Original Article

Discordance between self-reported premarital and post-marital parental sickle cell status

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ABSTRACT

Background: Sickle cell disease (SCD) is an autosomal recessive disorder with mutation in the hemoglobin gene. Sickle cell anemia (SCA), the homozygous state, has adverse effects. Community knowledge regarding personal sickle cell status and the inheritance pattern of SCD remain inadequate. Moreover, the influence of wrong laboratory sickle screening result has not been elucidated. **Objectives:** The objectives of the study were to determine the impact of self-reported parental sickle cell screening, parental understanding of the inheritance pattern of SCA, and prevalence of discordant screen results. **Materials and Methods:** A cross-sectional clinic-based survey was conducted. Short interviewer-administered questionnaire was used to obtain biodata, history and availability of parental screening and results, understanding of the mode of inheritance of SCA, and decisions about marriage with at-risk partners before marriage. There were 74 parents enrolled by consecutive sampling. Chi-square and Fisher's exact test were used to analyze inferential variables such as discordant premarital screen result, relationship between premarital screening, and knowledge of mode of inheritance. The prevalence of screening, knowledge of mode of inheritance, and other descriptive data were analyzed with frequency and percentage tables using SPSS version 25. **Results:** Parents with premarital screen were 39 (52.7%) and 51 (68.9%) had post-marital screen. Discordance was observed between premarital (AS/AA and AA/AA) and post-marital (AS/AS) screen results ([32 (82.1%); 7 (17.9%)] [$p<0.001$]). A significant relationship existed between knowledge of mode of inheritance and premarital screening in fathers and mothers ([85.0%; 87.5%] [$p\leq0.001$; 0.003], respectively) as well as socioeconomic class ($p=0.010$; 0.019). The difference between unwillingness to marry 57 (81.4%) and willingness to marry 13 (18.6%) was significant ($p\leq0.001$). **Conclusion:** Knowledge of personal sickle cell status seems to be marred by poor access to proper diagnostic tools. This supports the need to enhance policy efforts toward proper diagnosis within the country.

Key words: Discordance, Parental, Screening, Self-report

Sickle cell anemia (SCA) is a common erythrocyte disorder caused by a homozygous point mutation in the hemoglobin beta gene with variable clinical manifestations [1,2]. Sickle cell mutations are common in sub-Saharan African region more-so in Nigeria. Recently, sickle cell disease (SCD) has been declared a public health problem [3]. Studies in the past decades suggest that community knowledge regarding personal sickle cell status and the inheritance pattern of SCD remain inadequate [4,5].

In addition, low-income countries like Nigeria, where the disease is prevalent, lack access to proper and sophisticated diagnostic tools [6]. In Nigeria, screening efforts have remained largely limited to the traditional hemoglobin solubility tests (HSTs) associated with false positives [7]. It is crucial to identify best screening methods for detecting sickle cell hemoglobin in high-risk populations [3,8,9].

To date, no studies have examined the impact of laboratory determined parental sickle cell screening status. The main objective of this study was to compare self-reported parental pre- and post-marital screen results, ascertain the relationship between parental understanding of inheritance pattern of SCA and premarital screening and that between premarital screen result and unwillingness to marry spouse using appropriate statistical tools for inferential and descriptive data.

MATERIALS AND METHODS

A cross-sectional study was conducted between March 2020 and June 2020 among parents of children with SCA attending the SCD clinic of the Department of Pediatrics of Enugu State University

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Teaching Hospital, Nigeria. The Institutional Review Board of the Enugu State University Teaching Hospital, Enugu, Southeast Nigeria, approved this study. Using the consecutive sampling technique, participants were consecutively enrolled at each clinic visit. A total of 100 parents accompanying their children to the clinic were seen over a 4-month period. A total of 80 parents consented after due information were given, six had incomplete data bringing the final sample size to 74. A parent was excluded if the spouse was not available or he/she had incomplete data.

A short questionnaire was then administered to obtain a history of parental screening and results and availability of results before marriage or birth of off-spring (premarital screening/premarital screen results/availability of premarital screen result). History of parental screening, screening results, and result availability after marriage, birth, or SCA diagnosis of off-springs were also obtained. The premarital screening results were compared with the post-marital results (discordant premarital screen result). Parents were asked if they understood the mode of inheritance of SCA before marriage (knowledge of mode of inheritance) and if they would have opted out of the marriage if appropriately informed before marriage (unwillingness to marry). Basic biodata of these parents such as age, highest educational level, and occupation was recorded. Social classification into Class I-IV was done using the parent's occupation and educational attainment as proposed by Oyedeji [10].

The information obtained were entered into Microsoft Excel sheet and analyzed using Statistical Package for the Social Sciences (SPSS) version 25. The statistics used was frequency and percentage for descriptive data such as prevalence of screening, knowledge of mode of inheritance, and unwillingness to marry. Chi-square test of independence, Chi-square multinomial test, and Fisher's exact test analyzed discordant premarital screening result, relationship between premarital screening and knowledge of mode of inheritance, and other inferential variables. The level of significance was 5%. $p<0.05$ was considered statistically significant.

RESULTS

Among the 80 respondents, six had incomplete data and were dropped. The age range of fathers and mothers was 28–70 and 22–58 years with mean and standard deviation of 44.57±9.34 and 37.04±8.17, respectively. The modal age group was 40–49 years (33.8%) for fathers and 30–39 years for mothers (41.9%).

A total of 39 (52.70%) parents indicated that they had undergone sickle cell screening test premaritally/preconceptually, 51 (68.9%) post-martially while 35 (47.30 %) had not undergone a premarital screening (Table 1).

A total of 32 (82.1%) of these self-reported premarital screening results (AA/AS or AA/AA) were discordant with their post-marital results (AS/AS). However, 7 (17.9%) were not discordant. Discordant result was significantly higher ($p<0.001$).

Table 2 shows a considerable number of parents 45 (60.8%), especially the mothers, 48 (64.9%) understood the mode of inheritance. More of the mothers 57 (77.0%) than the fathers 51 (68.9) would have opted out of the union if they knew better. Few parents could present either their premarital reports 15 (20.3%) or the post-marital reports 23 (31.1%).

On comparing the willingness and unwillingness to marry, a significantly large number of parents compared to what can be expected by chance would have opted out of marriage if they knew the status premaritally (81.4% vs. 18.6%); ($p\leq0.001$). Although 27 of the 32 (79.4%) parents with discordant premarital screen results had knowledge of mode of inheritance, this was not statistically significant than those with no knowledge.

However, Table 3 shows that premarital screening was significantly related with knowledge of mode of inheritance in both mothers and fathers (87.5 % vs. 85.0%); ($p\leq.001$, 0.003). For both, premarital screening was seen more among those that had knowledge of mode of inheritance. Socioeconomic class (SEC) had no influence on either having a premarital screening or unwillingness to marry.

Conversely, fathers and mothers in SEC 2 had more knowledge of mode of inheritance ($p=0.010$; 0.019), respectively (Table 4).

DISCUSSION

SCD is the most common genetic disorder in Nigeria and has been estimated to be the sixth leading cause of death in children aged

Table 1: Premarital and post-marital screening

Screening	Mothers (n=74)	Fathers (n=74)	Parent (n=74)
Premarital screening			
Yes	40 (54.1)	40 (54.1)	39 (52.7)
No	30 (40.5)	26 (35.1)	31 (41.9)
Not known	4 (5.4)	8 (10.8)	4 (5.4)
Post-marital screening			
Yes	55 (74.3)	52 (70.3)	51 (68.9)
No	16 (21.6)	14 (18.9)	16 (21.6)
Not known	3 (4.1)	8 (10.8)	7 (9.5)

Table 2: Knowledge of mode of inheritance, unwillingness to marry, and availability of screen results

Parameters	Mother (n=74)	Father (n=74)	Parent (n=74)
Knowledge of mode of inheritance			
Yes	48 (64.9)	45 (60.8)	45 (60.8)
No	22 (29.7)	21 (28.4)	24 (32.4)
Not known	4 (5.4)	8 (10.8)	5 (6.8)
Unwillingness to marry			
Yes	57 (77.0)	51 (68.9)	57 (81.4)
No	13 (17.6)	13 (17.6)	13 (18.6)
Not known	4 (5.4)	10 (13.5)	4 (5.4)
Availability of premarital screen result			
Yes	15 (20.3)	15 (20.3)	15 (20.3)
No	56 (75.7)	51 (68.9)	56 (75.7)
Not known	3 (4.1)	8 (10.8)	3 (4.1)
Availability of post-marital screen result			
Yes	27 (36.5)	23 (31.1)	23 (31.1)
No	42 (56.8)	42 (56.8)	44 (59.5)
Not known	5 (6.8)	9 (12.2)	7 (9.5)

<5 years [11]. The proportion of parents tested for this disorder before marriage is an indication that community awareness has not improved much as compared to studies a few decades back [4,5]. Obaro in North-Central Nigeria observed that only 13% of children aged <5 years had previously been tested for SCD concluding that screening is not available to the vast majority of infants in Nigeria [11]. The study underlined the need for provision of appropriate counseling, affordable testing followed by the provision of treatment centers for those diagnosed with SCD.

However, a significant proportion (82.1%) of these parents was given initial sickle screening results different from the repeat done following having an affected offspring. "Misreporting" of SCD is more common in older adult populations [12]. This could possibly be due to wrong performance of test results [11] as observed in the present study. While the discordant results underline the need for more reliable testing, the "misreporting" of adult sickle status may contribute to poor testing of their offsprings who are erroneously thought to have no risk. Other plausible reasons for misreporting of sickle cell status are the lack of verifiable documentation making the interpretation open to speculation [11], as observed in this study as many could not present the documents. Some parents may deny their test results, especially in communities, where the myth about SCD still exists [12].

Similar to a previous report in the United States [12], there was no significant difference by gender or education level in those misreporting SCD status, although adult population have previously been reported to commonly misreport their sickle cell status [12].

Table 3: Relationship between premarital screening and knowledge mode of inheritance

Premarital screening	Knowledge mode of inheritance			Chi-square	p value
	Yes	No	Total		
Mothers				12.287	<0.001
Yes	35 (87.5)	5 (12.5)	40		
No	13 (48.1)	14 (51.9)	27		
Fathers				8.737	0.003
Yes	34 (85.0)	6 (15.0)	40		
No	11 (50.0)	11 (50.0)	22		

Table 4: Relationship between SEC and knowledge of mode of inheritance

SEC	Knowledge of mode of inheritance			Fisher's test	p value
	Yes	No	Total		
Mothers				8.878	0.019
SEC 2	22 (88.0)	3 (12.0)	25		
SEC 3	16 (61.5)	10 (38.5)	26		
SEC 4	9 (69.2)	4 (30.8)	13		
SEC 5	0 (0.0)	2 (100.0)	2		
Fathers				10.202	0.010
SEC 2	21 (87.5)	3 (12.5)	24		
SEC 3	15 (62.5)	9 (37.5)	24		
SEC 4	8 (72.7)	3 (27.3)	11		
SEC 5	0 (0.0)	3 (100.0)	3		

Higher educational status in the higher SEC 2 may explain better knowledge of the mode of inheritance while additional factors such as coercion may have influenced premarital screening. Another survey of parents also reported significant misunderstanding of the mode of inheritance of SCD, although parents of affected children had a better understanding due to increased awareness in the affected families [13].

There are a few reports on the "validation" of self-report of SCD in the literature. In a recent report from the United States on the discordance between self-report and genetic confirmation of SCD status in African-American adults, Bean *et al*. observed discordance of 94.1% more than 82.1% of this study [12]. The lower level may be due to comparison with self-reported post-marital screen result rather than the highly reliable DNA genotyping. However, the high level of discordance observed by them was unexpected; coming from an affluent setting, where universal newborn screening has been established for several years and national awareness about the knowledge of SCD has been raised. They concluded that there is a need for increased efforts to raise community awareness and knowledge of SCD.

In a survey restricted to postpartum African-American women, 37% could not recall their results and 4% incorrectly reported their status [14]. In contrast, the parents in this study could recall screening and screen results, but a significant number could not present their results for verification.

Obaro *et al*. in Nigeria identified high-performance liquid chromatography (HPLC) a better screening tool than alkaline gel electrophoresis used by the subjects [11]. Of 163 (15.3%) parents, 25 reported incorrect hemoglobin phenotype of their offsprings obtained by electrophoresis from those obtained by HPLC. It was concluded that quality assurance in laboratory diagnosis should be promoted. Thus, wrong laboratory diagnosis could contribute to "misreporting" of sickle cell status. This scenario may be partly applicable to the present study because the error prone electrophoresis has been the standard in Nigeria. Further study is needed to validate this. The wide variation in the level of discordance between this study and that of Obaro *et al.* implies that affected, and thus, better informed parents may have done the post-marital test at more reliable centers [11].

Other affordable and reliable screening methods to minimize "false reports" in resource-limited countries include the use of insoluble hemoglobin add-on (modified HST) [15,16]. This was noted to be the most accurate when compared with DNA genotyping results. The study followed the observation of 88.1% discordance between self-reported screen results and that of traditional HST. This can be compared to 82.1% in the present study. There is, therefore, similarity in discordance when self-reported sickle cell screening results are compared with traditional screening tools in the community.

The study had a few limitations. The limited financial resources and equipment would not permit the validation of self-reported results.

CONCLUSION

Improved screening efforts and understanding of the inheritance pattern of SCD should be supported by enhanced quality assurance in laboratory diagnosis. Further studies on validation of self-reported SCD status are required.

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