Surveillance for sickle cell disease, United Republic of Tanzania

Emmanuela E Ambrose,a Luke R Smart,b Mwesige Charles,c Arielle G Hernandez,b Teresa Latham,b Adolfine Hokororo,b Medard Beyanga,c Thad A Howard,b Erasmus Kamugisha,d Kathryn E McElhinney,b Erius Tebuka&a Russell E Wareb

Objective To determine the regional- and district-level newborn prevalence of sickle cell trait and disease, and the prevalence of haemoglobin variants and genetic modifiers of sickle cell disease, in the nine regions of north-western United Republic of Tanzania.

Methods We repurposed dried blood spot samples from children (aged 0–24 months) born to mothers living with human immunodeficiency virus (HIV), collected as part of the HIV Early Infant Diagnosis programme, for sickle cell diagnosis. We performed isoelectric focusing to determine whether samples had normal haemoglobin, sickle cell trait, sickle cell disease or a rare haemoglobin variant. We shipped samples diagnosed as disease or variant to Cincinnati Children’s Hospital in the United States of America for deoxyribonucleic-acid-based analyses to determine the prevalence of α-thalassaemia, glucose-6-phosphate dehydrogenase (G6PD) deficiency or fetal haemoglobin genetic modifiers.

Findings We analysed a total of 17 200 specimens during February 2017–May 2018. We observed a prevalence of sickle cell trait and disease of 20.3% (3492/17 200) and 1.2% (210/17 200), respectively. District-level trait varied from 8.6% (5/58) to 28.1% (77/274). Among confirmed sickle cell disease specimens, we noted 42.7% (61/143) had 1-gene deletion and 14.7% (21/143) had 2-gene deletion α-thalassaemia trait. We documented G6PD A− deficiency in 19.2% (14/73) of males.

Conclusion Our calculated prevalence is twice as high as previously reported and reinforces the need for enhanced sickle cell diagnostic services. Our district-level data will inform public health policy, allowing screening and disease-modifying hydroxyurea therapy to be focused on high-prevalence areas, until universal newborn screening is available.

Introduction

Sickle cell disease is an inherited disorder of haemoglobin, caused by a mutation in the β-globin subunit of adult haemoglobin. In classic autosomal recessive fashion, inheritance of one abnormal and one normal allele confers sickle cell trait, a carrier state without clinical symptoms. Inheritance of two mutated alleles causes sickle cell disease, characterized by varying amounts of chronic haemolytic anaemia, recurrent debilitating pain and an array of clinical sequelae, including increased risk of infection, stroke, lung disease, splenic dysfunction and bone infarction.

Sickle cell disease imposes a significant global burden of disease that remains underrecognized, especially in Africa. Approximately 400 000 infants are born each year with sickle cell disease;3–5 75% of these infants are born in the tropical regions of sub-Saharan Africa,3 home to most of the > 25 million people who live with sickle cell disease globally.7 Sickle cell disease causes substantial morbidity8 and is responsible for 5–16% of mortality in children younger than 5 years.9,10 Cumulative data from prior studies suggest that more than half of the children with sickle cell disease in sub-Saharan Africa die in early childhood, with substantial differences in mortality between historic rural communities11 and modern urban centres.12 Early enrolment in a comprehensive care programme that includes preventive care (immunizations and prophylactic antimicrobials) and disease-modifying therapy (hydroxyurea or prophylactic blood transfusions) can reduce symptoms and improve survival.

The World Health Organization acknowledged the global importance of addressing sickle cell disease almost 15 years ago,10,14,15 and in 2010 African leaders formally proposed sickle cell disease prevention and control strategies for the African Region.6 In response, the United Republic of Tanzania has embedded sickle cell disease targets within the national non-communicable disease policy,16 increased advocacy,17 created a centre of excellence,18 educated health-care workers and increased research output.19 The majority of these efforts have been focused in Muhimbili National Hospital in the coastal city of Dar es Salaam, but prevalence estimates suggest that the greatest burden of sickle cell disease is in the north-western regions of the country around Lake Victoria.9,21,22

The United Republic of Tanzania does not yet have a national newborn screening programme. In the absence of recent reports, Tanzanian estimates of sickle cell disease are based on sparse data from studies performed over the past 65 years in only seven of the 30 regions of the country.2,23,24 Recognizing that data extracted from isolated reports can poorly reflect variation within a country,12,15 we initiated and conducted the United Republic of Tanzania Sickle Surveillance Study in the north-western regions of the country. Our primary objective was to provide contemporary regional- and district-level data on the newborn prevalence of sickle cell trait and disease to inform the national noncommunicable disease policy goals.
Our study used existing public health infrastructure developed as part of the human immunodeficiency virus (HIV) Early Infant Diagnosis programme, while aiming to build local capacity for the accurate diagnosis of sickle cell disease. Our secondary objectives included characterization of rare haemoglobin variants and the prevalence of co-inherited genetic disorders that may affect sickle cell disease phenotypes and response to hydroxyurea treatment.

Methods

HIV Early Infant Diagnosis

In 2006, the International Center for AIDS Care and Treatment Programs, the Tanzanian Ministry of Health and Social Welfare, Bugando Medical Centre and the United States Centers for Disease Control and Prevention implemented the HIV Early Infant Diagnosis programme with the aim of preventing mother-to-child transmission of HIV. The country operates a decentralized testing structure with four reference laboratories. The Bugando Medical Centre, a zonal referral and teaching hospital located in the city of Mwanza, serves as the reference laboratory for the north-western catchment area, and is also the designated sickle cell centre of excellence for this area. The Bugando catchment area includes a population of approximately 17.6 million people within nine regions, who collectively represent 39.2% (17.6 million people within nine regions, who collectively represent 39.2% (17 623 047/44 928 923) of the country’s total population. An infant born to a mother living with HIV is brought to a Reproductive and Child Health clinic at 4–6 weeks of age for the first preventive health visit. A dried blood spot is collected from the infant, and transported to a reference laboratory for detection of HIV using a polymerase chain reaction (PCR). The dried blood spots are labelled with key demographic information including date of birth, sex, referring health facility, date of collection, date of dispatch and date of receipt at the laboratory. HIV results are communicated to the referring health facility for prompt initiation of antiretroviral medication. Dried blood spots are then stored at room temperature and made available for additional testing for sickle cell trait and disease.

Sickle cell diagnosis

We analysed all repurposed dried blood spots collected as part of the HIV Early Infant Diagnosis programme during February 2017–May 2018 by using the isoelectric focusing technique. Our laboratory equipment included Resolve Hemoglobin kits and JB-2 Staining System reagents (both PerkinElmer, Inc., Waltham, United States of America, USA), as well as control specimens and other consumables, all donated to the haematology section of the Bugando laboratory. Staff were trained on-site by a board-certified haematologist, and attended a 2-day seminar in Dar es Salaam, organized by the equipment manufacturer and funded jointly by the manufacturer and the United States Association of Public Health Laboratories. At the seminar, staff acquired theoretical knowledge of the isoelectric focusing technique and had the opportunity to process samples while supervised by an experienced manufacturer representative. The senior Tanzanian paediatrician leading the haematology clinic also completed a further two months of clinical and laboratory training funded and hosted by Cincinnati Children’s Hospital, USA.

All dried blood spots were analysed with a standard control specimen containing adult, fetal and sickling haemoglobin (haemoglobin A, F and S) and haemoglobin C. Isoelectric focusing results were scored independently by two Bugando Medical Centre staff for the presence and abundance of each type of haemoglobin. The results were interpreted as: normal if haemoglobin A (± haemoglobin F) was present; sickle cell disease if haemoglobin S (± haemoglobin F) was present; sickle cell trait if both haemoglobin A and S (± haemoglobin F) were present; variant if a band was present at any location other than haemoglobin A, S or C (± haemoglobin F); and uninterpretable if poor quality precluded interpretation. Dried blood spot analyses interpreted as sickle cell disease, variant or uninterpretable were repeated for confirmation and frozen for later deoxyribonucleic acid (DNA) studies. Regular teleconferences were convened with collaborators based in the Cincinnati Children’s Hospital, USA, to provide ongoing feedback on the quality of laboratory techniques and interpretation of gels; however, the Tanzanian team was responsible for all final interpretations.

DNA-based testing

Any dried blood spot diagnosed as sickle cell disease or variant was stored at −20 °C then shipped to the USA for future DNA testing. Upon arrival, we stored dried blood spots at −80 °C until testing could be performed. We extracted DNA from dried blood spots using an adapted protocol from InstaGene (Bio-Rad Laboratories, Hercules, USA). We performed amplification of β-globin gene exons 1 and 2 using a PCR, and confirmed the presence of a haemoglobin S mutation at rs334 (c.334T > A;p.GluVal) using a custom TaqMan PCR probe (Applied Biosystems, Foster City, USA). We analysed specimens interpreted as uncommon and atypical haemoglobin variants by isoelectric focusing via the previously published algorithm used to investigate uncommon variants in East Africa. Uncommon variants include the α-chain variants haemoglobin G-Pest (HBA1: p .Asp75Asn) and haemoglobin Stanleyville II (HBA1:p .Asn79Lys), and the fusion variants haemoglobin P-Nilotic (β-globin gene (HBB)–δ-globin gene (HBD) fusion: β31–δ50) and haemoglobin Kenya (γ-globin gene (HBG1)–HBB fusion: γ81–β86). We detected α-thalassaemia trait resulting from the 3.7-kilobase α-globin gene deletion and glucose-6-phosphate dehydrogenase (G6PD) A- variant using DNA-based techniques, and determined the modifiers of baseline haemoglobin F production.

We genotyped the BCLI1A polymorphisms (rs1427407, rs7557939 and rs11886868) and HBS1L-MYB intergenic polymorphisms (HMIP) (rs28384513 and rs9399137) using commercially available real-time PCR assays (Applied Biosystems, Foster City, USA). To identify the Xmnl single-nucleotide polymorphism at −158 basepairs to G-γ globin (rs7482144), we amplified the G-γ gene (HGB2) using PCR with G-γ-specific forward and reverse primers to ensure that the G-γ rather than an A-γ product was isolated. We then further amplified this product by performing PCR with Classic 1 forward and reverse primers. We genotyped the final product using a custom-made TaqMan PCR probe set (Applied Biosystems, Foster City, USA).
Data analysis
We entered data into an Excel database (Microsoft, Redmond, USA), treating age as a continuous variable (summarized using median and interquartile range) and treating haemoglobin type, HIV status, sex, region of origin, district of origin, G6PD status and α-thalassaemia status as categorical variables (summarized using frequencies). We calculated the prevalence of sickle cell trait and disease by dividing the number of specimens with sickle cell trait and disease by the total number of non-missing specimens with interpretable results. We determined allelic frequency by dividing the number of times that an allele was observed (once in heterozygotes, twice in homozygotes) by the total number of all alleles (twice the total number of specimens). We compared the proportions of participants living with HIV with and without sickle cell disease using a χ² test.

Ethical considerations
Our study protocol was approved with a waiver for informed consent by the joint Catholic University of Health and Allied Sciences–Bugando Medical Centre Research and Ethics Committee, as well as the Tanzanian National Institute for Medical Research, to perform disease surveillance on de-identified archived dried blood spots previously collected by the HIV Early Infant Diagnosis programme. The study was also approved by the Cincinnati Children’s Hospital Medical Center Institutional Review Board. A formal material transfer agreement was obtained so that specimens could be shipped to the USA for genetic analysis.

Results
Sample collection and testing
Our local Bugando Medical Centre staff completed a total of 232 isoelectric focusing gels during February 2017–May 2018. After samples from children older than 24 months were excluded to obtain a more accurate prevalence for infants, the median age of infants included in the sampling population was 52 days (interquartile range, 41–93 days). Staff scored a total of 17 274 unique dried blood spot specimens from the catchment area. The quality of laboratory testing was extremely high with only 20 specimens scored as uninterpretable and 54 with missing results, meaning that we performed our primary analysis on 17 200 specimens.

Prevalence
We observed an overall prevalence of sickle cell trait and disease in our cohort of 20.3% (3 492/17 200) and 1.2% (210/17 200), respectively, with a 0.1% (17/17 200) prevalence of atypical or uncommon haemoglobin variants. Our data yielded an allelic frequency of 0.114 (210/17 200) for the sickle gene (haemoglobin S) mutation, and demonstrate perfect Hardy–Weinberg equilibrium, as expected in a stable population. We did not identify any haemoglobin C or other common β-globin variants. Our geospatial mapping revealed mild variation between regions, with the prevalence of sickle cell trait and disease ranging from 16.6% (146/880) to 22.5% (253/1126) and 0.5% (4/880) to 1.5% (17/1126), respectively (Table 1). Analysis of individual districts that provided more than 48 specimens (i.e. excluding Bugihwe, from which only 12 samples were provided) revealed a wider geographic variability, with sickle cell trait and disease ranging from 8.6% (5/58) to 28.1% (77/274) and from zero to 4.3% (9/208), respectively (Fig. 1 and Table 1).

Using our regional prevalence estimates of sickle cell trait and disease, and regional census data from the 2012 Population and Housing Census for the United Republic of Tanzania, we calculated the estimated number of annual births with sickle cell trait or disease in each region within the study area (Table 2). We estimated that the number of births with sickle cell disease per year was 10056 within the nine regions comprising the study area. Contributions varied by region according to their population size and sickle cell disease prevalence. We projected the lowest number of births with sickle cell disease per year for the region of Singida (526 births), and the highest for the region of Mwanza (1730 births; Table 2).

Relation to HIV status
For the 16 479 samples for which HIV results were available, we analysed the co-morbidity of HIV and sickle cell disease to compare the potential effect of HIV status on mortality, as previously performed in Uganda. The prevalence of sickle cell disease was 1.2% among both HIV-infected (9/732) and HIV-negative (192/15 747) infants, indicating that HIV status has no effect on early mortality (Table 3).

DNA-based analysis
Of the 210 specimens that were interpreted as sickle cell disease by isoelectric focusing, 143 were genotype-confirmed and made available for further DNA-based testing. Uncommon or atypical haemoglobin variants were rare (0.1%; 17/17 200) and included four haemoglobin G-Pest (HBA1:p.Asp75Asn), two haemoglobin Kenya (HBBG1–HBB fusion gene Δγ81-β86) and a haemoglobin P-Nilotic (HBB–HBD fusion β31-δ50). We identified 1-gene deletion α-thalassaemia trait in 42.7% (61/143) and 2-gene deletion α-thalassaemia trait in 14.7% (21/143).

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We detected G6PD A– deficiency in 42.7% (61/143) and 2-gene deletion α-thalassaemia trait in 15.4% (22/143) and 0.5% (4/880) in regions with high prevalence of sickle cell disease. We performed an matched case–control analysis of the 143 specimens that were genotype-confirmed revealing mild variation between regions, with the prevalence of sickle cell trait and disease ranging from 16.6% (146/880) to 22.5% (253/1126) and 0.5% (4/880) to 1.5% (17/1126), respectively (Table 1). Analysis of individual districts that provided more than 48 specimens (i.e. excluding Bugihwe, from which only 12 samples were provided) revealed a wider geographic variability, with sickle cell trait and disease ranging from 8.6% (5/58) to 28.1% (77/274) and from zero to 4.3% (9/208), respectively (Fig. 1 and Table 1).

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Table 1. Regional and district prevalence of haemoglobin types in infants identified, north-western United Republic of Tanzania, February 2017–May 2018

| Region or district | Total | Normal | Sickle cell trait | Sickle cell disease | Variant |
|-------------------|-------|--------|------------------|--------------------|---------|
| **Region**        |       |        |                  |                    |         |
| Geita             | 2 436 | 1 918  | 495 (20.3)       | 23 (0.9)           | 0 (0.0) |
| Kagera            | 880   | 729    | 146 (16.6)       | 4 (0.5)            | 1 (0.1) |
| Kigoma            | 683   | 550    | 123 (18.0)       | 10 (1.5)           | 0 (0.0) |
| Mara              | 1 837 | 1 422  | 388 (21.1)       | 23 (1.3)           | 4 (0.2) |
| Mwanza            | 3 847 | 3 013  | 778 (20.2)       | 51 (1.3)           | 5 (0.1) |
| Shinyanga         | 2 800 | 2 158  | 598 (21.4)       | 41 (1.5)           | 3 (0.1) |
| Simiyu            | 1 126 | 855    | 253 (22.5)       | 17 (1.5)           | 1 (0.1) |
| Singida           | 1 141 | 906    | 226 (18.9)       | 9 (0.8)            | 0 (0.0) |
| Tabora            | 2 450 | 1 930  | 485 (19.8)       | 32 (1.3)           | 3 (0.1) |
| **Total**         | 17 200| 13 481 | 3492 (20.3)      | 210 (1.2)          | 17 (0.1)|

| District          |       |        |                  |                    |         |
|-------------------|-------|--------|------------------|--------------------|---------|
| Bariadi           | 261   | 206    | 52 (19.9)        | 2 (0.8)            | 1 (0.4) |
| Biharamulo        | 135   | 111    | 24 (17.8)        | 0 (0.0)            | 0 (0.0) |
| Buhiwgwe*         | 12    | 11     | 1 (8.3)          | 0 (0.0)            | 0 (0.0) |
| Bukoba            | 174   | 142    | 30 (17.2)        | 1 (0.6)            | 1 (0.6) |
| Bukombe           | 394   | 294    | 97 (24.6)        | 3 (0.8)            | 0 (0.0) |
| Bunda             | 378   | 301    | 73 (19.3)        | 3 (0.8)            | 1 (0.3) |
| Busega            | 274   | 195    | 77 (28.1)        | 2 (0.7)            | 0 (0.0) |
| Butiama           | 208   | 161    | 38 (18.3)        | 9 (4.3)            | 0 (0.0) |
| Chato             | 514   | 399    | 108 (21.0)       | 7 (1.4)            | 0 (0.0) |
| Geita             | 1 156 | 929    | 219 (18.9)       | 8 (0.7)            | 0 (0.0) |
| Igunga            | 539   | 426    | 107 (19.9)       | 4 (0.7)            | 2 (0.4) |
| Ikungi            | 135   | 110    | 23 (17.0)        | 2 (1.5)            | 0 (0.0) |
| Ilemela           | 513   | 394    | 110 (21.4)       | 9 (1.8)            | 0 (0.0) |
| Iramba            | 291   | 230    | 60 (20.6)        | 1 (0.3)            | 0 (0.0) |
| Itilima           | 152   | 120    | 29 (19.1)        | 3 (2.0)            | 0 (0.0) |
| Kahama            | 1 683 | 1 281  | 374 (22.2)       | 25 (1.5)           | 3 (0.2) |
| Kakonko           | 49    | 39     | 10 (20.4)        | 0 (0.0)            | 0 (0.0) |
| Kaliua            | 374   | 284    | 83 (22.2)        | 7 (1.9)            | 0 (0.0) |
| Karagwe           | 95    | 81     | 14 (14.7)        | 0 (0.0)            | 0 (0.0) |
| Kasulu            | 159   | 120    | 34 (21.4)        | 5 (3.1)            | 0 (0.0) |
| Kibondo           | 162   | 129    | 31 (19.1)        | 2 (1.2)            | 0 (0.0) |
| Kigoma            | 207   | 171    | 34 (16.4)        | 2 (1.0)            | 0 (0.0) |
| Kishapu           | 424   | 333    | 87 (20.5)        | 4 (0.9)            | 0 (0.0) |
| Kwimba            | 282   | 230    | 50 (17.7)        | 2 (0.7)            | 0 (0.0) |
| Kyerwa            | 58    | 53     | 5 (8.6)          | 0 (0.0)            | 0 (0.0) |
| Magu              | 664   | 541    | 116 (17.5)       | 7 (1.1)            | 0 (0.0) |
| Manyoni           | 285   | 223    | 60 (21.1)        | 2 (0.7)            | 0 (0.0) |
| Maswa             | 216   | 167    | 45 (20.8)        | 4 (1.9)            | 0 (0.0) |
| Mboogwe           | 273   | 215    | 53 (19.4)        | 5 (1.8)            | 0 (0.0) |
| Meatu             | 223   | 167    | 50 (22.4)        | 6 (2.7)            | 0 (0.0) |
| Missenyi          | 163   | 134    | 29 (17.8)        | 0 (0.0)            | 0 (0.0) |
| Msungwi           | 429   | 334    | 86 (20.0)        | 6 (1.4)            | 3 (0.7) |
| Mkalamu           | 100   | 76     | 23 (23.0)        | 1 (1.0)            | 0 (0.0) |
| Muleba            | 191   | 155    | 34 (17.8)        | 2 (1.0)            | 0 (0.0) |
| Musoma            | 461   | 352    | 103 (22.3)       | 4 (0.9)            | 2 (0.4) |
| Ngara             | 64    | 53     | 10 (16.5)        | 1 (1.6)            | 0 (0.0) |
| Nyamagana         | 1 107 | 876    | 216 (19.5)       | 13 (1.2)           | 2 (0.2) |
| Nyang’hwale       | 99    | 81     | 18 (18.2)        | 0 (0.0)            | 0 (0.0) |

(continues...)
An important strength of our study is that we developed a sickle cell disease diagnostic service using existing infrastructure used for HIV infant diagnosis, demonstrating a potential of using this approach across sub-Saharan Africa. For example, in Uganda decision-makers have successfully expanded the use of their HIV infant diagnosis screening platform for sickle cell disease diagnosis, and have launched focused screening in 18 high-prevalence areas. Until the emergence of government-sponsored universal screening, local providers can implement their own strategies for optimal screening. Regardless of the location (e.g. hospitals, schools, or reproductive and child health clinics), population (e.g. all patients, mothers, newborns or children) or testing modality (isoelectric focusing, electrophoresis, point-of-care testing or high-performance liquid chromatography) used for initial screen-

### Region or district

| Region or district | Total | Normal | Sickle cell trait | Sickle cell disease | Variant |
|--------------------|-------|--------|-------------------|--------------------|---------|
| Nzega              | 459   | 366 (79.7) | 88 (19.2) | 5 (1.1) | 0 (0.0) |
| Rorya              | 486   | 371 (76.3) | 108 (22.2) | 6 (1.2) | 1 (0.2) |
| Sengerema          | 705   | 525 (74.5) | 169 (24.0) | 11 (1.6) | 0 (0.0) |
| Serengeti          | 89    | 73 (82.0)  | 15 (16.9)  | 1 (1.1)  | 0 (0.0) |
| Shinyanga          | 692   | 543 (78.5) | 137 (19.8) | 12 (1.7) | 0 (0.0) |
| Sikonge            | 233   | 182 (78.1) | 50 (21.5)  | 0 (0.0)  | 1 (0.4) |
| Songida            | 330   | 267 (80.9) | 60 (18.2)  | 3 (0.9)  | 0 (0.0) |
| Tabora             | 347   | 288 (83.0) | 53 (15.3)  | 6 (1.7)  | 0 (0.0) |
| Tarime             | 215   | 164 (76.3) | 51 (23.7)  | 0 (0.0)  | 0 (0.0) |
| Ukerewe            | 147   | 113 (76.9) | 31 (21.1)  | 3 (2.0)  | 0 (0.0) |
| Urambo             | 211   | 165 (78.2) | 41 (19.4)  | 5 (2.4)  | 0 (0.0) |
| Uvinza             | 94    | 80 (85.1)  | 13 (13.8)  | 1 (1.1)  | 0 (0.0) |
| Uyui               | 288   | 220 (76.4) | 63 (21.9)  | 5 (1.7)  | 0 (0.0) |
| **Total**          | **17 200** | **13 481 (78.4)** | **3492 (20.3)** | **210 (1.2)** | **17 (0.1)** |

* We considered the number of samples returned from Buhigwe (12) to be too small to be statistically representative; all other districts returned ≥ 49 samples.

Note: We used isoelectric focusing to detect different haemoglobin types in infants aged 0–24 months.

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**Fig. 1.** District-level prevalence of sickle cell trait in infants, north-western United Republic of Tanzania, February 2017–May 2018

Note: We only included districts that provided a minimum of 49 specimens.

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Table 2. Estimated annual region-specific numbers of infants with sickle cell trait and disease, north-western United Republic of Tanzania, February 2017–May 2018

| Region      | Population* | Crude birth rate per 1 000 population* | Estimated annual no. of births with sickle cell traita | Estimated annual no. of births with sickle cell diseasea |
|-------------|-------------|----------------------------------------|-------------------------------------------------------|--------------------------------------------------------|
| Geita       | 1 739 530   | 56                                     | 19 775                                                | 877                                                    |
| Kagera      | 2 458 023   | 44                                     | 17 953                                                | 541                                                    |
| Kigoma      | 2 127 930   | 48                                     | 18 385                                                | 1 532                                                  |
| Mara        | 1 743 830   | 49                                     | 18 029                                                | 1 111                                                  |
| Mwanza      | 2 772 509   | 48                                     | 26 882                                                | 1 730                                                  |
| Shinyanga   | 1 534 808   | 44                                     | 14 452                                                | 1 013                                                  |
| Simiyu      | 1 584 157   | 52                                     | 18 535                                                | 1 236                                                  |
| Singida     | 1 370 637   | 48                                     | 13 027                                                | 526                                                    |
| Tabora      | 2 291 623   | 50                                     | 22 687                                                | 1 490                                                  |
| Total       | –           | –                                      | 169 725                                               | 10 056                                                  |

* From 2012 Population and Housing Census for the United Republic of Tanzania.36
a Estimated from population, crude birth rate and prevalence as calculated in Table 1.

Table 3. HIV-specific prevalence of haemoglobin types in infants, north-western United Republic of Tanzania, February 2017–May 2018

| HIV status | Total | Normal | Sickle cell trait | Sickle cell disease |
|------------|-------|--------|-------------------|--------------------|
| Negative   | 15 747 | 12 388 (78.7) | 3167 (20.1) | 192 (1.2) |
| Positive   | 732    | 563 (76.9) | 160 (21.9) | 9 (1.2) |
| Total      | 16 479* | 12 951 (78.6) | 3327 (20.2) | 201 (1.2) |

HIV: human immunodeficiency virus.
a Only specimens for which HIV test results were available are included.
Note: We used isoelectric focusing to detect different haemoglobin types in infants aged 0–24 months.

Table 4. Prevalence of α-thalassaemia and G6PD deficiency observed in infants, north-western United Republic of Tanzania, February 2017–May 2018

| Genotype           | Clinical effect                        | No. (%) |
|--------------------|----------------------------------------|---------|
| α-thalassaemia (n = 143) |                                       |         |
| 5 copies, αα/αα    | 1-gene duplication, unaffected         | 0 (0.0) |
| 4 copies, αα/αα    | 0-gene deletion, unaffected            | 61 (42.7) |
| 3 copies, αα/−α−/−α− | 1-gene deletion, α-thalassaemia minima | 61 (42.7) |
| 2 copies, −α−/−α− | 2-gene deletion, α-thalassaemia trait | 21 (14.7) |
| G6PD deficiency (n = 143) |                                       |         |
| Males (n = 73)     | B                                      | 52 (71.2) |
|                   | A+                                     | 7 (9.6)  |
|                   | A−                                     | 14 (19.2) |
| Females (n = 70)   | BB                                     | 33 (47.1) |
|                   | BA+                                    | 16 (22.9) |
|                   | A⁺A⁺                                   | 3 (4.3)  |
|                   | BA−                                    | 15 (21.4) |
|                   | A⁺A−                                   | 3 (4.3)  |
|                   | A⁺A⁺                                   | 0 (0.0)  |

G6PD: glucose-6-phosphate dehydrogenase.
Note: We analysed dried blood spots from infants aged 0–24 months.
imperative that health ministries and international organizations such as the Global Burden of Disease project receive high-quality district-level data to guide global health priorities and public health policy; our data will inform such strategies.

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Table 5. Prevalence of haemoglobin modifiers observed in infants, north-western United Republic of Tanzania, February 2017–May 2018

| Chromosome | Gene | Single-nucleotide polymorphism | Allele change | Higher fetal haemoglobin allele frequency |
|------------|------|-------------------------------|--------------|------------------------------------------|
| 2          | BCL11A | rs1188688 T → C              | 0.322 = C    |                                          |
| 2          | BCL11A | rs1427407 G → T              | 0.266 = T    |                                          |
| 2          | BCL11A | rs4671393 G → A              | 0.325 = A    |                                          |
| 6          | HBS1L-MYB | rs28384513 T → G       | 0.238 = G    |                                          |
| 6          | HBS1L-MYB | rs9399137 T → C       | 0.045 = C    |                                          |
| 11         | HBG2   | rs7482144 G → A              | 0.000 = A    |                                          |

Competing interests: None declared.

ملخص
الرصد لمرض الخلايا المتجولة، جمهورية تنزانيا المتحدة

المرض محدود معدل انتشار سمات ومرض الخلايا المتجولة لدى حديثي الولادة على مستوى الأقاليم والمناطق، وانتشار متغيرات الهيموجلوبين والعدلات الجينية для مرض فيروس الدم المتجول، في المناطق الشمالية مهيئة غرب جمهورية تنزانيا المتحدة. الجملة: بناءً على استخدام عينات تم تجميعها كجزء من برنامج التشخيص المبكر لمرض الخلايا المتجولة، أجرينا تحليلات باستخدام حمض الديوكسي ريبونيوكليك لتحديد ما إذا كانت العينات تحتوي على مصابات بفيروس نقص المناعة البشرية (HIV)، والتي تم جمعها كجزء من برنامج التشخيص المبكر لفِيروس نقص أنتِعَة البَشِرية للرضع، لتشخيص مرض الخلايا المتجولة. أجرينا تركيزًا متساويًا بين العينات على مستوى المناطق من أقاليم تنزانيا المتحدة، أو مرض الخلايا المتجولة، أو أحد التغيرات النادرة للهيموجلوبين. كنما نشئهم على زيادة الانتشار النادر للهيموجلوبين، عينات تم تشخيصها على أنها مصابات بإمراض أخرى، ويتم تشخيصها بناءً على بيانات مساعدة مرض فيروس الدم المتجول، أو أحد التغيرات النادرة للهيموجلوبين. ونص على أن العينات كانت على مستوى المناطق من أقاليم تنزانيا المتحدة، أو مرض الخلايا المتجولة، أو أحد التغيرات النادرة للهيموجلوبين.

النتائج
رصدًا على النتائج جمعنا تحليل إجمالي 17200 عينة منها في فبراير/نوفمبر 2017 ، ولاحظنا انتشار سمة ومرض الخلايا المتجولة بنسبة 20.3% (17200/83492) و1.2% (1206/101575) على الترتيب. نتائج السوات على مستوى المناطق من 6.6% (274/4195) إلى 28.1% (58/207) على الترتيب. ولنا أن عينات من بين عينات مرض الخلايا المتجولة، على سبيل المثال (143/61) 42.2% (21/42) عانت من حذف جين ت. ونتيجة لزيادة المجموع حوالي 19.2% (14/73) في G6PD A. ونتيجة لزيادة المجموع حوالي 20.3% (1206/5950) عن الانتهاء عن مستويات عينات مرض الخلايا المتجولة، وسوق البيانات على مستوى الاقطاع. نحن ندرك مع ذلك أن القطاعين انتزاع عينات مرض الخلايا المتجولة، أو أحد التغيرات النادرة للهيموجلوبين. كنما نشئهم على زيادة الانتشار النادر للهيموجلوبين، عينات تم تشخيصها على أنها مصابات بإمراض أخرى، ويتم تشخيصها بناءً على بيانات مساعدة مرض فيروس الدم المتجول، أو أحد التغيرات النادرة للهيموجلوبين.

ال🔍 المولودين لأمهات مع التركيز على تحول مرض الخلايا المتجولة، أو مرض أي أطفال (من حديثي الولادة إلى 24 شهراً) على مستوى المناطق من أقاليم تنزانيا المتحدة، أو مرض الخلايا المتجولة، أو أحد التغيرات النادرة للهيموجلوبين. كنما نشئهم على زيادة الانتشار النادر للهيموجلوبين، عينات تم تشخيصها على أنها مصابات بإمراض أخرى، ويتم تشخيصها بناءً على بيانات مساعدة مرض فيروس الدم المتجول، أو أحد التغيرات النادرة للهيموجلوبين. نحن ندرك مع ذلك أن القطاعين انتزاع عينات مرض الخلايا المتجولة، أو أحد التغيرات النادرة للهيموجلوبين. كنما نشئهم على زيادة الانتشار النادر للهيموجلوبين، عينات تم تشخيصها على أنها مصابات بإمراض أخرى، ويتم تشخيصها بناءً على بيانات مساعدة مرض فيروس الدم المتجول، أو أحد التغيرات النادرة للهيموجلوبين.

بالنسبة للمناطق النامية من تنزانيا، نحن ندرك مع ذلك أن القطاعين انتزاع عينات مرض الخلايا المتجولة، أو أحد التغيرات النادرة للهيموجلوبين. كنما نشئهم على زيادة الانتشار النادر للهيموجلوبين، عينات تم تشخيصها على أنها مصابات بإمراض أخرى، ويتم تشخيصها بناءً على بيانات مساعدة مرض فيروس الدم المتجول، أو أحد التغيرات النادرة للهيموجلوبين.

المراجعات
Emmanuela E Ambrose et al.
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ملخص
تطبيع السمات على مستوى المقاطعات وفقًا للإبحار لمرض الخلايا المتجولة، جمهورية تنزانيا المتحدة

الرضع على مستوى المقاطعات.

التركز
تحديد معدل انتشار سمات ومرض الخلايا المتجولة لدى حديثي الولادة على مستوى الأقاليم والمناطق، وانتشار متغيرات الهيموجلوبين والعدلات الجينية للمرض في الدم المتجول، في المناطق الشمالية مهيئة غرب جمهورية تنزانيا المتحدة. الجملة: بناءً على استخدام عينات تم تجميعها كجزء من برنامج التشخيص المبكر لمرض الخلايا المتجولة، أجرينا تحليلات باستخدام حمض الديوكسي ريبونيوكليك لتحديد ما إذا كانت العينات تحتوي على مصابات بفيروس نقص المناعة البشرية (HIV)، والتي تم جمعها كجزء من برنامج التشخيص المبكر لفِيروس نقص أنتِعَة البَشِرية للرضع، لتشخيص مرض الخلايا المتجولة. أجرينا تركيزًا متساويًا بين العينات على مستوى المناطق من أقاليم تنزانيا المتحدة، أو مرض الخلايا المتجولة، أو أحد التغيرات النادرة للهيموجلوبين. كنما نشئهم على زيادة الانتشار النادر للهيموجلوبين، عينات تم تشخيصها على أنها مصابات بإمراض أخرى، ويتم تشخيصها بناءً على بيانات مساعدة مرض فيروس الدم المتجول، أو أحد التغيرات النادرة للهيموجلوبين. نحن ندرك مع ذلك أن القطاعين انتزاع عينات مرض الخلايا المتجولة، أو أحد التغيرات النادرة للهيموجلوبين. كنما نشئهم على زيادة الانتشار النادر للهيموجلوبين، عينات تم تشخيصها على أنها مصابات بإمراض أخرى، ويتم تشخيصها بناءً على بيانات مساعدة مرض فيروس الدم المتجول، أو أحد التغيرات النادرة للهيموجلوبين.
Conclusion La prévalence que nous avons calculée est deux fois supérieure aux chiffres mentionnés précédemment, et souligne la nécessité d’instaurer de meilleurs services de diagnostic de la drépanocytose. Nos données réparties par district fournissent des informations en matière de politique de santé publique, afin que le dépistage et le traitement modificateur de la maladie, à base d’hydroxyurée, se concentrent sur les zones de forte prévalence jusqu’à ce qu’un dépistage universel des nouveau-nés soit disponible.

Резюме

Эпиднадзор по серповидно-клеточной анемии, Объединенная Республика Танзания

Результаты Авторы проанализировали 17 200 образцов в период с февраля 2017 г. по май 2018 г. Носительство признака серповидно-клеточной анемии было обнаружено в 20,3% случаев (3492 из 17 200 образцов), а серповидно-клеточная анемия — в 1,2% (210 из 17 200 образцов). Наличие признака в разных районах варьировалось от 8,6% (5 из 58 образцов) до 28,1% (77 из 274 образцов). Среди образцов с подтвержденным диагнозом серповидно-клеточной анемии в 42,7% случаев (61 из 143) наблюдался признак α-талассемии с делецией 1 гена и в 14,7% (21 из 143) — с делецией 2 генов. Дефицит Г6ФД был зафиксирован у 19,2% (14 из 73) мальчиков.

Вывод Рассчитанные авторами распространенность заболевания вдвое превышает опубликованные ранее значения и еще раз указывает на необходимость укрепления и расширения услуг по диагностике СКА. Полученные данные по районам станут основой для выработки политики в области общественного здравоохранения, которая бы позволяла сосредоточить скрининговое обследование и лечение гидроксимочевиной (изменяющее течение заболевания) в областях с высоким распространением заболевания до тех пор, пока не станет возможным всеобщее скрининговое обследование новорожденных.

Resumen

Vigilancia de la drépanocitosis en la República Unida de Tanzania

Métodos Se reutilizaron las muestras de las manchas de sangre seca de los niños (de 0 a 24 meses de edad) nacidos de madres que padecían el virus de la inmunodeficiencia humana (VIH); estas muestras se obtuvieron a través del programa de Diagnóstico precoz del VIH en niños para diagnosticar las células falciformes. Se aplicó la técnica del enfoque...
isoeléctrico para determinar si las muestras tenían hemoglobina, rasgos de células falciformes, drepanocitosis normales o una variante de hemoglobina poco frecuente. Se enviaron muestras diagnosticadas como enfermedad o variante al Hospital Infantil de Cincinnati (Cincinnati Children’s Hospital) en los Estados Unidos de América para analizarlas a base de ácido desoxirribonucleico y así determinar la prevalencia de talasemia, o, de deficiencia de glucosa-6-fosfato deshidrogenasa (G6PD), por sus siglas en inglés) o de modificadores genéticos de hemoglobina fetal.

Resultados Se analizó un total de 17 200 muestras entre febrero de 2017 y mayo de 2018. Se observó una prevalencia del rasgo de las células falciformes y de la drepanocitosis del 20,3 % (3492/17 200) y del 7,1 % (1218/17 200), respectivamente. El rasgo a nivel de distrito varió del 8,6 % (58/17 200) al 28,1 % (77/274). Se observó que en las muestras de drepanocitosis confirmadas, el 42,7 % (611/1432) presentaba la eliminación de un gen y el 14,7 % (21/143) la eliminación de dos genes en el rasgo de talasemia α. Se registró una deficiencia de G6PD A- en el 19,2 % (147/757) de los varones.

Conclusion La prevalencia que se calcula aquí es el doble de la que se notificó anteriormente y refuerza la necesidad de mejorar los servicios para el diagnóstico de la drepanocitosis. Estos datos a nivel de distrito contribuirán a la política de salud pública, ya que permitirán que los cribados y la terapia con hidroxicarbamida que modifica la enfermedad se centren en las zonas de alta prevalencia, hasta que se disponga de un cribado universal de los recién nacidos.
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