tertiary health facility located in Nnewi, Anambra State, a semi urban centre in the south eastern part of Nigeria. The inhabitants of the town were predominantly Christians, traders, while some others were farmers. The Catholics were more in number than other Christian denominations, which included Anglican, Pentecostal and Sabbath followers. Premarital couples from both Nnewi and other nearby towns came to the hospital for premarital health screening.

Sampling method

Systematic sampling method was used to select every third prospective couples who visited the General outpatient clinics of the hospital with the sole purpose of premarital screening for Sickle cell disease from November 2010 to October 2011. A consulting room was designated for these patients during the period of the study for the purposes of data collection and counselling. The first set of couples to arrive for premarital screening balloted for "Yes" and "No" in order to determine the first for the day and thereafter every third prospective couple were enrolled. Those selected were enrolled after their verbal informed consents were obtained individually. The selected couples were interviewed individually to elicit answers to intimate questions contained in the interview protocol. The contents of the interview protocol were not made known to the other partner.

Inclusion criteria

Prospective husbands and wives were included.

Exclusion criteria

Couples who were already married either by traditional methods or court marriage were excluded.

Determination of haemoglobin genotype

Blood sample was obtained by venepuncture of the antecubital vein and 3ml of blood was collected in ethylenediaminetetraacetic acid (EDTA) bottles for determination of haemoglobin genotype using the usual electrophoretic method (electrophoretic equipment model MUPID-EXU, Japan). A small quantity of blood haemolysate from each subject was placed on the cellulose acetate membrane and carefully introduced into the electrophoretic tank containing Tris-EDTA borate buffer at PH 8.9. The electrophoresis was allowed to run for 15 minutes at 160V. Haemolysates from blood samples of known genotypes (HbAA, HbAS, HbSS and HbSC) were run as reference standards. The results were read according to the migration pattern of the haemoglobin variant. The results were treated with utmost confidentiality.

Ethical issues

Informed consent of the participants was obtained before enrolment into the study. They were assured of confidentiality of the information obtained from them during and after the study. They were informed of their right to withdraw from the study at any time before its conclusion without fear of repercussion from the researchers. They were assured that their decision not to participate would not attract any loss of rights and privileges to appropriate clinical service. The post test counselling was done individually and confidentially.

Ethical approval was obtained from the Ethical committee of the teaching hospital.

Sample size determination

Cochran (1963:75) developed the equation no = Z^2pq/e^2 to yield a minimum sample size for proportions.[11] Where no= sample size; Z^2= abscissa of the normal curve that cuts off an area at the tails (equals the desired confidence levels e.g. 95%).

E = desired level of precision; *P* = estimated proportion of an attribute that is present in the population (if not known maximum variabilty of 0.5 is use) q = *P*–1.

Substituting in the above equation $\text{no} = \frac{(1.96)^2(.5)(.5)}{(.05)^2}$

Minimum size =385

This figure was adjusted to 385/0.9 = 427 (approximately 10%) and rounded up to 430 in order to provide for non response by some participants and pairing of subjects during sampling. If the client picked based on the systematic sampling withheld consent the next couple would be selected.

Data collection and analysis

The questionnaire was pre-tested on twenty medical students and validated by a consultant Family Physician. The interview protocol covered the demographic data, period of courtship, the knowledge of SCD transmission and what would happen if both prospective partners were carriers. Data analysis was done using version 16 of SPSS. Frequency distribution tables, and chi-square tests were used in the data analysis. Statistical testing was based on *P* value of 0.05 and confidence interval of 95%.

Results

A total of 430 questionnaires were distributed between November 2010 and October 2011, 424 were analyzed, six were rejected on account of mistakes and wrong entries in the questionnaires, giving a response rate of 98.6% or 424/430.

The mean ± SD of the ages of the male subjects was 33.58 ± 7.346 years, while that of the females was 26.28 ± 4.377 years [Table 1]. The mean ± SD of period of courtship was 10.64 ± 16.809 months, ranging from 0 to 120 months.

The most frequent age group (age groups in decades) of the male respondents (58.5%) was 31-40 years ($X^2 = 183.623$, df = 3, $P = 0.000$) while that of the female respondents (75.5%) was 21-30 years ($X^2 = 169.509$, df = 2, $P = 0.000$) [Table 2]. Most male respondents (93.4%) were ≤ 40 years, while female respondents were mostly (86.6%) ≤ 30 years. The most frequent period of courtship (54.7%) among the subjects was one to six months followed by seven to twelve months group. The analysis showed that most partners (81.1%) had period of courtship ≤12 months ($X^2 = 194.792$, $df = 4$, $P = 0.000$).

There was a significant correlation (2- tailed) between the male age and that of the female ($P = 0.000$), [Table 3].

Marched haemoglobin genotype showed 48.1% or 102/212 of the prospective couples were HbAA/AA with no risk of SCT to their offspring, while in 47.2% or 100/212, one of the prospective partners had HbAA, and the other had HbAS (i.e. HbAA/AS combined) with a 50:50 chance of their offspring being carrier of the SCD and normal genotype [illustrated in Figure 1]. Added together, 95.3% or 202/212 couples have no risk of having offspring with sickle cell anaemia. In 1.9% or 4/212 of couples one prospective partner was HbAA, while the other partner was HbSS (i.e. HbAA/SS combined). There was a hundred percent chance of their offspring being carriers of the SCD (i.e. HbAS) [Figure 2]. In 2.8% or 6/212 of the couples each of the partners was HbAS (i.e. combined HbAS/AS). There was 1:4 chance of their offspring being HbSS (SCA) and normal phenotype (HbAA), respectively, while there was 50% chance of their offspring being HbAS (SCT), [Figure 3].

The male:female ratio of Hb AA was 1: 1.05, or 48.7% and 51.3% respectively, while the male: female ratio of Hb AS was 1:0.87 or 53.65 and 46.4% respectively [Table 4]. There was an equal ratio of HbSS (0.9%) for both sexes.

Majority (72.6% or 308/424) of the respondents had HbAA (normal genotype), 26.4% or 112/424 were HbAS (SCT), while 0.94% or 4/424 were HbSS (SCA). A higher percentage of females than males were HbAA, 51.3% and 48.7%, respectively. A higher percentage of males compared to the females were HbAS, 53.6% and 46.4%, respectively.

Higher percentage of the males from Sabbath (100% or 2/2)

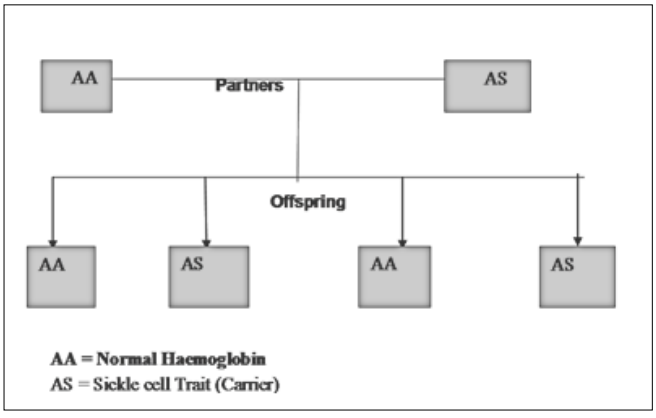

Figure 1: Genetic inheritance from parent by offspring (normal and carrier) partnersoffspring

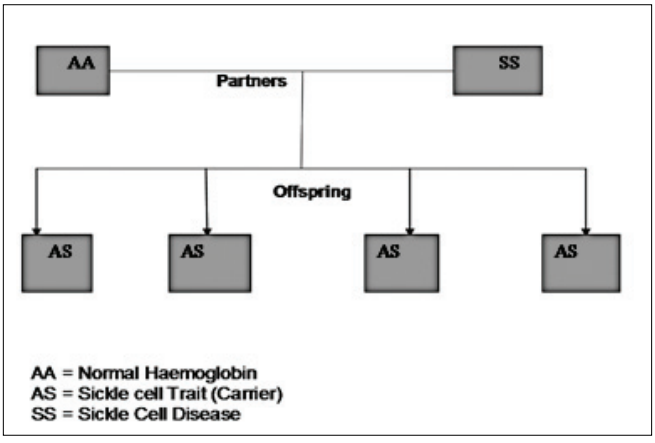

Figure 2: Geneti inheritance in offspring (normal and SCA) partners offspring

and Catholics churches (77.3% or 68/88) admitted that they would change their decision and stop the marriage if the test proved that both partners were carriers HbAS. This was followed by the Anglicans and finally the Pentecostals [Table 5]. The difference was statistically significant ($X^2 = 24.704$; df = 6; $P = 0.000$).

Table 1: Descriptive statistics of subjects

	Age of male	Age of female	Period of courtship
N	212	212	212
Mean	33.58	26.28	10.64
Std. deviation	7.346	4.377	16.809
Skewness	2.707	0.490	3.850
Std. error of skewness	0.167	0.167	0.167
Range	52	22	120
Minimum	23	18	0
Maximum	75	40	120

Table 2: Frequency distribution of age group and period of courtship among subjects

	Frequency	Percentage	Cumulative percentage	⊠²	Df	*P* value
Male age group (years)						
21-30	74	34.9	34.9	183.623	3	0.000
31-40	124	58.5	93.4			
41-50	10	4.7	98.1			
>50	4	1.9	100.0			
Female age group (years)						
≤20	24	11.3	11.3	169.509	2	0.000
21-30	160	75.5	86.8			
31-40	28	13.2	100.0			
Period of courtship (months)						
0	2	0.9	0.9	194.792	4	0.000
1-6	116	54.7	55.7			
7-12	54	25.5	81.1			
13-24	26	12.3	93.4			
≥25	14	6.6	100.0			

Similarly, a higher percentage of Catholic females (78.6% or 66/84) admitted that they would stop the marriage if both partners were found to be carriers (HbAS). This was followed by Anglican (69.2% or 36/52) and Pentecostals (55.6% or 40/72) and Sabbath 50% [Table 5]. The difference was statistically significant ($X^2 = 12.684$; df 6; $P = 0.048$).

Discussion

The analysis in this study was done using data from interviewer administered questionnaire on 212 prospective couples (i.e. 424 subjects) studied between November 2010 and October 2011. It was not surprising that the mean age of the males was higher than that of the females. It appeared plausible that the females reach physiological maturity faster than the males. On the average, female subjects tended to marry at a much younger age than the males. This tendency was observed in this study and

Table 3: Correlations test between the ages of males and females prospective couples

		Age of the male spouse	Age of the female spouse
Age of the male spouse	Pearson Correlation	1	0.478**
	Sig. (2-tailed)		0.000
	N	212	212
Age of the female spouse	Pearson Correlation	0.478**	1
	Sig. (2-tailed)	0.000	
	N	212	212

**Correlation is significant at the 0.01 level (2-tailed)

Table 4: Frequency distribution of Hb genotype according to the sex of respondents

Hb Genotype	Hb AA (%)	Hb AS (%)	Hb SS (%)	Total
Male	150 (48.7)	60 (53.6)	2 (50.0)	212
Female	158 (51.3)	52 (46.4)	2 (50.0)	212
Total	308 (100.0)	112 (100.0)	4 (100.0)	424

Table 5: Cross tabulation of religious denomination and decision to complete the marriage

	Will your decision to marry change						
Religious denomination	Don't know (%)	No (%)	Yes (%)	Total	⊠²	Df	*P* value
Male response							
Anglican	0 (0.0)	18 (33.3)	36 (66.7)	54	24.704	6	0.000
Catholic	12 (13.6)	8 (9.1)	68 (77.3)	88			
Pentecostal	14 (20.6)	16 (23.5)	38 (55.9)	68			
Sabbath	0 (0.0)	0 (0.0)	2 (100.0)	2			
Total	26 (12.3)	42 (19.8)	144 (67.9)	212			
Female response							
Anglican	6 (11.5)	10 (19.2)	36 (69.2)	52	12.684	6	0.048
Catholic	6 (7.1)	12 (14.3)	66 (78.6)	84			
Pentecostal	14 (19.4)	18 (25.0)	40 (55.6)	72			
Sabbath	0 (0.0)	2 (50.0)	2 (50.0)	4			
Total	26 (12.3)	42 (19.8)	144 (67.9)	212			

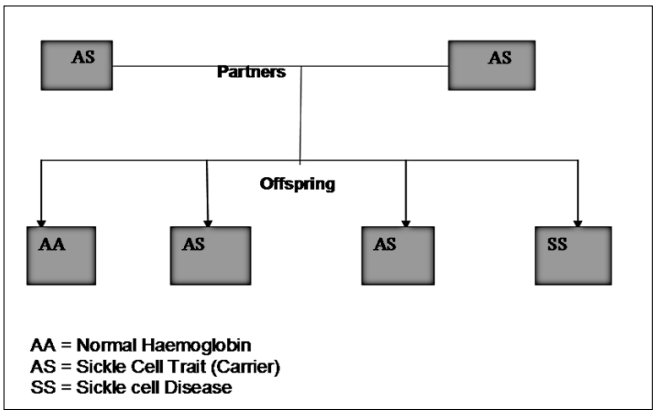

Figure 3: Genetic inheritance (carrier or SCT in both partners) partn ers offspring

reported by UNICEF.[12] The most frequent age group of the male subjects was about 10 years older than the most frequent age group of the female subjects. This finding coupled with the difference in the mean ages of both sexes went further to confirm the difference in the gender age at which marriage was contemplated in African traditional setting. There was a statistically significant correlation ($P = 0.000$) between the age of the male and their female partners such that both increased or decreased together. In the case of the male subjects, societal expectation was that they would have achieved socio-psychological maturity, and economic independence to be able to fend for their wives, and members of the extended family system, which characterized the traditional African society.[13,14] This implied that the male subjects should have completed their education or trade apprenticeship before contemplating marriage. This would probably not happen before the third decade of life (i.e. between 30 to 40 years of age).

The period of courtship found in this study agreed with what was found in the modern African setting in which the period of courtship was supervised by the parents of the prospective couple to ensure that sexual intercourse was restricted.[13] Modernization and Christianity have brought a lot of influence on the tradition of the people. All the subjects were Christians from different denominations.

The frequency of HbAS/AS (2.8%) found in this study was slightly higher than 2.3% found in Turkey by Altay *et al*.[6] These findings coupled with the finding that a high rate of respondents admitted that they would call-off the marriage if both couples were carriers of SCD (HbAS) was an indication that awareness of the transmission of SCD among premarital couples was high. This study did not find any other variants of haemoglobinopathies. This finding agrees with views expressed in many literature that other variants of haemoglobinopathies were very rare in this environment when compared to the Mediterranean region.[1,10]

There was a statistically significant association between the decision to discontinue the marriage and the Christian denomination of each partner. This could be attributed to the efforts of the churches in creating awareness among their faithful on how sickle cell disease could be transmitted and the need for premarital screening and control of SCD. Further studies would be needed to examine the effect of the churches on premarital screening of their faithful.

The frequency of subjects with normal genotype (72.6%) and carrier (26.4%) were comparable to the finding in other studies in Nigeria. Taiwo *et al*. found 73.1% and 24.5% for normal genotype and carriers, respectively.[10] However, the frequency of SCA in this study was lowest when compared with other studies in this environment. The reason is probably because majority of children born with SCA die before the age of five years so that the age specific prevalence of SCA would fall as the age of subjects increased. This figure was higher than the figure reported by Alhamdan in Saudi Arabia.[8] The probable explanation being that SCA was commoner than other haemoblobinopathies in sub Saharan Africa than the Mediterranean region where Thalassemia and other variants of haemoglobinpathies were commoner.[15] This finding agrees with the reports that approximately one quarter of the population was carrier of the SCD trait especially in sub Saharan Africa.[16]

Genetic counselling of these set of prospective spouses would require skill and knowledge on how to convey the facts, while allowing the prospective couples make well informed decision. The physician's role during the counselling would be to guide the prospective partners to make well informed decision and to avoid imposition of decisions with its attendant consequences.

In conclusion, a low percentage of prospective couples (2.8%) were found to have 1:4 chances of their offspring inheriting SCA (HbSS), while an overwhelming majority of the couples (95.3%) did not have risk of their offspring inheriting SCA. Majority of the respondents would call-off their proposed marriage if there was risk of their offspring having SCA. This study found a high proportion of premarital couple (72.6%) having normal haemoglobin genotype (HbAA), while slightly more than one quarter (26.42%) had SCT.

Recommendation: Further studies would be needed to examine the effect of the churches on premarital screening of their faithful. There is need for haemoglobin screening in adolescents to prevent premarital couples from frustrations and other emotional problems of having to reject prospective partners after screening.

Limitations of this study include counselling of the couples

and maintenance of confidentiality between the couples. However, these did not affect the results of the study.

References

1. Ohls RK, Christensen RD. Development of Haematopoeitic system. In: Behram RE, Kliegman RM, Jenson HB, editors. Nelson Textbook of Paediatrics. 17th ed. Philadelphia: Saunders; 2004. p. 1601-4.
2. Serjeant GR, Serjeant BE. Sickle Cell Disease. 3rd ed. Oxford: Oxford University Press.; 2001.
3. Weatherall D, Akinyanju O, Fucharoen S, Olivieri N, Musgrove P. In: *Disease* Control Priorities in Developing Countries. Jamison DT, *et al.* editors. Oxford University Press; 2006. p. 663-80.
4. Acharya K, Lang LW, Ross LF. A pilot study to explore knowledge, attitudes and beliefs about sickle cell trait and disease. J Natl Med Assoc 2009;101:1163-72.
5. Alao OO, Araoye M, Ojabo C. Knowledge of sickle cell disease and haemoglobin electrophoresis: A survey of students of a tertiary institution. Niger J Med 2009;18:326-9.
6. Altay C, Yilgor E, Beksac S, Gurgey A. Premarital screening of haemoglobinopathies: A pilot study in Turkey. Hum Hered 1996;46:112-4.
7. Guler E, Caliskan U, Ucar Albayrak C, Karacan M. Prevalence of beta- thalassemia and sickle cell anaemia trait in premarital screening in Konya urban area, Turkey. J Pediatr Hematol Oncol 2007;29:783-5.
8. Alhamdan NA, Almazrou YY, Alswiadi FM, Choudrhry AJ. Premarital screening for thalassemia and sickle cell disease in Saudi Arabia. Genet Med 2007;9:372-7.
9. Al-Arrayed SS, Hafadh N, Al-serafi S. Premarital counseling and experience from Bahrain. East Mediterr Health J 1997;3:415-9.
10. Taiwo IA, Oloyede OA, Dosumu AO. Frequency of sickle cell genotype among the Yorubas in Lagos: Implications for the level of awareness and genetic counseling for sickle cell disease in Nigeria. J Community Genet 2011;2:13-8.
11. Cochran WG. Sampling techniques. 2nd ed. New York: John Whiley and Sons Inc; 1963.
12. UNICEF Innocenti Research Centre. Early Marriage. Child Spouses. Innocenti Digest, 2001: (7); 4-7.
13. 'Final Report on National Baseline Survey of Positive and Harmful Traditional Practices Affecting Women and Girls in Nigeria, Centre for Gender and Social Policy Studies. Ile-Ife: Obafemi Awolowo University; 1998.
14. Caldwell JC. Caldwell P. 'Role of Marital Sexual Abstinence in Determining Fertility: A Study of the Yoruba in Nigeria'. Popul Stud (Camb) 1977;31:193-217.
15. Esan GJ. The Thalasaemia syndromes in Nigeria. Br J Haematol 1970;19:47-56.
16. Omotade OO, Kayode CM, Falade SL, Ikpeme S, Adeyemo AA, Akinkugbe FM. Routine screening for sickle cell haemoglobinopathy by electrophoresis in an infant welfare clinic. West Afr J Med 1998;17:91-4.

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