Performance evaluation of the Mini-Lab, an all-in-one clinical bacteriology laboratory adapted to low-resource settings, in a district hospital in Central African Republic: a prospective descriptive study

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Highlights

- The Mini-Lab is a simplified and all-in-one microbiology laboratory for remote areas
- It showed good performances for bacterial identification in blood culture
- Antibiotic susceptibility results were concordant with reference for most antibiotics
- The Mini-Lab was perceived as easy to use by the non-expert laboratory technicians.
- It improves access to quality microbiological diagnostics in resource-limited setting

Performance evaluation of the Mini-Lab, an all-in-one clinical bacteriology laboratory adapted to low-resource settings, in a district hospital in Central African Republic: a prospective descriptive study

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ABSTRACT

Background

Médecins sans Frontières designed an all-in-one microbiology laboratory (the "Mini-Lab") to improve bacterial infections diagnosis in low-resource settings by non-expert laboratory staff. We assessed the diagnostic performance of the Mini-Lab in its final intended use.

Methods

This was a prospective descriptive study at a District Hospital in Central African Republic. We included hospitalised patients who had a blood culture prescription. Bacteria isolated in the Mini-Lab were sent to a reference laboratory for confirmation. Ease of use was assessed using a self-administered questionnaire after training and up to 8 months after.

Results

Isolated from 960 blood cultures between Sept 2021 and Feb 2022, 76 pathogens were sent for confirmation. The concordance of bacterial identification between the Mini-Lab and the reference method was 97% (74/76) at genus level and 90% (68/76) at species level. Antibiogram showed very good category concordances (≥90%) between the Mini-Lab and the reference methods for most antibiotics. The Mini-Lab was perceived as easy to use by the laboratory technicians.

Conclusion

The Mini-Lab, routinely implemented in a district hospital in combination with an antimicrobial stewardship programme showed good performances and usability by non-expert laboratory staff. It is a promising solution to improve access to microbiological diagnostics in remote areas.

Keywords: microbiology laboratory; antimicrobial resistance; low-resource settings; blood culture; sepsis

Words 4168

INTRODUCTION

The global increasing threat of antibiotic-resistant bacterial infections, both among hospitalised patients and in the community, has led to the development of the WHO Global Action Plan, which calls for a multi-sectorial strategy against antimicrobial resistance (AMR) at national and international levels [1]. An essential element of this strategy is improving access to diagnostics, as a microbiology laboratory supports antimicrobial stewardship (AMS) and infection prevention and control (IPC) programmes [2]. However, laboratory diagnosis is challenging to implement in low-resource settings (LRSs) [3,4] and therefore few hospitals in LRSs are properly equipped with microbiology laboratories because of the limitations of funds and trained staff, with access to diagnostics even more limited at the peripheral (district) level.

By operating mainly in LRSs, Médecins Sans Frontières (MSF) has witnessed first-hand the detrimental impact of increasing AMR on patient management [5]. As part of a comprehensive strategy, including IPC and AMS, MSF has been exploring ways to increase access to diagnostics at the district level. Among them, MSF and external partners developed a simplified all-in-one clinical laboratory for field bacteriology, the Mini-Lab [6,7]. It is composed of six boxes that unfold into a fully equipped and ready-to-use workstation, where bacterial cultures, identification and antibiotic susceptibility testing (AST) can be performed. The diagnostic accuracy and robustness in tropical conditions were validated for each component, including the blood culture bottles [8,9], the subculture units [10], the identification system [11], and the susceptibility testing [12]. The Mini-Lab was designed to be used by a minimum of two non-expert laboratory

technicians and one laboratory supervisor with no previous experience in microbiology but trained to work in the Mini-Lab. The quality of the results is ensured by an internal Quality Management System, including a full laboratory manual, an equipment monitoring system and twelve internal quality control reference strains (ATCC, KWIK-STIK, Microbiologics, USA) to test process components at least with one Gram-negative and one Gram-positive organism weekly. Stock management requires 2 fridges for the storage of materials for 800 samples and a small fridge in the Mini-Lab for everyday activities. A re-supply is advised every 4-6 months. Educational and informatics materials are included with the Mini-Lab. In addition, there is a laboratory information management system (the Mini-LIMS), which integrates an assisted reading system (ARS) based on comparison of test results with an atlas of images, and includes an expert system that helps users interpret identification and AST results as well as alerts when results are inconsistent.

In September 2019, the Mini-Lab was piloted in a field implementation evaluation in MSF Drouillard Hospital in Port-au-Prince, Haiti. In this first field feasibility study, the Mini-Lab showed good usability and ease-of-use by non-expert laboratory technicians after a 1-month training (unpublished). Compared with reference methods, pre-identification, identification, and AST methods were generally acceptable, although sample size was too small to reach definitive conclusions.

Here, we evaluated the performance of the Mini-Lab implemented as part of routine patient care in the Central African Republic (CAR). The objectives of this field implementation study were to assess the diagnostic performance of the Mini-Lab in its intended use, to assess its ease-of-use by non-expert laboratory staff, and to evaluate the effect of bacteriological results on antibiotics prescription by the clinicians.

METHODS

Study design and setting

This prospective descriptive study took place in the Carnot District Hospital (CDH), in Carnot, southwest of Central African Republic (CAR). MSF has supported paediatric units in CDH since 2014 (76 beds, 4957 admissions in 2021), including emergency, intensive care, neonatology, and therapeutic feeding centre, as well as an internal medicine ward for HIV/TB adult patients (20 beds, 890 admissions in 2021). On site, there is also a laboratory with routine tests like biochemistry and haematology, but no bacteriological culture before the Mini-Lab.

The implementation of the Mini-Lab was part of a formal AMS programme that started in April 2021, with the arrival of an infectious disease specialist to the hospital to train and mentor an AMS focal point. A microbiologist trained two newly recruited laboratory technicians and one supervisor with no previous experience in microbiology from May to June 2021. He trained a third newly recruited laboratory technician in November and December 2021 while the routine activities continued. The training covered all the technical procedures implemented at the Mini-Lab, from the reception of blood cultures to the delivery of final results, including waste management and quality control. The initial training of clinicians on blood culture prescription and of nurses on blood culture sampling was conducted in June 2021, and a pilot phase with blood culture collection and analysis in the Mini-Lab was implemented for 1 week. The microbiologist coordinated the Mini-Lab until the end of the study in February 2022.

Recruitment process

Patient recruitment started on September 13, 2021 and ended on February 13, 2022. Patients were eligible if they had been admitted as inpatients to the CDH and if they had blood culture samples taken, which had been prescribed either on admission or during hospitalisation according to clinical criteria (supplementary panel, appendix). There were no pre-identified exclusion criteria.

Bacteriological testing in the Mini-Lab

Blood sampling was performed using bi-phasic blood culture bottles (Autobio Diagnostics, Zheng Zhou City, China). The recommendations were to collect one set of aerobic bottles per patient: one bottle per set for children (2–5 mL of blood per bottle, maximum 2 mL for neonates) and two bottles per set for adults (8–10 mL of blood per bottle) [13]. Blood volumes were calculated by weighing the bottles before and after blood collection. After registration in the Mini-Lab, the bottles were incubated at 35±1°C until signs of growth, or up to 7 consecutive days if no signs of growth. Blood cultures were visually inspected for signs of growth daily. Blood cultures with signs of growth were subcultured on both InTray®MH Chocolate agar and InTray®Colorex Screen (BioMed Diagnostics, White City OR, USA). All blood cultures were also blindly subcultured after 24 h of incubation, even if no signs of growth were observed. Preliminary identification (pre-identification) consisted of a combination of: Gram staining, oxidase (OxiSticks™ Oxidase Swabs, Hardy Diagnostics, Santa Maria CA, USA), catalase (Catalase Reagent, Liofilchem, Roseto degli Abruzzi TE, Italy), aminopeptidase (Gram Test Stick, Liofilchem), and coagulase (Coagulase Plasma, Oxoid Thermo Fisher Scientific, Waltham MA, USA). A pre-identification algorithm (Supplementary figure 1) was used to guide the process and interpret these tests

results, bacterial morphology, and colony colour on InTray®Colorex Screen media. Bacterial identification was performed on a single Gram-positive and Gram-negative panel (MSF Neg/Pos ID type 2 panel, Beckman Coulter, Sacramento CA, USA), and AST was performed on either Gram-positive (MSF Pos MIC type 2 panel), Gram-negative (MSF Neg MIC type 2 panel), or fastidious panels (MSF FAST MIC panel). All Gram staining, culture plates, and identification/AST plates were photographed and recorded in the Mini-LIMS to help with results interpretation using the ARS and for study purposes.

All isolated bacterial strains were stored in cryobeads vials (Technical Service Consultants Ltd, Lancashire, UK) containing brain heart infusion and 15% glycerol in a –80°C freezer and shipped at –20°C to the reference laboratory in France.

Reference testing

Reference pre-identification, identification and AST were performed at the French National Reference Centre for antimicrobial resistance in the Bicêtre Hospital, Paris, France. All blinded bacterial isolates were identified using MALDI-TOF (MALDI Biotyper, Bruker, Palaiseau, France). The AST was performed using disk diffusion method (for most antibiotics), agar gradient diffusion method (teicoplanin /vancomycin for *Staphylococcus sp.*), broth microdilution (amoxicillin-clavulanate, piperacillin-tazobactam, colistin for Gram-negative bacilli, daptomycin for *Enterococcus* and *Staphylococcus*) and agar-based dilution (fosfomycin for *Staphylococcus* and *Enterococcus*) to determine the minimum inhibition concentration (MIC) or the diameter of inhibition as per EUCAST v11.0 breakpoints [14]. The reference AST was performed only on isolates identified as pathogens and a random selection of coagulase-negative *Staphylococcus*.

Data collection procedures

The bacteriological results from the Mini-Lab were made available to clinicians on paper report and recorded on the Mini-LIMS by the laboratory technicians. All records from patients with positive blood cultures were evaluated by the AMS focal point to classify the organism as a pathogen or contaminant based on the isolate type and clinical and therapeutic considerations. Therapeutic data from patients with pathogen-positive blood cultures were collected by the AMS focal point on a standardised questionnaire using patient records. He decided on the appropriateness of the empiric and targeted antibiotic treatment based on the culture/AST results and according to the supporting guidelines for AMS programme (MSF Paediatric guidelines and MSF Targeted Antibiotic Therapy Guide). He may have offered guidance to clinicians regarding antimicrobial management before data collection.

Ease-of use of each component of the Mini-Lab was assessed using a self-administered user experience questionnaire. We used a four-point Likert scale (1=strongly disagree; 2=disagree; 3=agree; 4=strongly agree) (supplementary table 1). This self-assessment was done at the end of the initial training (June 2021 for technicians 1 and 2, December for technician 3), 3 months (September 2021 for technicians 1 and 2, February 2022 for technician 3) and 8 months (February 2022 for technicians 1 and 2) after initial training. The study ended before the technician 3 had 8-month experience.

Data analysis

The pseudonymised clinical data were entered on site into the REDCap software (http://project-redcap.org/). Data were analysed using Stata® 16 software (Stata Corporation, College Station, Texas, USA). The bacteriological data were exported from the Mini-LIMS for the patients included in the study. For continuous variables, the

average, median, standard deviation, minimum and maximum were given; categorical variables were described using percentages.

To assess Mini-Lab performance, we compared key performance indicators with those reported in the literature: pathogen positivity rate, range of pathogens detected, average filling volume of blood culture bottles, and turn-around time (supplementary table 2). For comparative analysis on bacteria identification, we assessed agreement between Mini-Lab and the reference methods at species and genus level, respectively. For comparative analysis on AST, we assessed categorical agreement as ratios for minor (false intermediate), major (false resistance), and very major discrepancies (false susceptibility) for each antibiotic of the three AST panels, as per criteria in ISO20776-2: 2007. Missing data were considered missing at random, and no imputation was applied. Identification and categorical agreements were considered poor (<75%), acceptable (75-85%), or good (>85%).

For ease-of-use evaluation, we calculated the median score of the answers (ordinal values) from a cluster of questions by topic for each laboratory technician and at each time point. Ease-of-use was considered good (median score 3 to 4) or not sufficient (median score 1 or 2).

Ethical considerations

Inclusion in the study was voluntary and required prior signed informed consent by adult participants or minors' parent(s)/caregiver(s) for data collection. The patient information sheet provided information in French or Songo. Each patient who had indications for blood culture sampling had a sample taken as part of the routine procedures before consenting for study participation. Consent was related to data collection, not to blood culture sampling.

RESULTS

This study includes eligible patients admitted to CDH between Sept 13, 2021, and Feb 13, 2022. Out of 1042 patients with at least one blood culture collected, 948 (91%) were investigated for eligibility (figure 1). 111 patients were not eligible. Among 837 eligible patients, 835 were included (two refused to participate). Among included patients, 574 (69%) were younger than 5 years (supplementary table 3).

Among the 835 included patients, 950 sampling episodes were performed for a total of 960 blood culture bottles processed (a set of two blood cultures was inoculated for ten episodes). After incubation, 271 (28%) of 960 blood cultures were positive, and 300 microorganisms were isolated. Of these, 124 were classified as pathogens by the AMS focal point and 176 as contaminants. In one blood culture, two different pathogens were isolated: non-typhoidal Salmonella and Klebsiella pneumoniae. The most frequently isolated pathogens were non-typhoidal Salmonella (44%), Escherichia coli (10%), and Streptococcus pneumoniae (9%). In total, 123 (13%) of 960 blood cultures were positive for at least one pathogen, which corresponded to 117 patients. Contamination rate at the site of collection was 16% (150 of 960), mainly due to coagulase-negative staphylococci (n=67, 38%) and Gram-positive bacilli (n=61, 35%), with two different contaminants in 26 blood cultures (figure 2 and supplementary table 4). We observed that 9 bacteria (5% of contaminants) commonly reported as pathogens were classified by the AMS focal point as contaminants (3 *Staphylococcus aureus*, 1 *Enterococcus faecalis*, 1 *Hafnia*, 1 *Salmonella* sp, 2 yeasts, and 1 *Providencia* sp). From a clinical perspective, these organisms were classified as contaminants because the blood culture results were not considered in treatment decisions, primarily due to the fact that patients had either died

or been discharged before the results became available. All the other key performance indicators fell within the limits seen in literature (supplementary table 2).

In total, 221 isolates were sent to the reference laboratory, of which 88 (40%) were pathogens and 133 (60%) were contaminants according to the AMS focal point classification. The remaining 79 isolates (36 pathogens and 43 contaminants) could not be sent to the reference laboratory due to shipment constraints (supplementary table 4). Of the 88 pathogen and 133 contaminant isolates, 6 and 7 respectively were non-viable upon arrival in France and were therefore excluded from the analysis (supplementary table 5).

Identification.

Over a total of 82 pathogen isolates tested for reference identification, the agreement to reference method was 90% (74/82) at genus level and 83% (68/82) at species level (table 1). A closer analysis of the discrepancies revealed that 6 reference results were completely inconsistent with the Mini-Lab results, which were supported by Gram stain and culture media photographs from the initial tests (Supplementary Table 5). These discrepancies may be due to incorrect or contaminated isolates being stored and/or shipped. After excluding these 6 isolates, the corrected agreement with the reference method was 97% (74/76) at the genus level and 90% (68/76) at the species level (Table 1). Among the remaining discrepancies, three misidentifications would have had an impact on the diagnosis and/or treatment of the patients: a Gram-negative coccus (given by the pre-identification but inconclusive by identification method), an *S. pneumoniae*, and an *Enterococcus faecium* were identified as *Micrococcus luteus, as Streptococcus oralis*, and as *Lactococcus garviae*, respectively, by the reference laboratory (supplementary table 6). All *S. aureus* isolates were identified correctly at species level.

Of the 126 contaminants tested for reference identification, the agreement was 71% (90/126) at genus level and 31% (39/126) at species level (table 1). Here again, 20 reference results were completely inconsistent with the Mini-Lab results, which were supported by Gram stain and culture media photographs from the initial tests (Supplementary Table 5). These discrepancies may be due to incorrect or contaminated isolates being stored and/or shipped. After excluding these 20 isolates, the corrected agreement with the reference method was 97% (90/106) at the genus level and 37% (39/106) at the species level (Table 1). Among the remaining discrepancies, seven misidentifications would have had an impact on the diagnosis and/or treatment of the patients (supplementary table 6): two Gram-positive bacilli were identified as *Salmonella* sp by the reference method (possible cause erroneous Gram interpretation); a Hafnia alvei was identified as *Salmonella* sp by the reference method; an unidentified Gram negative bacillus was confirmed *Acinetobacter baumannii* by the reference method; a yeast and a *Providencia rustigianii* were identified as *Bacillus* sp by the reference method, and a *Micrococcus* sp was identified *Enterococcus faecium* in the reference laboratory (possible Gram misinterpretation and polymicrobial culture).

Antibiotic susceptibility testing

The Gram-negative AST panel showed good categorical agreement (>85%) for all antibiotics except for colistin (table 2). However, colistin was interpreted on only 20 isolates since the manufacturer of AST panel recommends not to report colistin for *Salmonella* sp., *Acinetobacter* sp. and *Enterobacter cloacae*. Major discrepancies on colistin concerned two *Pseudomonas aeruginosa* (n=2) and *K. pneumoniae (n=1*). Two very major discrepancies were observed for piperacillin-tazobactam, based on a low number of resistant isolates (n=16).

The categorical agreement of the Gram-positive AST panel with *Staphylococcus* sp. was good (>85%), except for cotrimoxazole, erythromycin, fosfomycin and ciprofloxacin (table 3). The major and very major discrepancies mainly involved coagulase-negative staphylococci, which are considered contaminants. The major discrepancies involving *S. aureus* were reported on the same isolate, except for daptomycin. This *S. aureus* had been identified as *S. simulans* by the Mini-Lab.

Categorical agreement for all antibiotics was 100% with *Enterococcus* sp. (n=4).

For the fastidious panel, the agreement was mostly acceptable (≥75%, n=8), except for cotrimoxazole (supplementary table 7).

Ease-of-use

At the end of the 2-month initial training, laboratory technicians 1 and 2 considered some pre-analytical, analytical and post-analytical aspects of the Mini-Lab not very easy to use (median<4, supplementary table 8). The identification and AST plate inoculation system, their reading and interpretation, and the use of the autoclave seemed challenging (median=3) after the first training, but not anymore later on. Technician 3, who joined the team later, had a far lower median score after the initial training than his colleagues at the same timepoint (median=1 or 2) but after three months of experience, all the components were considered much easier to use (median=3 or 4, supplementary table 8).

Antibiotic prescription

Among the 117 patients with pathogen-positive blood culture, we recorded the antibiotic prescription of 105 patients (90%). Of these, 81 (77%) had received empiric antimicrobial treatment before reception of bacteriological results (mainly ceftriaxone, amoxicillin, or ceftriaxone/cloxacillin). After reception of results, the empiric treatment

was considered appropriate based on culture/AST results for 28 (35%) of these 81 patients (25 of them were receiving ceftriaxone). Among the 53 patients who received empiric antibiotics that were inappropriate based on culture/AST results, 40 (75%) changed to the appropriate treatment. Most changes were escalations from penicillins (ampicillin, amoxicillin, cloxacillin) to third-generation cephalosporins, meropenem, or vancomycin. Among the 13 patients who did not change their treatment, three had died and two were discharged before receiving the results. The remaining eight patients were considered cured and were discharged after completing their treatment.

Among the 24 patients who did not receive empiric treatment, 14 (58%) started antibiotic treatment after receiving the results (all included at least ceftriaxone) and ten (42%) did not start any antibiotic treatment despite a positive result (3 non-Typhi *Salmonella*, 2 *S. pneumoniae*, 2 *E. faecium*, 1 *E. coli*, 1 *Acinetobacter* sp., 1 *S. aureus*) including those who were discharged before reception of results. None of these 24 patients died during hospitalisation.

DISCUSSION

This study represents the final step of the evaluation process of the Mini-Lab, as routinely integrated in the clinical practice of an MSF-supported district hospital, in a remote area.

Overall, we showed the Mini-Lab key performance indicators were comparable to the benchmark, except for the contamination rate, which was higher than the acceptable value of 3% [15,16] and requires a collaborative effort between laboratory and nursing teams. This is, however, a challenging aspect for a microbiology laboratory, recognised in both high- and low-resource settings [13,17,18]. Multi-sampling strategy (multiple

blood cultures from separate venipunctures) does not seem applicable, specifically in paediatric populations, in LRSs, leading to possible misclassification of contaminants vs pathogenic infections.

The performance of the pathogen identification system and of the Gram-positive and Gram-negative AST panels was overall consistent with the results of the analytical validation studies previously performed [11,12]. The poor performance of the Gram-positive identification panel with *Streptococcus* and *Enterococcus* species confirmed again the intrinsic limitation of the system. As a mitigation measure, the Mini-Lab introduced an agglutination test for the identification of *S. pneumoniae* and *S. agalactiae* (Pastorex Meningitis - Bio-Rad®). However, careful attention should be paid because an erroneous interpretation of this test may lead to an erroneous diagnosis. Other pathogen misidentifications were mostly caused by pre-identification errors, mainly misinterpretation and over-decolourised Gram staining, which is a common mistake among non-expert users [19]. Additional problems were related to polymicrobial culture due to contamination at sampling or at storage level [12]. Also, for the AST panels, discrepancies found in this study were mostly inherent to the method and well-known (eg, for amoxicillin-clavulanate [20] or colistin [21–23]). In particular, the colistin test on the Gram-negative AST panel showed 15% of major errors, concerning important species such as *P. aeruginosa*. As a mitigation measure, replacing it with a broth microdilution assay for colistin susceptibility confirmation is being considered. Important discrepancies in the Gram-positive AST panel for cotrimoxazole, erythromycin, fosfomycin and ciprofloxacin, may have been due to a misreading or misreporting by the laboratory technician into the Mini-LIMS. The discrepancies of penicillin for *S. aureus* are of little relevance since penicillin will not be given in routine care. During the initial

training, particular attention should be given to AST reading and reporting. Because the AST panel for fastidious organisms was evaluated on a small number of isolates, it is difficult to draw any conclusion on its performance. Nevertheless, due to short reagents' shelve life and to low sample throughput, for routine diagnostic purposes of *Haemophilus* sp., the Mini-Lab includes a beta-lactamase disk (Cefinase disk, Becton Dickinson) whereas the AST panel for fastidious organisms is used for surveillance only. Three months after completing the specific eight-week-long initial training, the Mini-Lab was considered easy to use by two laboratory technicians who had no previous experience in microbiology, indicating that the day-by-day use of the Mini-Lab helped them become more confident with these techniques. However, the training of the third technician, who arrived four months after the initial training, was less effective, suggesting that several factors may have influenced the outcome, not only the format of the training (in-service vs. dedicated, lecture-based sessions), but also individual factors such as motivation, engagement, and learning capacity. These elements should be taken into account by the trainer in order to tailor the approach to the audience's specific needs and context.

In our study conditions, the blood culture results from the Mini-Lab were well accepted by the clinical team and acted upon for appropriate patient treatment. Overall, 51% of patients with pathogen-positive blood culture benefited from a change or initiation of antibiotic treatment upon reception of bacteriological results, while already 27% were receiving appropriate empiric treatment, mainly with ceftriaxone. The on-site AMS focal point, supported by an AMS expert advisor off-site, was the cornerstone for an efficient and sustainable implementation of a bacteriology laboratory in a health facility, by strengthening an essential cross-team collaboration, involving the laboratory, the IPC

measures, and the clinical team. However, in LRSs, AMS expertise is often limited, while training clinicians in AMS takes time and requires sustained support and coordination between medical and laboratory teams. Clinicians in LRSs can receive remote support and guidance from AMS specialists located elsewhere, facilitating decision-making and best practice implementation.

This study has some limitations. Firstly, eligibility assessment was not performed for about 100 individuals with at least one blood culture (20% of the total) due to work overload during peak activities. Secondly, several isolates sent for reference testing could not be used due to contamination at arrival, suspected involuntary swapping at origin, or loss of viability at arrival. Furthermore, some isolates from January and February 2022 could not be sent to the reference laboratory within an acceptable delay due to shipment constraints. However, the composition of these untested isolates was similar to those tested in the reference laboratory (Supplementary Table 4). Thus, we assume that all these constraints may have affected the representativeness of the isolate distribution within the study setting, but they may probably not have affected the interpretation and conclusion of the study results. Furthermore, the classification of contaminants and pathogens relied only on the AMS focal point on site, which we acknowledge could have led to misinterpretation, in particular when the patients were discharged or died before the reception of the laboratory results. However, according to the severity of the patients included and the non-recommended paired blood cultures for children in local procedures, we feel that, overall, it would be more appropriate to use a classification based on the patient's clinical condition than one defined by the laboratory consideration.

The recommendations identified during our study have been taken into account for a new version of the Mini-Lab that is currently being used in ten laboratories in MSF-supported hospitals across Africa and Middle East, and in three health structures supported by non-MSF partners. The improvement perspectives in the short term are to include urine analysis and sterile body fluids cultures, as well as rapid lateral flow immunoassay to confirm antimicrobial resistance [24–26]. Despite efforts to limit the use of reagents requiring cold-chain storage or having short shelf-lives, supply and storage remain challenging. Further development of tropicalized reagents and investment in local distribution systems are needed, as laboratory-level adaptations and current market options remain insufficient.

In conclusion, the Mini-Lab is a promising solution to improve access to microbiology laboratories and responds adequately to the needs of health structures in remote areas. Along with individual care, it could also contribute to AMR surveillance in rural settings and, ultimately, to the elaboration of antibiotic guidelines based on local epidemiological data. However, interpretation and utilisation of results require AMS and IPC capacity building, which should accompany scale-up of microbiology laboratory activities in LRSs.

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Declaration of interests

The authors declare no competing interests.

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Ethical approval statement

The study was conducted in accordance with ethical principles of the Declaration of Helsinki along with good clinical practice guidelines. The study protocol was approved by the “Comité Ethique et Scientifique de République Centrafricaine” (May 17th, 2021) and Médecins Sans Frontières Ethics Review Board. Written informed consent was obtained from all participants or representatives.

Authors’ contributions

CL, AN, CDR, JJ, TN, and OV conceived and designed the study. J-BR, TV, HK, SO, BB, FK, and KD performed the experiment. CL, AN, J-BR, SO and TN analysed the data. CL, J-BR, and AN wrote the first draft of the manuscript. CL, J-BR, AN, TV, CF, FK, CDR, RK, JM, JJ, TN, and OV contributed to the writing of the manuscript. All authors contributed to data interpretation. All the authors critically reviewed and approved the final version of the manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Data sharing

Epicentre and Médecins Sans Frontières (MSF) are committed to sharing and disseminating health data from its research in an open, timely, and transparent manner to promote health for populations while respecting ethical and legal obligations towards patients, research participants, and their communities. Upon publication and for as long as the ethical authorization permits it, the participant data set underlying the findings of this study, a data dictionary defining each field in the set, as well as the study protocol will be made available on request. If scientifically relevant, the request may be granted in accordance with legal framework set forth by Epicentre data sharing policy available on its website (https://epicentre.msf.org/en/ongoing-projects/study-data-access-request). The MSF data sharing policy ensures that data will be available upon request to interested researchers while addressing all security, legal, and ethical concerns. All data access request for non-commercial and academic research can be addressed to epimail@epicentre.msf.org or the corresponding authors. Such request will be submitted to the medical departments of MSF and Epicentre. In case of approval of the request, the data will be shared with researchers, subject to the establishment, within a reasonable timeline, of a data sharing agreement to provide the legal framework for data sharing – including any applicable data protection laws. Such data sharing agreement may differ depending on the nature of the data to be shared – pseudonymized or anonymized – and the sensitivity of the data.

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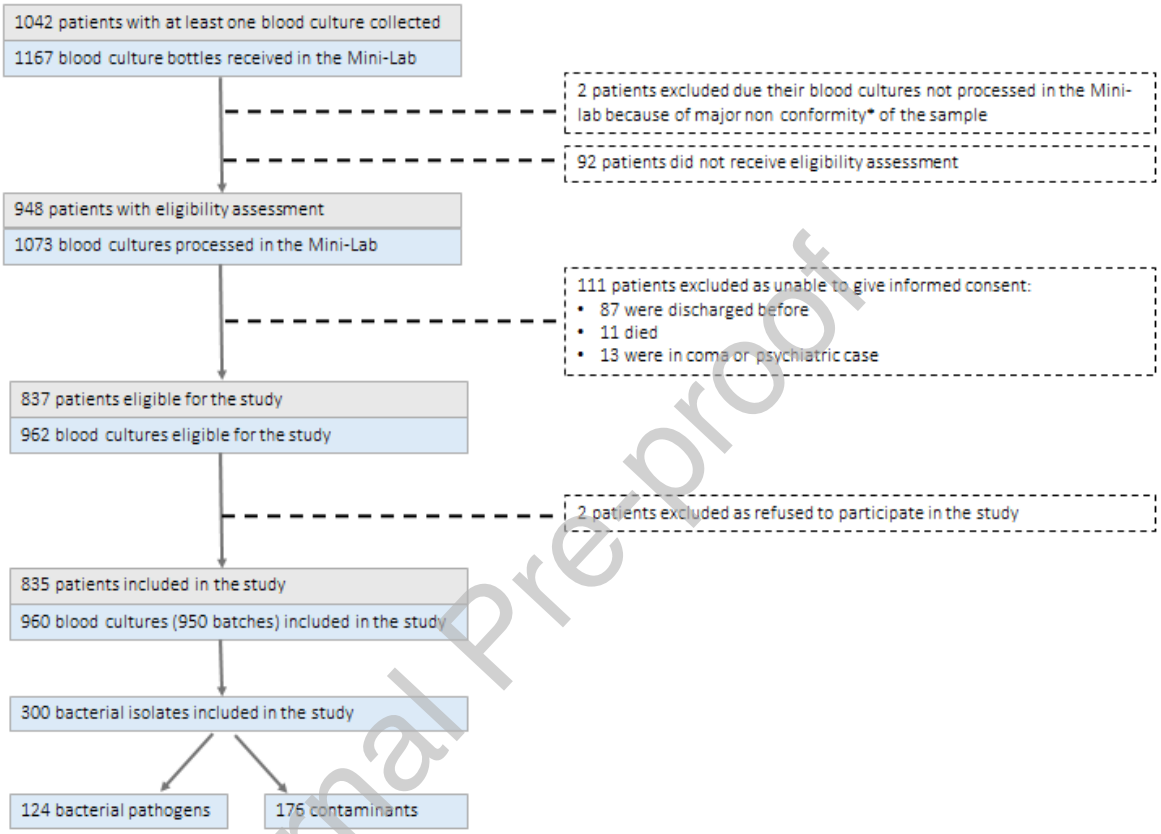

Figure 1. Study flowchart for inclusion and exclusion of patients and corresponding blood cultures processed in the Mini-Lab. *Major non-conformities are defined as per laboratory procedures, e.g. when a sample presents major spillage of blood outside the bottle or the bottle itself is broken, so that the integrity of the sample is hampered.

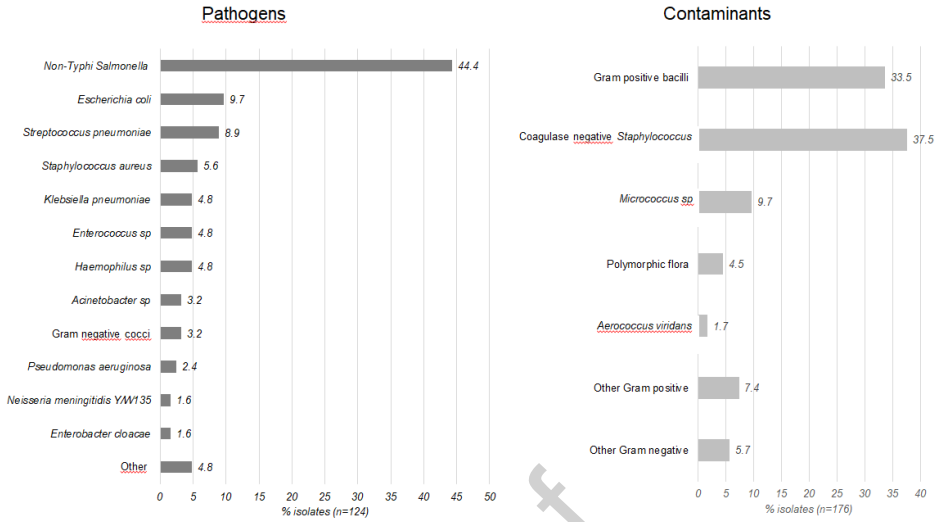

Figure 2. Proportion of pathogens (n=124) and contaminants (n=176) isolated in the Mini-Lab during the study period. Complete list of pathogens and contaminants is available in Supplementary materials.

Table 1. Agreement between the Mini-Lab (MSF Neg/Pos ID Panel Type 2) and the reference method results (MALDI-TOF) for the identification of organisms

	Agreement for genus and species		Agreement for genus only	
	Absolute	**Corrected**	**Absolute**	**Corrected**
Pathogens				
Over agreement, % (n/N tested)	83% (68/82)	90% (68/76)	90% (74/82)	97% (74/76)
Agreement Gram positive, % (n/N tested)	61% (11/18)	73% (11/15)	72% (13/18)	87% (13/15)
Agreement Gram negative, % (n/N tested)	89% (57/64)	93% (57/61)	95% (61/64)	100% (61/61)
Contaminants				
Over agreement, % (n/N tested)	31% (39/126)	37% (39/106)	71% (90/126)	85% (90/106)
Agreement Gram positive, % (n/N tested)	33% (37/111)	37% (37/100)	79% (88/111)	88% (88/100)
Agreement Gram negative, % (n/N tested)	13% (2/15)	33% (2/6)	13% (2/15)	33% (2/6)

[a]One Gram-positive organism did not give valid result with MSF Neg/Pos ID Panel Type 2 in the reference laboratory

Table 2. Agreement between the results of the Gram-negative AST panel (MSF Neg MIC type 2) in the Mini-Lab and the reference methods

Antibiotic	Categorical agreement[a], % (n/N)	Minor discrepancy[a]		Major discrepancy[b]		Very major discrepancy[c]	
		% (n/N)	Organism (n)	% (n/N_{Sref})	Organism (n)	% (n/N_{Rref})	Organism (n)
Ampicillin	100 (51/51)	0	..	0	..	0	..
Amoxicillin-Clavulanate	100 (51/51)	0	..	0	..	0	..
Ceftriaxone	98 (50/50)	0	..	2 (1/41)	*E. xiangfangensis* non ESBL (1)	0	..
Ceftazidime	96 (52/54)	4 (2/54)	Non-typhoidal *Salmonella* (1); *E. coli* ESBL (1)	2 (1/41)	*E. xiangfangensis* non ESBL (1)	0	..
Piperacillin-Tazobactam	89 (48/54)	6 (3/54)	Non-typhoidal *Salmonella* (1); *P. aeruginosa* (2)	3 (1/36)	Non-typhoidal *Salmonella* (1)	13 (2/16)	*E. coli* non-ESBL (2)
Imipenem	100 (56/56)	0	..	0	..	0	..
Meropenem	96 (54/56)	4 (2/56)	*A.baumannii* (1); *E. xiangfangensis* non-ESBL (1)	0	..	0	..
Colistin	85 (17/20)	0	..	15 (3/20)	*K. pneumoniae* ESBL (1); *P. aeruginosa* (2)	0	..
Ciprofloxacin	95 (53/56)	0	..	7 (3/45)	*K. pneumoniae* ESBL (1); *E. coli* ESBL (1); *E. xiangfangensis* non-ESBL (1)	0	..
Gentamicin	92 (49/53)	4 (2/53)	*E. coli* non-ESBL (2)	4 (2/45)	*Acinetobacter sp.* (1); *E. xiangfangensis* non-ESBL (1)	0	..
Amikacin	96 (54/56)	0	..	4 (2/56)	E. coli ESBL (1); *E. xiangfangensis* non-ESBL (1)	0	..
Cotrimoxazole	98 (52/53)	0	..	0	..	2 (1/49)	Non-typhoidal *Salmonella* (1)
Chloramphenicol	94 (47/50)	0	..	7 (1/15)	Non-typhoidal *Salmonella* (1)	6 (2/35)	Non-typhoidal *Salmonella* (1)

Tigecycline	100 (36/36)	0	..	0	..	0	..

ESBL: Extended-Spectrum Beta-Lactamase
[a] N= total number of isolates tested with final interpretation possible depending on the tested organism and manufacturer recommendations
[b] n/N_{Sref}= number of isolates that result in a major discrepancy divided by the number of susceptible isolates as determined by the reference method (ISO 20886-2:2007)
[c] n/N_{Rref}= number of isolates that result in a very major discrepancy divided by the number of resistant isolates as determined by the reference method (ISO 20886-2:2007)
Note: AST reference method was disk diffusion method, except for amoxicillin-clavulanate, piperacillin-tazobactam, colistin (micro-broth dilution).
Two carbapenem-resistant *Acinetobacter baumannii* (CRAB). 10 extended spectrum beta-lactamase (ESBL)-producing Enterobacterales were confirmed by the reference method.

Table 3. Agreement between the Gram-positive AST panel (MSF Pos MIC type 2) for *Staphylococcus* sp. in the Mini-Lab and AST reference methods, for antibiotics used for treatments

Antibiotic	Categorical agreement[a], % (n/N)	Minor discrepancy[a]		Major discrepancy[b]		Very major discrepancy[c]	
		% (n/N)	Organism (n)	% (n/N_{Sref})	Organism (n)	% (n/N_{Rref})	Organism (n)
Penicillin	88 (7/8)	0	..	33 (1/3)	*S. aureus* (1)	..	..
Cefoxitin	100 (11/11)	0	..	0	..	..	..
Cotrimoxazole	81 (17/21)	0	..	21 (3/14)	CNS (3)	14 (1/7)	CNS (1)
Clindamycin	86 (18/21)	5 (1/21)	CNS (1)	13 (2/16)	*S. aureus* (2)	..	..
Vancomycin	100 (21/21)	0	..	0	..	..	..
Teicoplanin	100 (21/21)	0	..	0	..	..	..
Tigecycline	95 (20/21)	0	..	5 (1/21)	CNS (1)	..	..
Tetracycline	90 (18/20)	0	..	22 (2/9)	*S. aureus* (1); CNS (1)	..	..
Erythromycin	77 (16/21)	0	..	36 (5/14)	*S. aureus* (1); CNS (4)	..	..
Fosfomycin	76 (13/17)	0	..	21 (3/14)	CNS (3)	33 (1/3)	CNS (1)
Linezolid	100 (25/25)	0	..	0	..	..	..
Ciprofloxacin	67 (14/21)	33 (7/21)	CNS (7)	0	..	..	..
Gentamycin	87 (20/23)	0	..	19 (3/16)	CNS (3)	..	..
Amikacin	95 (20/21)	0	..	5 (1/20)	*S. aureus* (1)	..	..
Quinupristin	88 (22/25)	8 (2/25)	*S. aureus* (1); CNS (2)	5 (1/21)	*S. aureus* (1)	..	..
Daptomycin	95 (20/21)	0	..	5 (1/21)	*S. aureus* (1)	..	..

CNS : Coagulase negative *Staphylococcus*
[a] N= total number of isolates tested with final interpretation possible depending on the tested organism and manufacturer recommendations
[b] n/N_{Sref}= number of isolates that result in a major discrepancy divided by the number of susceptible isolates as determined by the reference method (ISO 20886-2:2007)

[c] n/N_{Rref}= number of isolates that result in a very major discrepancy divided by the number of resistant isolates as determined by the reference method (ISO 20886-2:2007)
Note: AST reference method was disk diffusion method, except for teicoplanin/vancomycin (agar gradient diffusion method), daptomycin (micro-broth dilution), fosfomycin *(*agar-based dilution) as per EUCAST v11

Declaration of Interest Statement

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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