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# Sickle cell disease: caregiver's awareness and phenotype distribution among children presenting to children emergency of a tertiary hospital in Lagos, Nigeria

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**Abstract***: Background:* Sickle cell disease accounts for significant morbidity and mortality in sub-Saharan Africa and the burden is expected to increase further by 2050. Nigeria is known to bear the highest burden of sickle cell disease in the world with about 2.69–5% of the population affected by the disease.
*Aim:* This study determined awareness of sickle cell disease among caregivers and phenotype distribution of children presenting to children emergency in Lagos University Teaching Hospital (LUTH), Nigeria.
*Methods:* The study was cross-sectional and descriptive in design and data was collected using a pretested, structured interviewer-administered questionnaire among 250 caregivers and children. HemoTypeSC™ rapid test kit was used to determine the hemoglobin phenotype in whole blood of the respondents who were consecutively recruited following the caregiver's consent. The Statistical Package for Social Sciences version 21 software was used for analysis.Univariate and bivariate analyses were carried out with a level of significance set at $p \leq 0.05$.
*Results:* The mean age of the children was 50.27±50.91 months. There were more females 141 (56.4%) than males. Almost all 242 (96.8%) caregivers did not know the children's Hb phenotype. Most 173 (69.2%) of the children had HbAA;55(22.0%) were HbAS; 6(2.4%) were HbAC; 15 and 1 (6.0% and 0.4%) were HbSS and HbSCphenotypes respectively. Education was statistically significant with awareness of SCD (p=0.002) and awareness of SCD was statistically significant with knowledge of prevention (**p<0.001**) among the caregivers.
*Conclusion:* Awareness of SCD among the caregivers of children was high, although the majority of them did not know the children's Hb phenotype. Most of the children had HbAA with a high proportion of HbSS and HbSC phenotypes. A routine neonatal/early infant screening program for SCD is highly recommended in Nigeria for early diagnosis and prevention of SCD complications.

**Keywords:** Sickle cell disease, awareness of caregivers, phenotype distribution of children.

## Introduction

Sickle cell disease (SCD) is a genetic disorder affecting red blood cells, with high morbidity and mortality rates.[1] The high morbidity and mortality caused by SCD and its significant social and economic impact have made the United Nations recognize SCD as a global public health concern.[2,3] The high prevalence of SCD in sub-Saharan Africa has been documented, where it accounts for significant morbidity and mortality, and the burden on sub-Saharan Africa is expected to increase to 88% of cases by 2050.[4,5,6] Nigeria is known to bear the highest burden of SCD in the world with about 2.69–5% of the population affected.[7,8] Early diagnosis of SCD is important as early commencement of appropriate standardized comprehensive care can reduce morbidity and mortality due to SCD.[9,10]

Despite having the highest burden of sickle cell disease in the world, Nigeria does not have routine haemoglobin (Hb)phenotype screening program and most people with SCD are identified when they present with symptoms and the diagnosis is usually confirmed by qualitative electrophoresis, which is difficult to access and very

costly.[11] A study in Nigeria among children with confirmed Hb phenotype found that none of the children aged eleven months to eighteen years presented for routine screening but the diagnosis was made following the development of symptoms and complications.[12]
The limitations of the usual diagnostic methods for SCD which include cellulose acetate electrophoresis, isoelectric focusing, mass spectrometry, and high-performance liquid chromatography (HPLC) have made early SCD screening difficult especially in low-income settings like Nigeria. However, inexpensive easy-to-use tests based on different diagnostic principles, which have been able to differentiate common haemoglobin phenotypes and can be used at remote sites, have been developed.[4] Studies in Nigeria have demonstrated the use of affordable, reliable, and accurate methods of diagnosis including an ELISA-based point-of-care test (HemoTypeSC), and documented that the HemoTypeSC test had 100% sensitivity and specificity for SCD in early infancy.[4,1314]

New potentially curative therapies for SCD are emerging with increasing evidence-based preventive strategies; therefore, new approaches may be required to increase the parents/caregivers' awareness of children's phenotype early enough to prevent complications, which could be detrimental. Hence, this study determined awareness of SCD among caregivers and phenotype distribution of children presenting to children emergency in Lagos University Teaching Hospital (LUTH), Nigeria with the use of a point-of-care screening test (HemoTypeSC) and follow-up of the children detected with SCD for early commencement of management.

## Materials and Methods

*Background information to study area*

This research was carried out at the children emergency (CHER) of the Lagos University Teaching Hospital (LUTH). Lagos University Teaching Hospital is a major referral center serving the whole of Lagos State and several adjoining states in the southwest geopolitical zone of Nigeria. It is an over 700-bed facility occupying 92 acres of land making it one of the largest teaching hospitals in Nigeria.

*Study design, data collection tool, and sample size calculation*

The study was a cross-sectional and descriptive design with quantitative data collection methods using a pretested, structured interviewer-administered questionnaire. Face validity of the questionnaire was done by the subject's expertise. It comprised four sections; section A consisted of socio-demographic characteristics of parents/caregivers. Section B assessed socio-demographic characteristics of the child, while section C assessed awareness of sickle cell disease among caregivers. The tool was pretested among 25 caregivers in a similar but different health institution for accuracy and adequacy. The questionnaire was written in the English Language.
The study took place between September and November 2020.The Cochran formula for the descriptive study was used for sample size calculation ($n=z^2pq/d^2$)[15] with a standard normal deviation at 95% confidence interval (1.96), the prevalence of SCD as 3% from a study on screening for sickle cell disease in a Nigerian hospital in Nigeria,[8] error of precision at 2.5% and an additional 20% to allow for missing or incompletely filled questionnaires, hence, 250 caregivers and children pairs were recruited for the study. Caregiver consent was adequately sought before recruitment and critically ill children were excluded.

*Selection of participants*

Eligible participants for the study were consecutively recruited based on the inclusion criteria until the sample size was attained.

*Testing procedures*
*HemoType SC Test Kits*

HemoTypeSC™ (Silver Lake Research Corp., USA)is a rapid test kit intended for in vitro diagnostic use by health professionals to determine the presence of hemoglobin A, S, and C in whole blood. It is based on competitive lateral flow immunoassay incorporating monoclonal antibodies for the determination of the presence of hemoglobins A, S, and C to provide rapid detection of hemoglobin phenotypes HbAA, HbSS, HbSC, HbCC, HbAS, and HbAC.

*Phenotype Testing*

Pre counseling was conducted by the trained counselor for each caregiver before the test was conducted on the child. Blood samples from babies six weeks and below were drawn by heel-prick, while those from older infants were collected by finger-prick. Approximately 1µl of blood was absorbed into the point of care testing device absorbent pad for testing. The result of the phenotype test was communicated to parents following a post counseling session. All infants positive of SCD with the rapid kit were referred for high-performance liquid chromatography Hemoglobin Testing (HPLC) diagnostic test at sickle cell foundation for Nigeria and following confirmation, were referred to the sickle cell disease clinic in Lagos University Teaching Hospital for management.

*Data analysis*

Data analysis was done using the Statistical Package for Social Sciences (SPSS) version 21. Univariate and bivariate analyses were conducted with a level of significance set at $p \leq 0.05$.

*Ethical considerations*

The nature of the study was explained to the participants and written; informed consent was obtained from each caregiver before recruitment into the survey. Ethical clearance was obtained from the Health Research and Ethics Committee of Lagos University Teaching Hospital (ADM/DCST/HREC/APP/3781).The participants were made to understand that participation was voluntary.

## Results

Table 1: Socio-demographics characteristics of caregivers and children
Table 1 shows that 181 (72.4%) of the caregivers were mothers and most 194 (77.6%) were between 31-50years with a mean age of 36.6±6.6years. About half 131 (52.4%) had a tertiary level of education. Furthermore, most 168(67.2%) of the children were between 0 and 60 months with a mean age of 50.27±50.91 months. There were more females 141 (56.4%) than males, and the majority 235 (94.0%) did not have a family history of SCD.

Table 2: Awareness of sickle cell disease among caregivers
Table 2 shows that almost all the caregivers 245 (98.0%) were aware of SCD. The major source of information was health professionals 175(70.0%). Almost all of the respondents 242 (96.8%) did not know the child's Hb phenotype. However, four (1.6%) of the children were known HbSS patients, and 2(50%) were diagnosed at 5years of age. The Hb phenotype of most mothers 138 (55.2%) and fathers 161(64.4%) was not known. Less than half 87 (34.8%) of the caregivers had premarital Hb phenotype screening done. Almost all the caregivers 242 (96.8%) did not know that SCD can be screened in the newborn period, while 181 (72.4%) did not think it was a good practice to screen newborn babies of Hb phenotype. However, the majority 233 (93.2%) knew that SCD can be prevented and all (100%) were willing to screen the children for Hb Phenotype.

**Table 1:** Socio-demographics characteristics of caregivers and children

| Variable | Frequency (N=250) | Percentage (%) |
|---|---|---|
| *Relationship of caregiver to child* | | |
| Father | 62 | 24.8 |
| Mother | 181 | 72.4 |
| Others | 7 | 2.8 |
| *Age of caregiver (years)* | | |
| 0-30 | 49 | 19.6 |
| 31-50 | 194 | 77.6 |
| >50 | 7 | 2.8 |
| Mean age = 36.6±6.6 | | |
| *Highest level of education of caregiver (completed)* | | |
| Primary | 10 | 4.0 |
| Secondary | 109 | 43.6 |
| Tertiary | 131 | 52.4 |
| *Age of child (months)* | | |
| 0-60 months | 168 | 67.2 |
| >60months | 82 | 32.8 |
| *Sex of child* | | |
| Female | 141 | 56.4 |
| Male | 109 | 43.6 |
| *Family history of SCD* | | |
| Yes | 15 | 6.0 |
| No | 235 | 94.0 |
| *Past illness in child* | | |
| Yes | 111 | 44.4 |
| No | 139 | 55.6 |
| *History of routine medication in child* | | |
| Yes | 59 | 23.6 |
| No | 191 | 76.4 |

**Table 3:** Association of socio-demographic characteristics of caregivers and awareness of SCD

| Socio demographic variables | Awareness of SCD | | | |
|---|---|---|---|---|
| | Yes Freq. (%) 245 (98.0%) | No Freq. (%) 5 (2.0%) | Total Freq. (%) 250 (100.0%) | Test Statistics |
| *Age of caregiver (years)* | | | | |
| 0-30 | 47 (95.9) | 2 (4.1) | 49 (100.0) | $x^2$=2.031 |
| 31-50 | 191 (98.5) | 3 (1.5) | 194 (100.0) | p=0.363* |
| >50 | 7 (100.0) | 0 (0.0) | 7 (100.0) | |
| *Marital status* | | | | |
| Single | 3(100.0) | 0(0.0) | 3(100.0) | $x^2$=4.401 |
| Married | 238 (97.9) | 5 (2.1) | 243 (100.0) | p=1.000* |
| Divorced/separated | 1 (100.0) | 0 (0.0) | 1 (100.0) | |
| Widowed | 3(100.0) | 0 (0.0) | 3(100.0) | |
| *Level of education* | | | | |
| Primary | 8 (80.0) | 2(20.0) | 10(100.0) | $x^2$=11.278 |
| Secondary | 106 (97.2) | 3(2.8) | 109 (100.0) | p=0.002* |
| Tertiary | 131(100.0) | 0 (0.0) | 131(100.0) | |
| *Religion* | | | | |
| Christianity | 186 (97.4) | 5 (2.6) | 191 (100.0) | $x^2$=1.567 |
| Islam | 59 (100.0) | 0 (0.0) | 59 (100.0) | p=0.594* |
| *Employment* | | | | |
| Self-employed | 148 (97.4) | 4(2.6) | 152 (100.0) | |
| Govt-employed | 45 (100.0) | 0 (0.0) | 45 (100.0) | $x^2$=2.551 |
| Private-employed | 35 (100.0) | 0 (0.0) | 35 (100.0) | p=0.402* |
| Unemployed | 17 (94.4) | 1 (5.6) | 18 (100.0) | |

*Fisher's exact test

**Table 2:** Awareness of sickle cell disease among caregivers

| Variables | Frequency (N=250) | Percentage (%) |
|---|---|---|
| *Aware of SCD* | | |
| Yes | 245 | 98.0 |
| No | 5 | 2.0 |
| *Source of information* | | |
| Health professional | 175 | 70.0 |
| Family/friends | 49 | 19.6 |
| Multiple sources | 26 | 10.4 |
| *Child's phenotype (known)* | | |
| AA | 3 | 1.2 |
| SS | 4 | 1.6 |
| Others | 1 | 0.4 |
| Don't know | 242 | 96.8 |
| *If child is known to have SCD, age at diagnosis(n=4)* | | |
| <6 months | 1 | 25.0 |
| <=1 year | 1 | 25.0 |
| >=5years | 2 | 50.0 |
| *Mother's phenotype* | | |
| AA | 67 | 26.8 |
| AS | 39 | 15.6 |
| AC | 6 | 2.4 |
| Don't know | 138 | 55.2 |
| *Father's phenotype* | | |
| AA | 46 | 18.4 |
| AS | 41 | 16.4 |
| AC | 2 | 0.8 |
| Don't know | 161 | 64.4 |
| *Premarital phenotype test* | | |
| Yes | 87 | 34.8 |
| No | 163 | 65.2 |
| *Knew that SCD can be screened in the new born period* | | |
| Yes | 8 | 3.2 |
| No | 242 | 96.8 |
| Thought it is a good practice to screen new-born of Hb phenotype | | |
| Yes | 52 | 20.8 |
| No | 17 | 6.8 |
| Don't know | 181 | 72.4 |
| Knew SCD could be prevented | | |
| Yes | 233 | 93.2 |
| No | 16 | 6.4 |
| Don't know | 1 | 0.4 |
| Agreed to screen child for Hb phenotype | 250 | 100.0 |
| Yes | | |

**Fig 1:** Phenotype distribution among participants

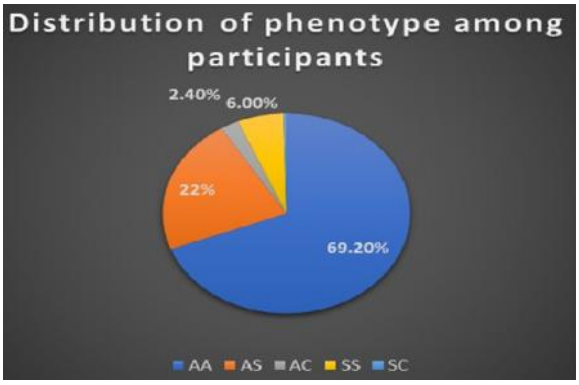


Figure 1:Phenotype distribution among participants

Figure 1 shows the majority 173 (69.2%) of the children were Hb phenotype AA, 55(22.0%) were AS; 6 (2.4%) were AC; 15 and 1 (6.0% and 0.4%) were SS and SC respectively. 4(25%) of the 16(100%) SS/SC children were already known SCD patients.

Table 3: Association of socio-demographic characteristics of caregivers and awareness of SCD

Table 3 shows an increase in the awareness of SCD among the caregivers with an increased level of education. Eight (80%) of those with primary education, 106 (97.2%) with secondary education, and all respondents who had tertiary education 131(100%) were aware of sickle cell disease. The association was statistically significant (p=0.002).

Table 4: Association of knowledge of prevention and awareness of SCD

Table 4 shows a statistically significant association between awareness of SCD and knowledge of its prevention (p<0.001). Almost all 232(99.6%) of the respondents who were aware of SCD knew that the disease could be prevented.

**Table 4:** Association of knowledge of prevention and awareness of SCD

| Variables | Awareness of SCD<br>Yes Freq. (%) 245 (98.0%) | No Freq. (%) 5 (2.0%) | Total Freq. (%) Freq (%) | Test Statistics |
|---|---|---|---|---|
| *Knew SCD could be prevented* | | | | |
| Yes | 232 (99.6) | 1 (0.4) | 233 (100.0) | $x^2$=21.130 |
| No | 12 (75.0) | 4 (25.0) | 16 (100.0) | p=0.000* |
| Don't know | 1 (100.0) | 0 (0.0)` | 1 (100.0) | |
| Had premarital screening for Hb phenotype | | | | |
| Yes | 87 (100.0) | 0 (0.0) | 87 (100.0) | $x^2$=2.723 |
| No | 158 (96.9) | 5 (3.1) | 163 (100.0) | p=0.166* |
| knew SCD can be screened in the new born period | | | | |
| Yes | 8 (100.0) | 0 (0.0) | 8(100.0) | $x^2$=0.169 |
| No | 237 (97.9) | 5 (2.1) | 242 (100.0) | p=1.000* |
| Good practice to screen newborn of Hb phenotype | | | | |
| Yes | 52 (100.0) | 0(0.0) | 52 (100.0) | $x^2$=2.455 |
| No | 16 (94.1) | 1 (5.9) | 17 (100.0) | p=0.242* |
| Don't know | 177 (97.8) | 4 (2.2) | 181 (100.0) | |

*Fisher's exact test

## Discussion

This study found a high prevalence of SCD among children attending children emergency in Lagos University Teaching Hospital and this is a pointer to the public health significance of SCD. The prevalence of the HbAA and HbSS/HbSC among the children was similar to a survey conducted in a teaching hospital in Lagos.[16] This is not a surprise as both studies were conducted in tertiary health institutions having specialists in the management of SCD and also serving as referral centers. The prevalence of HbAC in both studies were also similar.

The prevalence of SCD found in the present study (6.4%) was lower compared to a similar study among 400 children admitted to a teaching Hospital in North Darfur State, Sudan(14.8%).[17] Also, another study on the prevalence of sickle cell disease among children attending Plateau specialist hospital, Jos, Nigeria revealed that the prevalence of SCD in Jos from 2012 to 2014 was 26.9/1000 population among pediatric patients. [18] The differences observed may be due to the differences in sample sizes of the studies.

In this study, the proportion of participants who had performed Hb genotype testing before the survey interview was low(25.0%) while 75.0% were newly diagnosed during the research. This finding is similar to that of a study in Lagos.[16] This may be due to the lack of availability, accessibility, and affordability of SCD diagnostic tests in Nigeria, because the cheap and rapid testing kits are not yet available. The average cost of a diagnostic test for SCD in Nigeria is about N8,000($16).This makes effective and efficient SCD diagnosis not easily accessible and affordable with most of the population living below one dollar per day.[16]

About half of the participants in the present study with known Hb phenotype had their status diagnosed at or after 5years of age. This is similar to that of the study in Lagos which reported that only one-ninth of the subjects with known Hb phenotype status at the commencement of the study had their status confirmed before the age of 1 year.[16] Another study on age at diagnosis of SCD in Lagos, reported 27.33months ±26.36months as the mean age at confirmation of Hb phenotype.[19] The delay in diagnosis of SCD due to the lack of neonatal/infant screening programs in Nigeria predisposes the affected children to many complications which could be prevented by parental education and early diagnosis and treatment.[24] Some studies have demonstrated the feasibility and acceptability to implement an SCD screening intervention program in early infancy in Nigeria.[4,13,14] The establishment of a neonatal/early infant screening program for SCD which could be included in preventive services like routine immunization will go a long way in the early detection and treatment of SCD and avoidance of complications.

Our study revealed the significance of education on awareness of SCD. The proportions of respondents who were aware of SCD increased with the level of education and all those who had tertiary level of education were aware of SCD. The significance of education and awareness of SCD has been documented by studies.[20,21, 22] Awareness of SCD is essential for early screening and detection. If caregivers are educated, they are more likely to be aware of SCD, hence, are more likely to take preventive actions. This study also found a statistically

significant association between awareness and knowledge of prevention of SCD among the respondents.

## Conclusion

Awareness of SCD among the caregivers of children presenting to children emergency in LUTH was high, and level of education was significant with SCD awareness. The majority of the caregivers did not know the children's Hb phenotype status. Most of the children were HbAA but a high proportions were HbSS and HbSC phenotypes. A routine neonatal/early infant screening program for SCD is highly recommended in Nigeria for early diagnosis and prevention of SCD complications.

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**Authors' contributions**

OEO was responsible for concept and design of study, acquisition of data, analysis and interpretation of data; drafting the article and critical review.

TAA participated in the concept and design of the study and critical review of manuscript

BO participated in the in the acquisition of data and review of manuscript

PA participated in the concept and design of the study and final review of manuscript

All the authors approved the final manuscript. The requirements for authorship have been met, and each author declares that the manuscript represents honest work.

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