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Institutionalising New-born Screening for Sickle Cell Disease at the Federal Medical Centre, Asaba, Nigeria

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Abstract

Background: In the bid to decrease infant mortality, we introduced New-born screening for sickle cell disease with parental education and enrolment of the early diagnosed child into comprehensive care program at the Federal Medical Centre, Asaba.

Methods: The institution's ethical review Board approved the proposal. We systematically collected samples on dry blood spots from consecutively delivered babies after informed parental consent. We thereafter, shipped them to a regional laboratory where they were eluted and analysed on HPLC machine, Newborn Hb variant. Statistical analysis was by simple frequencies, means and standard deviations and chi square test. The level of significance was set at $p< 0.05$

Results: Two thousand four hundred and fifty one babies were delivered over 1st March 2017 to 28th February 2019. One thousand and thirty three of the total 2451 (42.2%) were sampled and results for 983 samples were available for the analysis. Seven different haemoglobin patterns were identified in these newborns. They are HbAA, HbAS, HbAC, HbAD, HbSS, HbAE and HbDD; and HbAA being the most predominant with a frequency of 74.9%.The prevalence of HbSS was 0.8% and the DD was 0.2% and 24. 2% were traits.

There was a high level of awareness of the disease among the mothers as many of them had knowledge of their Hb Phenotype before marriage. Eight hundred and forty-four (844) 81.7% knew about phenotype test while 706 (68.3%) had prior knowledge of their Hb phenotype.

Conclusion: The low prevalence of HbSS in this survey might have resulted from the high level of parental awareness and also from the fact that only 42.2% of births were screened. This emphasises the role of societal education and awareness for decreasing the prevalence of the disease.

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Introduction

Over 300,000 babies with sickle cell disease (SCD) are born annually, the majority in sub-Saharan Africa. The world's SCD population is concentrated in three countries: Nigeria, India, and the Democratic Republic of Congo where the disease affects up to 2 percent of the population and the carrier prevalence rate (sickle cell trait) is as high as 10 to 30 percent [1-3].

Systematic reviews suggest that universal screening is especially cost effective in populations with a high frequency of the prevalence of SCD >0.2 to 0.5 per 1000 births [4]. The threshold for screening for SCD (0.5 per 1000 births) in many countries in Africa far exceeds the minimum threshold for cost-effectiveness for new-born screening. In Nigeria the rate of SCD is estimated to be 300 per 1000 births [5]. New-born screening (NBS) programs allow for early detection and intervention, a method for primary prevention is included. This is actually the basis for the screening that exists in all the states of the United States of America [6-7]. World Health Organization (WHO) had actually identified the need for primary prevention of SCD screening in new-born period, genetic counselling, and accessible comprehensive care [8]. Yet in Sub-Saharan Africa, it is only available in a few centres that have been able to introduce this program [9-11].

Some of the countries of the Caribbean's and Jamaica have had long standing NBS screening programs and are able to show the impact of early diagnosis, education and early child care on mortality and morbidity [12,13]. SCD contributes significantly to infant and young child mortality particularly in Malaria endemic regions [14]. Sufferers of sickle cell disease are also highly susceptible to infections with encapsulated bacteria hence such infants succumb from these bacterial infections in early life. Infections have been implicated in as much as 20 to 50% of these deaths [15]. The increased susceptibility has been traced to impaired splenic function [15].

The Concept of NBS for sickle cell disease (SCD) arose because of various reasons. One of this is to inculcate appropriate health seeking behaviour through parental education on the underlying nature of the disease and thorough understanding of the causes of mortality and morbidity in this disorder. Studies of the splenic function had shown that complete waning can occur even by the end of the 3rd month of life and thereafter the risk of death from invasive Pneumococcal disease increases [16,17]. This strengthened the idea of the need for early identification and initiation of preventive measures soon after the birth for the affected infant. Early diagnosis and comprehensive care is currently the standard of care package for the affected child [16]. In 1986, Gasto MH and co-workers demonsrated that prophylactic penicillin markedly reduces the incidence of pneumococcal sepsis, [17] this provided a powerful incentive for the widespread

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implementation of neonatal screening for SCD [18]. New-born screening for haemoglobinopathies is now increasingly practiced globally. This is due to the numerous benefits accrued from the early diagnosis of haemoglobinopathies and related disorders through this genetic screening when done early enough, especially in the neonatal period [1,18,19] SCD contributes significantly to morbidity and mortality particularly in children who reside in malaria endemic regions [14].

The processes for the diagnosis of this disease has also gone through evolutionary process. Currently practices for screening include Hemoglobin electrophoresis through to High performance liquid chromatography (HPLC) [20]. Such HPLC techniques available for Newborn screening of Hemoglobin variants offer advantage for mass screening but are expensive to maintain [21]. More recently several point of care test kits have been evaluated and validated for use in mass screening. Such test kits are of particular interest in developing countries as they offer potentials for reduced cost of HPLC in mass screening of individuals. Whatever the tests, these would require confirmatory tests ulteriorly [20-24].

Federal Medical Centre Asaba, Delta State, Nigeria in March 2017 commenced systematic New Born Screening Programme (NBS) for haemoglobin phenotypes. We set out to provide new-born screening (NBS) services for all babies born at the FMC Asaba. This was in a bid to set up NBS for sickle cell disease Comprehensive care and early parental education.

The purpose of screening is to identify early infants with abnormal haemoglobin so as to enrol them into a comprehensive care, and provide parental education and follow up program a as well as to describe the patterns of the major haemoglobin phenotype patterns and other forms of identifiable haemoglobinopathies and ultimately to institutionalise NBS program.

Hitherto in Nigeria, systematic screening for the newborn has not become the norm because of financial constraints. Even though the important contribution of SCD to infant and U-5 mortality had been recognised and the contribution of hemoglobinopathy as a public health problem in the non communicable diseses in our communities had been recognised, it has not received the deserved attention because of various factors. The hemoglobinopathies are coming into focus as the communicable diseases of infancy are being tackled. In a bid to tackle this child survival issue of infancy, it is behoving to introduce this best practice that has contributed significantly to curtailment of infant and young child mortality to our environment with a projected high population of carrier individuals.

Materials and Method

The Proposal was approved by the Ethical review Board of the institution. Consecutively delibered newborns of consenting parents were recruited into the study. Blood samples from heel stics were obtained unto whartmans 903 protein server papers, dried and shipped in batches to the regional Laboratory. The High Performance Liquid Chromatography (HPLC) was the screening method utilised. All specimens were processed and analysed using the variant Newborn Screening (VARIANT™ nbs) HPLC machine (Bio-Rad, Hercules, California, USA). REF-NUMBER 250-3000. This system utilises standard techniques of electrophoresis using cation-exchange resin as the chromatographic column and two buffer reagents of sodium phosphate containing Sodium azide, pH 6.5 and pH 6.6 for establishing an HPLC gradient. These tests were performed according to the HPLC machine's manufacturer's instructions [21].

This machine and the technique is now widely available in Nigeria. The use of HPLC is a good choice to give reliable results, but it is recommended to validate screening results by a second method. Due to financial constraints, it was not done for these patients. Test results were sent electronically within 2 weeks of sample collection and parents were contacted upon receipt to return as they had been initially informed at home discharge from hospital. Upon receipt of the result, each parent was counselled by the NBS program Paediatric Haematologist irrespective of their status. The affected infants were then recruited into the comprehensive care program which refocssed parental education and recognition of the danger signs. The educational program equally highlighted the importance of good hydration, nutritious dietary and the importance of Immunisation in infancy and beyond. The importance of antimalarial therapy and attendance at regular clinic follow up clinic was equally emphasised. All SCD diagnosed infants had a second test with Hemo Type SC but could not have the DNA confirmatory test.

Prior parental awareness of Sickle cell disease was assessed through direct questioning at the point of newborn screening. The Hb electrophoresis of parents was not re-verified by laboratory testing.

The data were collected onto survey questionnaires. These were entered on Excell spread sheet and analysed using Statistical Package for Social Sciences (SPSS) software, version 22 (IBM, Armonk, NY, USA). Frequencies, Means and standared deviation were studied for categorical variables; chi square test was used for comparison of means. Statistical significance was set at $P< 0.05$.

Results

Two thousand four hundred and fifty one (2451) babies were delivered in the Centre during the period of this survey. However, only 1033 babies were screened, giving a screening rate of 42.15%. Of this one thousand, and thirty three (1033) babies that were screened, data for 983 babies are available for analysis.

General characteristics of the population

They were 520 (50.3%) males and 513 (49.7%) females giving a male to female ratio of 1.01:1.

Nine hundred and twenty-five (925) neonates representing 89.5% were sampled on the their first week of life. The mean age of population at screening was 2.1±3.7 days. Their weight ranged from 0.8- 5.2 kg with a mean weight of 3.02±0.84 Kg.

Five hundred and seventy-six (576/1033) 55.8% neonates are of Delta State origin, giving a ratio of indigene to non-indigene of 1.2: 1, and a proportion of 0.6. For every two babies screened, one is from Delta state as 62% of client of Department of Obstetrics, FMC Asaba are Delta Indigenes.

Phenotypes identified

Seven different haemoglobin pattern were identified in these newborns. They are HbAA, HbAS, HbAC, HbAD, HbSS, HbAE and HbDD, with HbAA with the highest frequency 74.9% Figure 1.

Figure 1 describes the haemoglobin variants of the studied newborns.

Classification of the Hb phenotypes

Seven hundred and thirty-six 736 (74.9%) babies had normal phenotype (AA), 273 (24.1%) were traits, while 10 (1.0%) had haemoglobinopathy (SS and DD) Figure 2.

Of the eight neonates identified with SCA, there were 5 males and 3 females .

One was a male, the first of a set of twins, who died of the complication of Birth Aphyxia in the neonatal period. The phenotype of the twin sister is AS, and the mother received counselling on the child's phenotype, the phenotype of the demised one was also conveyed to her.

Three out of the babies with haemoglobinopathy are presently enrolled on comprehensive healthcare program of the institution. Parents of one have relocated to another town and they were counselled on the importance of the follow-up. Parents of two babies refused to accept the result. One of the Parents who gave wrong address could not be reached.

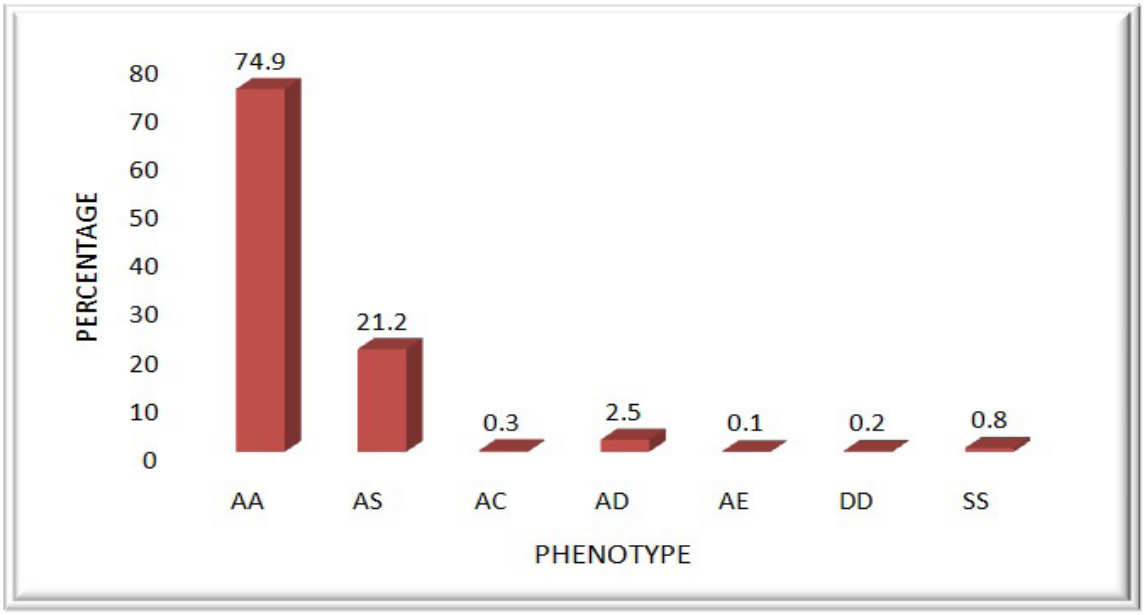

Figure 1: Prevalence of different haemoglobin phenotype.

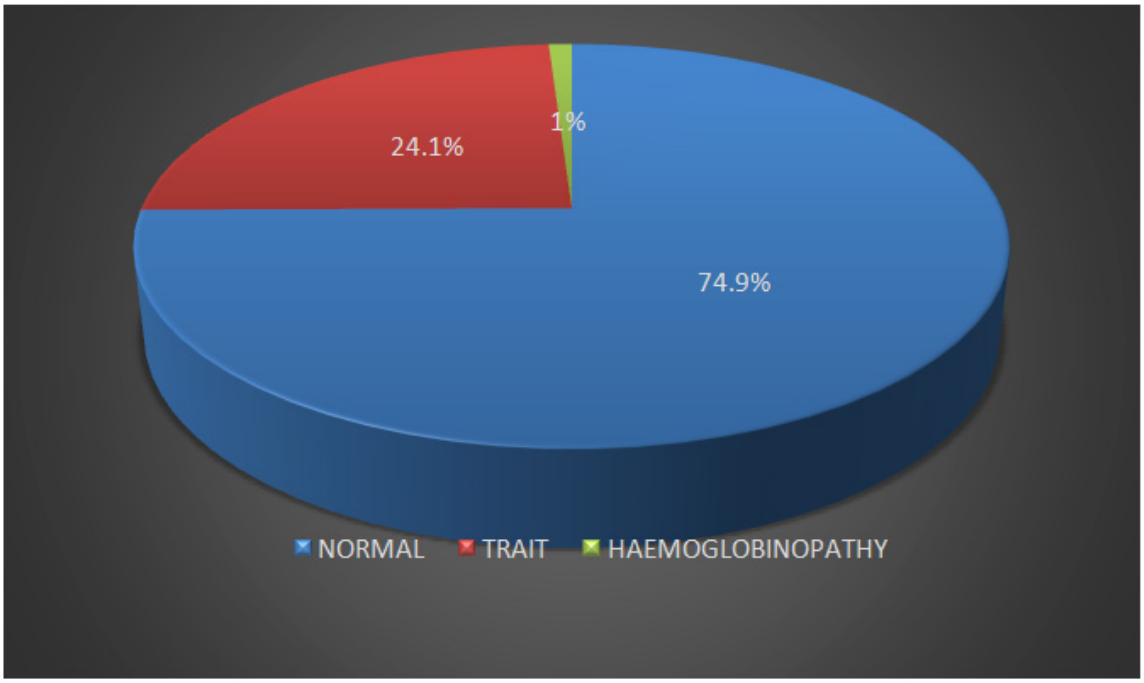

Figure 2: Classification of Phenotypes.

Three of the newborns identified to have HbAC are from Delta State (2) and the other from Imo State.

Prior parental knowledge of their genotypes

Eight hundred and forty-four (844) representing 81.7% knew about phenotype test while 706 of them respresenting 68.3% knew their Hb phenotype.

Discussion

The HbAA frequency of 74.9% is similar to what is identified in the general population in Nigeria [13-16]. Though this result is from the NBS it conforms with the findings from other studies. It may represent an indirect reflection of the acknowledged fact that up to 25 to 30 percent of the local population have abnormal Hb variants. The freqency of S phenotype, the traits, identified is 21.6%. This also similar to what is obtainable in the general population in Nigeria [26-29]. It is however lower than what has been described elsewhere in Nigeria [28,29]. This difference might have arisen due to the low numbers of newborns screened. Despite this low proportion of 0.81%, it is noted that this figure represents a high incidence when 1 of every 123 newborns screened has SCD. Despite the low numbers, it still justifies the initiation of newborn screening according to the WHO guidelines [8]. When compared to what has been reported by some authors in Nigeria [14,24,26-32] and some other parts of Africa [25,31,2] it is quite low. Relative to the other reports, this is a hospital based survey of newborns whereas those other surveys are from older age groups and are population based survey. This survey may therefore not convey the true picture of the burden of this problem. Community-based survey reflects the burden of any condition better than Hospital-based [29]. Thus there is therefore the need to extend the action to involve the community. Again, bearing in mind that only about 40% of deliveries occur in health facilities in Nigeria, [32] the rest are either at home with the help of the elderly women, or by Traditional Birth Attendents (TBAs). More efforts should be focused on how to reach these non facility delivered newborns.

The prevalence of SCD in this study is higher than what is observed for developed countries. This again reflects the population dynamics of the environment of such studies where the ethnic black population is low. In such climes, the introduction of NBS and comprehensive care for the newborn diagnosed child with SCD have significantly reduced mortality and morbidity from the burden of this disease [7,19,31-33]. The SCD high burden Low Middle Income countries(LMICS) of sub Saharan Africa to enable attainment of the sustainable development goals should adopt and implement this strategy.It therefore calls for the LMICS policy makers to refocus their attention to the public health needs of infants and young children.

It can also be inferred that another reason for the observed low prevalence of SCD in this survey is the high awareness of the mothers of their phenotype before marriage. Sixty eight point three percent of mothers claimed that they knew their Hb phenotype prior to marriage .Their claim was not authenthicated by the performance of a concurrent laboratory test. It therefore limits the extent to which the observed low prevalence can be ascribed to this information.

Given that the number and the percentage of deliveries screened was low, the smaal size of the population screened could have influenced the low incidence reported.It is however worthy of note that 1 out of 123 babies tested has sickle cell anaemia. This is a very high incidence and supports the idea of systematic screening of the newborn for SCD and enrollment into the comprehensive care. Diverse pattern of hemoglobin variants have been identified in this survey. This is because of the high precission of the HPLC machine used in these assay [28].

Of the traits with Hb C, two were from Delta state whreas the other is from the East of the Niger. Hitherto , Hb C was rarely found across the Niger [34]. This therfore shows that genes which were concentrated to some regions are now spreading due to ease of movement and inter-ethnic marriages [37].

The prevalence of phenotype D is higher than what is reported in most local studies [24,35,36,37] and some African studies [26,28,38,39]. This high prevalence may be attributed to the HPLC method used for the screening. This is a more sensitive method in the newborn period [40,-42]. Two neonates have double homozygous D.

One baby had Hb AE, this variant is rare. The implications of these findings have to be closely studied. We attribute this finding to the sensitivity of the method employed in the seperation of the haemoglobins HPLC [28,34]. It is a very useful tool that can be used in mass screening of newborn in the community. However, it is recommended that further tests should always be carried out to confirm the presumed identity of abnormal haemoglobin. It was not done in this survey and thus limits the extent of the results.

Conclusions

We conclude that NBS has been institutionalised at the FMC Asaba, Nigeria. Seven variants of Hb have been identified in this survey because of the methodology utilised. It can be stated that such high precision techincs should be utilised for large population surveys.

Competing Interests

The authors declare that they have no competing interests.

Author's Contributions

All authors made equal contributions.

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