

Point-of-care testing allows successful simultaneous screening of sickle cell disease, HIV, and tuberculosis for households in rural Guinea-Bissau, West Africa

Federica Menzato¹ | Luca Bosa¹ | Armando Sifna² | Luisa Da Silva² |
Elena Gasperoni^{3,4} | Maddalena Martella¹ | Alfa Mustik⁵ | Liviana Da Dalt¹ |
Giulia Reggiani¹ | Vania Munaretto¹ | Giuseppe Liotta⁶ | Fabio Riccardi^{3,6} |
Raffaella Colombatti^{1,3}

¹Department of Woman's and Child's Health, Università di Padova, Padua, Italy

²Hospital Raoul Follereau (HRF), Centro de Referencia Nacional para Tuberculose, Bissau, Guinea-Bissau

³Aid Health and Development Onlus (AHEAD), Rome, Italy

⁴San Marino Hospital, San Marino, San Marino

⁵Non-profit organization "Amici della Guinea-Bissau", Milan, Italy

⁶Department of Biomedicine and Prevention, Tor Vergata University of Rome, Rome, Italy

Correspondence

Raffaella Colombatti, Department of Woman's and Child's Health, University of Padova, Via Giustiniani 3, 35128, Padua, Italy.
Email: raffaella.colombatti@unipd.it

Abstract

Diagnosis of noncommunicable genetic diseases like sickle cell disease (SCD) and communicable diseases such as human immunodeficiency virus (HIV) or tuberculosis (TB) is often difficult in rural areas of Africa due to the lack of infrastructures, trained staff, or capacity to involve families living in remote areas. The availability of point-of-care (POC) tests for the above diseases offers the opportunity to build joint programs to tackle all conditions. We report successful simultaneous screening of SCD, HIV, and TB utilizing POC tests in 898 subjects in Fanhe, in rural Guinea-Bissau. Adherence was 100% and all diagnosed subjects were enrolled in care programs.

KEYWORDS

Guinea-Bissau, HIV, point of care, sickle cell disease, tuberculosis

Abbreviations: AHEAD, Aid Health and Development Onlus; Hb, hemoglobin; HIV, human immunodeficiency virus; HRF, Hospital Raoul Follereau; NGO, non-governmental organization; POC, point of care; SCD, sickle cell disease; TB, tuberculosis.

Federica Menzato and Luca Bosa contributed equally to this work.

This manuscript was presented as a poster at the American Society of Hematology (ASH) Meeting December 2018: Menzato F et al. Successful simultaneous screening of sickle cell disease, HIV and tuberculosis in rural Guinea-Bissau, West Africa through rapid tests and a standardized clinical questionnaire: An outreach program due to a public-private partnership. <https://ashpublications.org/blood/article/132/Supplement%201/4715/262460/Successful-Simultaneous-Screening-of-Sickle-Cell>

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial](https://creativecommons.org/licenses/by-nc/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2022 The Authors. *Pediatric Blood & Cancer* published by Wiley Periodicals LLC.

1 | INTRODUCTION

Several "big killers" have been identified in Africa, some of which are infectious diseases that are widespread in African countries, like malaria, human immunodeficiency virus (HIV) infection, or tuberculosis (TB), while others are genetic disorders like sickle cell disease (SCD). All present a high morbidity and mortality toll^{1,2} and challenges for the fragmented and overburdened African health systems. Access to health services for rural populations is further limited and, in some

villages, basic health care and routine screening are seldom available due to limited diagnostic capacity, lack of specialized staff or other resources.³ Therefore, people are not diagnosed or are diagnosed late for SCD, HIV, TB, resulting in high morbidity and mortality. Recently, rapid tests for both HIV and SCD have become available in the market and one for TB is currently under development,^{4,5} offering the opportunity to plan screening programs at the point of care (POC) in rural areas, reaching underserved populations. Tackling diseases with different etiologies (SCD is a genetic noncommunicable disease, while HIV and TB are infectious communicable diseases with different mechanisms of spread) should include joint and coordinated actions among specific disease programs, which, unfortunately, often proceed separately. Nevertheless, a trend in this direction has recently become more evident, with joint efforts to combine HIV, TB, and SCD programs in order to benefit from joint support of infrastructures and networking of sample collection.^{6,7} Simultaneous screening of three big diseases at the POC in rural areas would save time and resources, while identifying people in need of further specialized diagnostic or follow-up.

Guinea-Bissau is a West African country with a high TB/HIV burden.⁸ Both HIV1 and HIV2 are present, with an overall HIV incidence per 1000 people (all ages) of 1.15 (95% CI: 0.92–1.41), although data collection has been hampered by chronic political instability and has been limited to the urban areas of Bissau, Gabu, and Bafatà.^{9,10} TB is widespread in the country with official data reporting TB rate at 361 (234–516)/100,000 population.⁸ There are National HIV and TB programs, but underdiagnosis and underreporting are common for both diseases due to limited infrastructure and limited screening in rural areas, often resulting in lack of access to health care or underdiagnosis when patients do access health centers.^{8,10,11} There is no National SCD screening program, and routine tests for SCD are not available, hence prevalence data are limited and come from pilot projects.¹² Several POC kits in Guinea-Bissau are available and currently used for routine diagnosis of HIV1 and HIV2 (determine HIV1/HIV2, Genie III HIV-1/HIV-2, Immunoflow HIV1-2, SD Bioline HIV-1/2 3.0),¹³ but not yet for TB and SCD screening.

In spite of the limited resources dedicated to the public health system, collaboration with the private sector, charities, and international institutions has allowed support of public health facilities with specific interventions, involving the National Reference Center for Tuberculosis Hospital Raoul Follereau (HRF), the Aid Health and Development Onlus (AHEAD), and the University of Padova.^{14–16} Building on this previously established network, we therefore designed a short-term intervention in the rural village of Fanhè (Figure 1) where the Italian non-governmental organization (NGO) “Friends of Guinea-Bissau” supports a local school and provides a nurse a couple of days per week. The primary objective was to evaluate the feasibility of utilizing simultaneously POC tests for SCD, HIV, and a questionnaire to screen for TB in a rural area of Guinea-Bissau during a health visit; secondly, we aimed to identify patients with SCD or HIV and enroll them in appropriate follow-up programs, as well as to identify suspected cases of TB eligible for indepth diagnostic screening; lastly, we wanted to determine hemoglobin (Hb)S prevalence in order to plan future interventions,

as epidemiological information is available only for the capital city of Bissau.¹²

2 | MATERIALS AND METHODS

The small rural village of Fanhe is in the countryside North-East of the capital city of Bissau. The village has a local school and a basic dispensary with a nurse a few days a week. A small regional hospital is present in Mansoa and a rural health center is in Nhacra, both at 25 km from Fanhe. The pilot screening intervention was designed in 2018 in three phases: preparatory phase (February–March), temporary outreach health post for screening (March), and follow-up for enrollment in dedicated programs (April–May).

2.1 | Preparatory phase

In preparation of the health post opening, the chiefs of the rural community villages and the local nurse informed the households through two collective meetings and home visits regarding the three objectives of the pilot project and its modalities after accepting the proposal made by the NGOs and the HRF staff (February–March 2018). The meetings were held in Portuguese-Creole and in one of the local languages, Balanta. The local chiefs organized the schedule of the health visits according to each household’s availability.

2.2 | Temporary outreach health post for screening

In the second phase a temporary health post was organized for 10 days: three nurses and two physicians from the HRF in Bissau, linguistically competent for Portuguese-Creole and local dialects, administered the standardized questionnaire (Supporting Material S1) and the physical examination, while two pediatric residents from Italy aided in the clinical examination. After performing the clinical visit and the TB standardized questionnaire, each patient was offered the possibility to perform the rapid tests for SCD (Sickle SCAN, BioMedomics, Inc, Morrisville, NC, USA) and HIV (Determine HIV-1/HIV-2, Alere Inc, Waltham, MA, USA). After oral informed consent collection, a previously trained local nurse supervised by two physicians of the international team collected the blood samples from a finger prick simultaneously for the SCD and the HIV tests; the procedure took less than 1 min for both and the average waiting time for the results was 20 minutes.

The results were communicated to all individuals immediately. Individuals with Sickle SCAN positive results underwent collection of a second blood sample on Guthrie card for confirmatory molecular analysis of the beta globin gene to be performed in Italy and received health education on SCD. Patients with HIV Determine positive test were informed of the results and advised to continue to the follow-up phase; patients with suspicion of TB were also advised to perform the appropriate diagnostic evaluation in the follow-up phase.



FIGURE 1 Map of Guinea-Bissau with the rural area of Fanhe

2.3 | Follow-up phase

During the third phase (April–May), subjects with suspected TB and/or HIV received free transportation to the HRF for TB diagnostic evaluation according to the national protocol or HIV confirmatory test. The timing of the follow-up and the visits were organized by the local nurse.

3 | RESULTS

All 898 inhabitants (32 families) living in Fanhe who were present at the time of the pilot project accepted to participate in the simultaneous screening program, underwent clinical examination, and responded to

the TB questionnaire; all performed the finger prick for HIV and SCD rapid test. Overall 395 were males (44%) and 503 females (56%), with mean age of 31.3 years (range: 2 months to 88 years).

3.1 | Sickle cell screening results and demographics

At Sickle SCAN, 16/898 (1.78%) were HbAS (children nine of 16); none were HbAC or HbSS. All 16 Sickle SCAN-positive HbAS samples underwent molecular analysis and the results were confirmed. All patients received information on the HbAS carrier state and health education on SCD in their local language. Demographics and characteristics of the individuals with HbAS are described in Table S1. Eight belonged to the

same three families (mother and two children for two families; mother with one child); the remaining were not related.

3.2 | HIV and tuberculosis screening results

At Determine HIV rapid test, 61/898 (6.79%) were HIV positive (children nine of 61). A total of 93/898 (10.35%) presented clinical suspicion of TB (children 33/93). Twelve (1.3%) had a suspicion of TB and were also HIV positive (children: 2/12). For subjects with a suspicion of TB or who were HIV positive, free transportation was arranged to the HRF for complete TB diagnostic workup and a second HIV confirmatory Rapid Test. All HIV-positive tests were confirmed and patients enrolled in clinical care in a nearby village dedicated HIV rural health clinic; 30% of patients with TB suspicion had the diagnosis confirmed by X-ray/sputum smear examination and were enrolled in appropriate care programs at the TB rural health clinic.

4 | DISCUSSION

Our pilot project demonstrates the feasibility of simultaneous POC testing for genetic and communicable diseases in rural Guinea-Bissau, with good capacity of the local staff to learn how to perform the rapid tests, willingness of families to undergo testing if adequately informed, and adherence of families to follow-up programs, in case of need.^{4,5} Dedicated staff training was possible in a short period of time and a brief supervision of 15 days allowed correct interpretation of POC test results in all cases but two, indicating that with long-distance supervision, results could even be improved. The rural community's acceptance of the screening project was satisfactory, with 100% households' participation, highlighting the importance of preliminary health information and community engagement in screening programs.¹⁷

Water and sanitation conditions in the Fanhe area were poor, as well as electricity support, similarly to other parts of the country.¹⁸ Moreover, rate of illiteracy was high, with low basic health knowledge and a high proportion of adults who spoke only local languages. These factors will need to be taken into consideration in planning more stable screening programs and follow-up care requiring adherence to treatment or health behaviors in SCD such as penicillin prophylaxis or prevention of vaso-occlusive crisis and spleen sequestration or fever management.

The frequency of HbAS in families (1.78%) was overall lower than the one reported recently in an urban pediatric population in Bissau, which was 6.95% HbAS, 0.94% SS, and 0.23% AC¹³; however, our sample is small and future studies including larger pediatric populations from different ethnic backgrounds and areas of the country are needed to describe the epidemiology of the sickle gene in Guinea-Bissau. None of the children in this group had SCD; no stillbirths or deaths in childhood occurred in the families with the sickle trait.

5 | CONCLUSIONS

This pilot study confirms the opportunity that rapid tests offer to scale-up diagnosis and treatment in Africa and the feasibility of a

simultaneous population screening at the POC in rural areas of Guinea-Bissau for three "big diseases" (SCD, HIV, and TB). The simultaneous screening with rapid test and standardized clinical examination is a model that could be replicated in other rural settings of Guinea-Bissau to benefit from joint communicable and noncommunicable disease programs.

ACKNOWLEDGMENTS

The project was supported by AHEAD Onlus. The authors would like to thank Guido Maruelli coordinator of "Friends of Guinea-Bissau" and Mamadu Saliu Sanha Representative of AHEAD for the support in the project, as well as the local logistic staff, nurses, and technicians who contributed to improving health care for the rural population. The pediatric residents involved in the project were part of an International Outreach Program of the Pediatric Residency School of the University of Padova.

CONFLICT OF INTEREST

The authors report no conflict of interest for the research reported in this manuscript.

REFERENCES

- Piel FB, Hay SI, Gupta S, Weatherall DJ, Williams TN. Global burden of sickle cell anaemia in children under five, 2010–2050: modelling based on demographics, excess mortality, and interventions. *PLoS Med.* 2013;10:e1001484.
- Sultana ZZ, Hoque FU, Beyene J, et al. HIV infection and multidrug resistant tuberculosis: a systematic review and meta-analysis. *BMC Infect Dis.* 2021;21(1):51.
- Udenigwe O, Okonofua FE, Ntoimo LFC, Imongan W, Igboin B, Yaya S. "We have either obsolete knowledge, obsolete equipment or obsolete skills": policy-makers and clinical managers' views on maternal health delivery in rural Nigeria. *Fam Med Community Health.* 2021;9(3):e000994.
- Dexter D, McGann PT. Saving lives through early diagnosis: the promise and role of point of care testing for sickle cell disease. *Br J Haematol.* 2022;196(1):63–69.
- Hong JM, Lee H, Menon NV, Lim CT, Lee LP, Ong CWM. Point-of-care diagnostic tests for tuberculosis disease. *Sci Transl Med.* 2022;14(639):eabj4124.
- Foo C, Shrestha P, Wang L, et al. Integrating tuberculosis and noncommunicable diseases care in low- and middle-income countries (LMICs): a systematic review. *PLoS Med.* 2022;19(1):e1003899.
- Kiyaga C, Hernandez AG, Ssewanyana I, et al. Sickle cell screening in Uganda: high burden, human immunodeficiency virus comorbidity, and genetic modifiers. *Pediatr Blood Cancer.* 2019;66(8):e27807.
- World Health Organization (WHO) global tuberculosis report 2018. WHO; 2018. Accessed August 9, 2022. <https://www.who.int/publications/i/item/9789241565646>
- UNAIDS country fact sheets. UNAIDS. Accessed August 9, 2022. <https://www.unaids.org/en/regionscountries/countries/guinea-bissau>
- Galjour J, Havik P, Aaby P, Rodrigues A, Mpinga EK. Chronic political instability and the HIV/AIDS response in Guinea-Bissau from 2000 to 2015: a systematic review. *Trop Med Infect Dis.* 2021;6(1):36
- Virenfeldt J, Rudolf F, Camara C, et al. Treatment delay affects clinical severity of tuberculosis: a longitudinal cohort study. *BMJ Open.* 2014;4(6):e004818.

12. Martella M, Campeggio M, Pulè G, et al. Distribution of HbS allele and haplotypes in a multi-ethnic population of Guinea-Bissau, West Africa: implications for public health screening. *Front Pediatr*. 2022;10:826262.
13. Esbjörnsson J, Månsson F, Kvist A, et al. Long-term follow-up of HIV-2-related AIDS and mortality in Guinea-Bissau: a prospective open cohort study. *Lancet HIV*. 2018;S2352-3018(18):30254-30256.
14. Rabna P, Ramos J, Ponce G, et al. Direct detection by the Xpert MTB/RIF assay and characterization of multi and poly drug-resistant tuberculosis in Guinea-Bissau, West Africa. *PLoS One*. 2015;10(5):e0127536.
15. Colombatti R, Coin A, Bestagini P, et al. A short-term intervention for the treatment of severe malnutrition in a post-conflict country: results of a survey in Guinea-Bissau. *Public Health Nutr*. 2008;11(12):1357-1364.
16. Colombatti R, Penazzato M, Bassani F, et al. Malaria prevention reduces in-hospital mortality among severely ill tuberculosis patients: a three-step intervention in Bissau, Guinea-Bissau. *BMC Infect Dis*. 2011;11:57.
17. Ankomah SE, Fusheini A, Ballard C, Kumah E, Gurung G, Derrett S. Patient-public engagement strategies for health system improvement in sub-Saharan Africa: a systematic scoping review. *BMC Health Serv Res*. 2021;21(1):1047.
18. Colombatti R, Vieira CS, Bassani F, et al. Contamination of drinking water sources during the rainy season in an urban post-conflict community in Guinea-Bissau: implications for sanitation priority. *Afr J Med Med Sci*. 2009;38(2):155-161.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Menzato F, Bosa L, Sifna A, et al. Point-of-care testing allows successful simultaneous screening of sickle cell disease, HIV, and tuberculosis for households in rural Guinea-Bissau, West Africa. *Pediatr Blood Cancer*. 2022:e30009. <https://doi.org/10.1002/pbc.30009>