NEWBORN SCREENING FOR SICKLE CELL DISEASE IN NIGERIA – CHALLENGES AND OPPORTUNITIES.

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ABSTRACT

Background:

Sickle cell disease (SCD) is an inherited autosomal recessive disorder affecting red blood cells with high morbidity and mortality worldwide. Sickle cell anaemia (SCA) is the most common and severe type of sickle cell disease. The United Nations has recognized SCD as a global public health problem and the World Health Organisation (WHO) has previously recommended that member states initiate National sickle cell control guidelines which are comprehensive by 2020.

While there has been significant improvement in outcomes for children with SCD in high-income countries due to factors such as early diagnosis through prenatal diagnosis, newborn screening programs, prophylactic therapy, hydroxyurea therapy and bone marrow transplant, low and middle-income countries such as Nigeria still have a high disease burden.

Body:

In most African countries including Nigeria, neither prenatal nor neonatal screening for sickle cell disease is readily available or affordable. Thus, in the absence of a routine newborn screening program, diagnoses are often made when patients present with suggestive clinical features or based on the request of parents or healthcare providers.

High Performance Liquid Chromatography is the gold standard for diagnosis of SCD in newborns, however inexpensive and easy to use point of care testing devices have also shown high sensitivity and specificity in the detection of haemoglobin genotype and can play a role in coordinated newborn screening for SCD in Nigeria.

Conclusion:

Morbidities and mortalities from SCD are preventable if children are started early on interventions like folic acid, administration of oral penicillin, immunizations, prevention and treatment of malaria. However, determining which child will benefit from such care will be challenging if routine screening of newborns for SCD is not instituted.

INTRODUCTION

Sickle cell disease (SCD) refers to a condition in which an individual inherits two abnormal haemoglobin (Hb) genes, one of which is HbS, with the resulting symptomatology or pathology attributable to the sickling phenomenon.[1] The most common and most severe form is Haemoglobin SS disease also known as Sickle cell anaemia (SCA)[1,2,3] which occurs in 3% of Nigerians.[3] Other less common conditions in the spectrum include HbSC disease, SB 0 (Beta- zero) thalassaemia and SB+ thalassaemia.[1] SCD is an autosomal recessive, genetically transmitted haemoglobinopathy responsible for significant morbidity and mortality.[4]

The disease affects red blood cells (RBCs) and is characterized by chronic haemolytic anaemia and several clinical consequences which include painful vaso-occlusive crises, acute anaemic crises and manifestations in different organs.[5,6] It has been documented that 50 – 80% of children born with SCD do not reach their fifth birthday due to lack of diagnosis and comprehensive health care and thus is regarded as a silent baby killer.[7]

The high mortality rate in sub-Saharan Africa is influenced by multiple factors which include limited resources, poor access to health care, lack of comprehensive SCD management programs and paucity of interventions that have been effective in reducing mortality among SCD patients in high-income countries. These interventions include newborn screening and prophylactic measures.[7, 8]

The burden of SCD in sub-Saharan Africa is of public health concern. In 2010, the region had nearly 80% of the projected 306,000 newborns with SCD worldwide. This has been projected to increase to 88% of the worldwide cases by 2050.[9,10,11,12]

In Nigeria, the prevalence of sickle cell trait (SCT) is about 23.7%, while the frequency of SCD is about 20 per 1000 births resulting in about 150,000 babies born annually.[9] This figure ranks Nigeria as a country with the largest burden of SCD globally with about 2.69 – 5% of the population being affected.[4,9,13]

Nigeria does not currently have a national neonatal screening program for SCD and in the majority of cases diagnoses are only made when patients present with suggestive symptoms and signs. The diagnosis of SCD is confirmed by haemoglobin electrophoresis which is expensive and often only available in tertiary hospitals.[13,14]

Studies have shown that in countries where universal newborn screening, early intervention and comprehensive care are effective, the morbidity and mortality of SCD is less than 1% of the global disease burden.[4,15,16] Also in such settings, more than 90% of the babies born with SCD survive into adulthood. Evidence of multiple benefits of universal newborn screening has been demonstrated in the United States, England, Jamaica and Brazil.[17,18,19]

Effective management of SCD revolves around genetic counselling, newborn screening and early diagnosis, immunizations, providing anti-malarial medications, antibiotics, hydroxyurea and prompt management of complications. Bone marrow transplantation in a selected segment of patients is the only proven cure for SCD to date[15,16,19] but this is an expensive treatment and not readily available in low and middle-income countries like Nigeria.

LITERATURE REVIEW

The newborn screening program (NSP) is a public health initiative,[20] and it refers to a set of special tests including blood, hearing and heart screening done at birth and usually before the

newborn leaves the hospital. In high-income countries, every newborn is tested for a group of health disorders which include newborn hearing assessment, genetic, hormone-related, and metabolic conditions that may cause serious health problems later in life.[19,20,21] Newborn screening is usually done at birth, 24 to 72 hours of life and within the neonatal period (first 28 days of life) or at most between six to eight weeks of life.[19]

Globally, sickle cell disease is the most common condition diagnosed by newborn screening.[20] This is performed by High Performance Liquid Chromatography (HPLC) to determine the presence of abnormal haemoglobins in whole blood.[22] HPLC is the gold standard for the diagnosis of SCD in the newborn period.[22] Specimens with HPLC profiles consistent with SCD, sickle cell trait, thalassemia or variant haemoglobins other than HbS can subsequently be analysed by Capillary Electrophoresis as a confirmatory method.[22]

Other screening methods include isoelectric focusing, cellulose acetate electrophoresis, citrate agar electrophoresis, capillary zone electrophoresis and more recent methods like molecular genetic analysis and mass spectroscopy.[7,19,22] Each of these methods has important limitations for scaling up to a wide reaching national programme in low-income setting.[7] In Nigeria, six special Millennium Developmental Goal (MDG) sickle cell centres were established across the six geo-political zones by the Federal Ministry of Health between 2011 and 2012.[7] Each of these centres was equipped with an HPLC machine, however challenges like inadequately trained personnel, limited government capacity and funding, expired reagents, limited availability of consumables, absence of mechanisms to collect samples from babies on a regular basis and erratic power supply have led to fewer than 2000 newborns being screened across the six MDG sickle cell centres.[7]

However, relatively new, inexpensive, and easy-to-use point of care testing (POCT) devices like the HemoType SC™ and Sickle SCAN™ have been developed which can differentiate common haemoglobin genotypes in newborns. Point of care testing devices are based on competitive lateral flow immunoassays incorporating monoclonal antibodies and have been shown to have high sensitivity (93.4%) and specificity (99.9%) in the detection of Hb genotypes.[4] Point of care testing can play a role in coordinated newborn screening for SCD in Nigeria as it can be used in remote sites[4,7,20] as against the current method of diagnosis (HPLC) which is expensive, costs between 5000 to 7000 Naira, usually paid out-of-pocket, and needs specially trained personnel and constant power source which are not readily available in Nigeria.

Newborn screening programs have been established in countries like Germany, the United States, England, France, Belgium, the Netherlands, Brazil and Jamaica.[19,23] Rahimy et al.[24] suggested that the introduction of newborn screening in these developed countries 20 years ago has reduced the mortality rate from 16% to less than 1%. Early neonatal screening for SCD enables implementation of a comprehensive care approach including prophylactic treatment, parental education, and initiation of a tracking and follow-up program for identified patients.[21,24]

In sub-Saharan Africa, access to newborn screening for SCD is limited due to varied reasons including economic constraints.[25] The Republic of Benin and Ghana are the only two countries in Africa that have comprehensive newborn screening programs.[21,24,25] The program in Benin is targeted at mothers with sickle cell trait.[21,24,25]

In March 2021, the American Society of Haematology (ASH) Consortium on Newborn Screening in Africa (CONSA) launched the sickle cell disease newborn screening programs in Ghana and Nigeria as an important step towards expanding access to early intervention and comprehensive care.[26] Five additional countries in the consortium – Kenya, Liberia, Tanzania, Uganda, and Zambia are also preparing to launch screening programs in 2021.[26]

Foundations like the Sickle Cell Foundation Nigeria (SCFN) in Lagos, Centre of Excellence for Sickle Cell Disease Research in Abuja and African Research and Innovative Initiative for Sickle cell Education (ARISE) have programmes aimed at education, research and empowering trainees with the necessary skills to implement newborn/infant screening, prophylaxis and management of SCD patients.[21,25]

A number of studies have been conducted to assess the efficacy of newborn screening programs in Africa.[10] These include studies done in Nigeria to determine the feasibility and acceptability of early infant screening for SCD, as well as studies in which newborn screening was done in some selected Nigerian hospitals.[4,19,21,25]. Odunvbun et al.[25] showed that newborn screening would be widely accepted by parents in Nigeria, as an acceptability rate of 99.7% was demonstrated in 630 - 649 mother-baby pairs studied.[25]

Similarly in a multi-centre study in Nigeria by Oluwole et al.[4] using a low cost POCT device to screen for SCD in infants aged two to ten weeks of age attending routine immunization clinic in Lagos, an acceptance rate of 86% out of the 291 mother-infant pairs was obtained.[4] Thus, the feasibility of early infant screening for SCD in this pilot study was assessed by > 80% acceptability rate.[4] These findings indicate that implementation of a national neonatal and early infant screening for SCD is likely to be widely accepted within Nigeria.

In any case, the establishment of a routine screening program which could be prenatal, neonatal or linked to child welfare services like immunization would significantly reduce the number of children with delayed diagnosis for any reason, reduce morbidity and mortality, improve the quality of life and life expectancy of these children.[3,4,19,21]

The life expectancy for people with SCD in the United States where routine newborn screening for SCD and comprehensive intervention and health care are available is 42 and 48 years for men and women respectively.[4,16,27] In Jamaica, the life expectancy stands at 53 and 58.5 years for men and women respectively.[28] In contrast, 50 to 80% of children born with SCD in Africa die before the age of five years.[4,7,8]

In a study on newborn screening and prophylactic interventions for sickle cell disease in 47 countries in sub-Saharan Africa, the mean life expectancy of unscreened newborns in both rural and urban areas was estimated at 1.7 years and 6.7 years respectively. However, the life expectancy of screened and treated infants ranged from 24.2 years in the Central African Republic to 32.4 years in Cape Verde with a mean age of 27.0 years.[10]

The age at which diagnosis of Sickle cell Disease is made in sub-Saharan Africa widely varies for two reasons. Firstly, due to the absence of routine screening programme for the diagnosis and secondly, because there is no specific age at which clinical manifestations may become apparent to parents and caregivers.[3,29] Nearly three quarters of most HbSS patients are diagnosed before the age of three years while more than 10% are diagnosed after their fifth birthday.[3,29]

Studies have also revealed that being in the upper socioeconomic class is associated with a younger age at diagnosis of sickle cell anaemia.[29]

Moving forwards, there is a need to identify better strategies to educate the public and major stakeholders on the importance of establishing a national newborn screening programme for sickle cell disease in Nigeria. Advocacy by paediatricians and all health care providers of children is pertinent. Efforts to scale up interventions such as the use of POCT devices even in remote locations and the institution of favourable payment mechanisms such as through a government-subsidised approach by way of insurance payments may improve demand and uptake of such services.

The role of the Government cannot be overemphasized. Good political will to fund the existing centres of excellence for research in SCD, provision of manpower and equipment, training and retraining of staff as well as the enactment of policies to ensure mandatory screening of newborns especially those whose mothers are sickle cell trait carriers will contribute to reduction in the disease burden.[7,10,12] Newborn screening can be incorporated into the package from antenatal/postnatal care through to immunization of the newborn.

Partnership with other stakeholders in health care, corporate organizations, philanthropists, and non-governmental organizations (NGOs) can facilitate access to funds, surveillance, and treatment of sickle cell disease. It should be noted that despite the absence of a national newborn screening programme in Nigeria, SCD patients who present to tertiary health institutions benefit from a holistic care.[30] These include malaria prophylaxis, provision of folic acid and vitamin C, use of anti-sickling agents like hydroxyurea, prompt treatment of acute crises, antibiotics and analgesic usage when indicated, acute and chronic transfusion therapy and transcranial doppler screening to assess risk for cerebrovascular accident. These measures have improved the quality of life of most SCD patients and have reduced mortality.[30]

Currently there are pilot projects for newborn screening for SCD in the University of Abuja Teaching Hospital and SCFN/ Lagos University Teaching Hospital (LUTH) and a bone marrow transplant centre set to kick off in June at LUTH.[31] These are steps in the right direction and all stakeholders must be lauded. However, as the world celebrates the World Sickle Cell Day on June 19th, all hands must be on deck to establish functional newborn screening programmes in all tertiary hospitals and gradually expand to all health facilities in the country.

CONCLUSION

In summary, the need for newborn screening programmes, especially for sickle cell disease is great in Nigeria. Efforts should be made to develop partnerships between countries where newborn screening and comprehensive care for SCD are well established to support training and re-training of health workers, research, and knowledge sharing to improve care and reduce the burden of SCD in Nigeria.

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