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The Role of Laboratory Supervision in Improving the Quality of Malaria Diagnosis: A Pilot Study in Huambo, Angola

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Abstract. In 2006, the Angolan National Malaria Control Program introduced clinical guidelines for malaria case management, which included diagnostic confirmation of malaria before administration of treatment; however, diagnostic practices were inconsistent and of unknown quality. In 2009, a laboratory supervision program was implemented in Huambo Province, with the goal of assessing and improving diagnosis of malaria within the confines of available in-country resources. Supervisions were carried out from 2009 to 2014 using a standardized supervision tool by national laboratory trainers. Data from the first supervision were compared with that from the final supervision. Over the study period, the number and level of training of laboratory technicians increased, and there was a nonstatistically significant trend toward improved laboratory conditions. There was a significant reduction in false-positive microscopy slide reading ($P = 0.0133$). Laboratory infrastructural capacity to diagnose other communicable diseases, including syphilis, human immunodeficiency virus and hepatitis B virus infections ($P = 0.0012$, 0.0233 and 0.0026, respectively), also improved significantly. Laboratory supervision for malaria diagnosis found significant areas for improvement, and in combination with concurrent capacity-building activities, it improved the diagnostic capacity for malaria and other diseases. Importantly, this study demonstrates that locally available resources can be used to improve the accuracy of malaria diagnosis.

INTRODUCTION

The Angolan Ministry of Health has worked over the past 12 years to rebuild the health-care infrastructure, which was decimated during its prolonged civil war.[1] During this time, health indicators have significantly improved, yet Angola continues to have among the highest child mortality rate (167/1,000) and maternal mortality rate (460/100,000) in the world. Average life expectancy is only 51 years.[2] Malaria significantly contributes to these poor health outcomes, and is estimated to be responsible for 35% of health-care visits, 20% of hospital admissions, 40% of perinatal deaths, and 25% of maternal deaths.[3,4]

Underlying these health statistics, however, is a lack of standardized diagnostic practices. In 2006, the Angolan National Malaria Control Program (NMCP) introduced clinical guidelines for malaria case management, including treatment with highly effective artemisinin-based combination therapies (ACTs).[5] Given the high cost of ACTs, fear of development of resistance to ACTs, and very low specificity of clinical diagnosis, the NMCP recommended diagnostic testing before administration of treatment.[6–8] Three years after these guidelines were disseminated, over half of providers continued to treat clinically suspected cases of malaria despite negative laboratory testing.[9] Fever alone is frequently the only clinical criterion for diagnosis, and yet one study showed that only 3.6% of fevers in children under 5 years of age in Luanda, the densely populated urban capital, had a positive malaria diagnostic test.[10] Misdiagnosis results in overrepresentation of the burden of malaria and derails clinical investigation into other, potentially life-threatening, causes of illness.[11]

The MENTOR Initiative (MENTOR) is an international nongovernmental organization that has worked in collaboration with the NMCP since 2003 to implement the national malaria control strategy. In 2009, MENTOR implemented a laboratory supervision program with the goal of improving diagnosis of malaria within the confines of available in-country resources. The goal of supervision was to gather baseline data on microscopic diagnosis of malaria, conduct on-the-job training for laboratory technicians, and provide the foundation for the development of a laboratory quality assurance program. The aim of this study is to describe the 5 years of experience in laboratory supervision and evaluate the improvement in laboratory capacity as it relates to malaria diagnosis over the study period.

MATERIALS AND METHODS

Setting. Laboratory supervision was carried out in Huambo Province, Angola. Huambo has a subtropical highland climate with stable meso-endemic transmission of malaria. The majority of laboratories are in public health facilities, including health centers, municipal and provincial hospitals, as well as a few private clinics. Laboratories provide services with low cost-sharing by patients.

Supervision intervention. Laboratory supervisions were conducted regularly over a 5-year period from 2009 to 2014. Laboratory supervisions were carried out by an expert team using a structured supervision guide for data collection. Supervisions were conducted by an integrated team of NMCP laboratory supervisors and MENTOR clinical supervisors. The NMCP laboratory supervisors are nationally certified laboratory trainers, who have received supplemental training from the United States Centers for Disease Control and Prevention (CDC) and the National Laboratory of Angola. Experienced clinical supervisors provided logistic and implementation support.

The laboratory supervisors conducted supervisions in a systematic manner using a supervision guide. The laboratory supervision guide was developed from November 2008 to February 2009 and collects data related to laboratory management best practice guidelines. The guide is composed of four main sections: laboratory technician demographic data, laboratory conditions, assessment of laboratory technician knowledge, and statistical information (see Supplemental Annex 1

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for full guide). The laboratory supervisors administered questions regarding demographic data of laboratory technicians. They inspected laboratory conditions, including biosafety, availability of electricity, and availability and quality of light microscopy. They assessed the diagnostic technical capacity of the laboratory technicians and conducted quality assurance of malaria microscopic diagnosis. Technical diagnostic capacity of the laboratory technicians was assessed by evaluation of microscopy slides prepared by the technician for quality and accuracy. Quality assurance was performed by review of slides diagnosed as positive or negative in the laboratory. In 2009, five slides that the laboratory had diagnosed as positive and five that the laboratory had diagnosed as negative were evaluated; in 2014, 10 of both positive and negative slides were evaluated for accuracy. If any slides were classified inaccurately, the laboratory was considered inaccurate for statistical analysis purposes.

Laboratory supervision was piloted with a first round of supervision of all laboratories in Huambo Province from March to June 2009. An additional round of supervision was conducted in 2009 at all laboratories in Huambo Province, and subsequently, supervisions with full data collection were conducted once a year at each facility.

Laboratory supervision was coupled with technical support, on-the-job training, and peer mentorship of laboratory technicians by the trained laboratory supervisors in general laboratory management, as well as proper slide preparation and reading.

Concurrent activities. From 2009 to 2014, the President's Malaria Initiative (PMI) also independently contributed to malaria diagnosis in the laboratories in Huambo in a number of ways. They provided 41 microscopy kits, which included microscopy slides, lancets, immersion oil, lens tissue, cell counter, staining materials, timer, pipettes, measuring cylinders, and replacement light bulbs. PMI also trained 90 laboratory technicians through an intensive 10-day training in malaria diagnosis based on curriculum developed by the CDC. With these trainings, laboratory technicians were given laboratory bench aids on the microscopic diagnosis of malaria. From 2013 to 2014, PMI/CDC distributed manuals on quality control, which were newly developed in collaboration with the NMCP, National Laboratory, and the National Malaria Control Program.

Statistical analysis. Data from the supervision guides were cleaned and recorded prospectively in a comprehensive Excel database (Microsoft Corp., Redmond, WA). Data from the first round of supervision in 2009 were compared with data from the final round of supervision in 2014. Data were analyzed using GraphPad Software (La Jolla, CA). The McNemar test of significance was used to compare the dependent, paired nominal data.

The results were presented to national and provincial partners, as well as the funding agency.

RESULTS

The first round of supervision in 2009 included 30 of the 33 operational laboratories in public health facilities in the province of Huambo. Three laboratories were not included because of unavailability of laboratory technician on the day of the supervision and transportation limitations. The final round of supervision in 2014 included 36 of the 39 laboratories operational in public health facilities. Three were not included because of temporary closure for rehabilitation or unavailability of laboratory technicians at the time of supervision. Analysis of the data was limited to the 25 laboratories that were supervised in both 2009 and 2014.

TABLE 1
Laboratory technician training

Technician training	2009 N^* = 109 (%)	2014 N = 163 (%)
Educational level		
Basic laboratory training†	26 (23.9)	20 (12.3)
Medium laboratory training‡	81 (74.3)	141 (86.5)
Other training	2 (1.8)	2 (1.2)
Refresher training on malaria diagnosis within the last year	61 (56.0)	148 (90.8)

*Number of laboratory technicians present at time of evaluation.
†10th grade educational level with an incorporated 2.5 years of training on laboratory technology.
‡12th grade educational level with an incorporated 4.5 years of training on laboratory technology.

The number of laboratory technicians increased dramatically over the study period (Table 1). The training level of laboratory technicians improved, with a greater proportion of medium-trained laboratory technicians, which is the highest attainable level of training within Angola. At the same time, a greater proportion of laboratory technicians had received refresher training in malaria diagnosis within the past year.

There was a nonsignificant improvement in availability of electricity in laboratories over the study period (Table 2), with seven laboratories becoming electrified (15 versus 22, $P = 0.0704$). Light microscopes became available in four additional facilities during the study period, leaving only two facilities necessitating use of mirror microscopy; however, this was not a statistically significant change (19 versus 23, $P = 0.2888$). The microscopes remained in overall good condition throughout the study period.

The technical capacity of laboratory technicians significantly improved over the study period (Table 3). There were no cases of false-negative slide reading identified by the laboratory supervisors, rather, the improvement in slide reading reflects a reduction in the proportion of facilities that produced false-positive slide reads. The percentage of facilities with 100% concordance increased from 16/25 (64%) to 23/25 (92%). While 28% of individual slides evaluated in 2009 were read as falsely positive, only 1.2% slides were read as falsely positive in 2014. The proportion of laboratory technicians performing rapid diagnostic tests (RDTs) did not change over the study period.

There was a marked increase in the availability of non-malaria diagnostic tests (Table 4). Laboratory infrastructural capacity for diagnosis of communicable diseases increased significantly over the study period, including syphilis ($P = 0.0012$),

TABLE 2
Laboratory and equipment conditions

	2009 N = 25 (%)	2014 N = 25 (%)	Significance McNemar test
Stable electricity	15 (60)	22 (88)	0.0704
Light microscope available	19 (76)	23 (92)	0.2888
Microscope functions well	23 (92)	25 (100)	0.4795
Laboratory meets all three of the above conditions	14 (56)	20 (80)	0.1489

TABLE 3
Technical ability of laboratory technician

Capacity assessment	2009 N* = 25 (%)	2014 N = 25 (%)	Significance McNemar test
Sample slides correctly assessed by technician	16 (64)	23 (92)	0.0133
Laboratory technicians conduct RDTs	8 (32)	4 (16)	0.2888

RDT = rapid diagnostic test for malaria.
*One representative laboratory technician at each laboratory.

human immunodeficiency virus (P = 0.0233) and hepatitis B (P = 0.0026) infections. Capacity to identify blood group (P = 0.0002), measure glucose (P = 0.0055), and diagnose pregnancy (P = 0.0005) also significantly increased.

DISCUSSION

The quality of microscopic diagnosis of malaria improved during the period of laboratory supervision in Huambo Province. This improvement is likely related to the combined interventions implemented during this time, including improved baseline education of laboratory technicians, provision of refresher trainings, supply of laboratory materials and equipment, and greater focus on laboratory quality control at the national level. Laboratory supervision supported these activities by providing concrete feedback to provincial partners, creating the awareness of needed improvements in laboratory infrastructure, and in some cases, providing logistical support to their implementation. Laboratory supervision also created the opportunity for one-on-one on-site clinical mentorship for laboratory technicians, which had never before been possible. Laboratory supervision provided the unique opportunity to gather information to document challenges and progress in laboratory diagnosis in a specific context, which guides programmatic planning for the future.[12,13] In the case of Angola, laboratory supervision has contributed to the development of a robust quality assurance program at the national level.[14]

Importantly, over the study period, the proportion of false-positive readings of slides was reduced. Improved accuracy reduces unnecessary treatment with antimalarials and pushes clinicians to find the real cause of patients' illnesses that present similarly to malaria. The reduction in false-positive readings corresponded to an overall improvement in laboratory capacity to diagnose other infectious etiologies of illness. Although improvement in diagnosis of other diseases was not an objective of the laboratory supervisions, the regular visits of laboratory supervisors through this program contributed to improved supply chain logistics, providing the opportunity for informal feedback to the provincial health department about laboratories' needs for general diagnostic materials, as well as providing the physical transport of some of these supplies. One of the greatest challenges for providers in resource-limited health-care settings is how to treat an ill patient with a negative malaria diagnostic. Having a greater capacity to evaluate other entities with malaria-like presentations serves to strengthen overall patient care.

TABLE 4
Availability of non-malaria diagnostic testing

Diagnostic test	2009 N = 25 (%)	2014 N = 25 (%)	Significance McNemar test
Syphilis	1 (4)	15 (60)	0.0012
Typhoid	9 (36)	15 (60)	0.1489
Human immunodeficiency virus	1 (4)	8 (32)	0.0233
Hepatitis B	0 (0)	11 (44)	0.0026
Tuberculosis	4 (16)	9 (36)	0.1306
Hemoglobin	19 (76)	21 (84)	0.6171
Hematocrit	0 (0)	5 (25)	0.736
Blood grouping	1 (4)	17 (68)	0.0002
Glucose	2 (8)	13 (52)	0.0055
Urine analysis	24 (96)	24 (96)	0.4795
Stool analysis	21 (84)	24 (96)	1.333
Rapid pregnancy test	5 (20)	19 (76)	0.0005

In Angola, there has been rapid adoption of RDTs, and a recent prevalence survey demonstrated that RDTs were more sensitive than microscopy (73% and 60%, respectively) without sacrificing specificity.[15] Although there is value in maintaining microscopic skills, the variability in technical capacity introduces a serious concern regarding diagnostic accuracy that has been reduced with the use of RDTs in other settings.[16–19] On the other hand, there are benefits of maintaining microscopy skills and not depending solely on RDTs. With microscopy, parasite density can be quantified. In addition, identification of the species of malaria parasite with microscopy in the clinical setting allows precise treatment to be prescribed, which is important, given that multiple species of malaria parasites have been identified in Angola.[20] Recording parasite density and species has only recently been made a technical requirement for laboratory technicians in Angola, coinciding with improved education and training of laboratory technicians. Improving and maintaining microscopic proficiency in malaria diagnosis through ongoing training and supervision not only serves to strengthen malaria diagnosis, but also adds value to general laboratory diagnosis in the long term.

There are limitations to this evaluation. It is observational and based on programmatic activities that were implemented in parallel to other local and national health systems interventions, making it difficult to isolate the effect of laboratory supervision alone. In addition, the conditions of Huambo Province during the study period are unique. In post-war Angola, infrastructure was in the process of being rebuilt: roads were poor, electricity limited, connectivity minimal outside the urban center, and water was scarce. A generation of skilled workers was missing as a result of the prolonged conflict. Therefore, the generalizability of this study may be limited.

These laboratory supervisions were the first of their kind in Angola and demonstrate how nongovernmental partners can strengthen and support national programming. Importantly, they demonstrate that locally available resources can be used to improve the accuracy of malaria diagnosis through relatively low-cost interventions.

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