Newborn screening for sickle cell disease in sub-Saharan Africa: Is the glass half-full yet?

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Abbreviations

LMIC	Low and Middle Income Countries
SCD	Sickle Cell Disease

The overwhelming majority of children with sickle cell disease (SCD) in the world are born, live, and die in low- and middle-income countries (LMIC) located within sub-Saharan Africa. [1] Tragically, outside of a few select African urban centers, almost none of these affected infants are ever diagnosed, and are thus unable to receive life-saving preventive care and survive past 5 years of age. [2] Newborn screening for SCD holds great promise for changing this unacceptable paradigm. Even before the widespread use of disease-modifying therapy with hydroxyurea, adoption of universal newborn screening for SCD in the United States saved lives by allowing early initiation of penicillin, pneumococcal immunization, and family education about early signs of life-threatening complications. [3-5] Although these simple interventions are potentially available in LMIC, most SCD screening in Africa to date has been in the form of pilot studies that primarily demonstrate feasibility and document a high burden of disease. [6-10]

In this issue of *Pediatric Blood and Cancer*, Segbefia et al describe their experience implementing a newborn SCD screening program at Korle Bu, the largest public hospital in Ghana. [11] Should we be encouraged by yet another pilot program in sub-Saharan Africa, when none of the prior programs has evolved into a national universal newborn screening policy? The halting success of the United States to adopt universal sickle cell newborn screening should temper our response. Despite pre-existing newborn screening infrastructure for metabolic conditions like phenylketonuria, [12] more than 30 years with tireless advocacy and significant federal funding were required before SCD was added to every state's screening program. [13] Although their experiences reveal some failures and gaps, the team in Ghana describes an early essential phase of implementation and provides an invaluable roadmap for hospitals in LMIC that seek to establish successful a public health intervention within their busy, complex medical environment. Their report is especially relevant as collaborative efforts are coalescing around the wider introduction of SCD screening across Africa, such as the CONSA program by the American Society of Hematology. [14]

This manuscript contains one of the most detailed accounts yet published of the programmatic structure, resources, personnel, and efforts needed to operationalize an LMIC newborn SCD screening program in its full breadth from sample collection to follow-up care. With support from government, academia, and industry, the team in Ghana set out to establish a robust SCD screening program to diagnose newborns on the hospital maternity ward and connect them to the SCD clinic at the same facility. Newborn screening in Africa is cost-effective, [15,16] but the startup phase can be especially resource intensive, and this team formed an impressive coalition to accomplish the task. The Ghana Ministry of Health and the Sickle Cell Foundation of Ghana provided necessary impetus; a north-south collaboration with The Hospital for Sick Children and Toronto University was established; and external funding was obtained from Pfizer. Care was taken to form appropriate local governance and supervision.

During an initial year-long demonstration phase, they tested only 45% of all newborns but still diagnosed 79 infants with presumed SCD, of whom 74 (94%) were contacted and 60 (79%) were linked to ongoing SCD care. After discovering that task-shifting was ineffective for already busy nurse-midwives, additional staff were hired to collect infant samples on the maternity wards. During the following year-long Phase 1 period, they managed to test 80% of newborns, diagnose 132 infants, contact 121 (92%), and link 62 (47%) to ongoing care. Perhaps not coincidentally, broader screening brought to scale meant only half of the babies were brought into care.

Linkage-to-care is an essential aspect of any screening program and perhaps its greatest challenge. Children diagnosed with SCD in sub-Saharan Africa will only benefit from the diagnosis when they regularly attend a dedicated SCD clinic that provides appropriate therapy. [17] The intuitive cascade of care from collection of specimens to prescription of medications contains numerous pitfalls that defy easy solutions and require adaptations tailored to the realities of each setting (Figure 1). Short-term successes in previous pilot screening programs have varied, but larger maternity-based programs have

experienced more challenges, averaging only around 50% in Angola, Liberia, and DRC. [6,7,18] Those reports provide few details about the strategies used to ensure clinic attendance and focused more on the optimal screening location (hospital-based, immunization clinic-based), timing (at birth, before 3 months of age), and methodology (point-of-care, hemoglobin electrophoresis, high performance liquid chromatography).

Accurate test results are important, but screening programs must recognize and address features that impede successful linkage-to-care. SCD screening in a major hospital provides an opportunity to diagnose children early in life, but delayed reporting of test results may prohibit timely notification and education of families before discharge. After babies leave the hospital, families are sometimes difficult to locate. Those who live far from the hospital and are unable to return for routine care may lack an appropriately equipped local SCD clinic. Utilizing immunization clinics more proximal to family homes can increase clinic attendance if local SCD clinics are available. [10] In Ghana, creative solutions included developing a relationship with the family before discharge, repeated contact attempts, tracking clinic no-shows, and employing public health nurses to locate families in the community.

While the long-term success of SCD screening programs in LMIC remains to be determined, these efforts provide some rays of hope for the future of children born with SCD in LMIC, especially within sub-Saharan Africa. The progress achieved in response to the global HIV pandemic displays the sustainable gains that can be accomplished with local-global partnerships. The American Society of Hematology, in partnership with PerkinElmer, has committed to helping with newborn screening in numerous African countries; continued external funding is needed to create SCD screening and treatment programs that extend beyond teaching hospitals. Despite numerous struggles and challenges, we see these ~50% success rates as a glass half-full, recognizing that ongoing partnerships, investment, and best practices

are needed to extend such programs beyond busy maternity wards in major cities to smaller hospitals, immunization clinics, and health outposts across each country.

Disclosures

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Figure 1. Steps in a successful newborn screening program and intervening aspects that affect completion of each step