RESEARCH ARTICLE

Identification of selected primary bloodstream infection pathogens in patients attending Kisii level five and Homa Bay county hospitals [version 1; peer review: 1 approved with reservations, 1 not approved]

Ronald Kirera ¹, Erick Kipkirui¹, Margaret Koech¹, Abigael Ombogo¹, Janet Ndongye¹, Mary Kirui¹, Cliff Odhiambo Philip¹, Nancy Kipkemoi¹, Elizabeth Odundo¹, Alexander F. Flynn¹, Christine Hulseberg¹, Judd Walson ^{2,3}, Joseph Nganga⁴, Daniel Kariuki⁴

¹United States Army Medical Research Directorate, Africa/Kenya, Kericho, Kenya, Kenya

²University of Washington, Seattle, WA, USA

³Childhood Acute Illness and Nutrition Network, Nairobi, Kenya

⁴School of Biomedical Sciences, Jomo Kenyatta University of Agriculture and Technology, Nairobi, Kenya

V1 First published: 12 Oct 2020, 9:1228
<https://doi.org/10.12688/f1000research.26300.1>
 Latest published: 28 Sep 2022, 9:1228
<https://doi.org/10.12688/f1000research.26300.2>

Abstract

Background: Bloodstream infection (BSI) contributes to a substantial proportion of mortality in sub-Saharan Africa and is marked by the presence of bacterial and/or fungal microorganisms in the blood. Because BSI can be life threatening, it requires a timely, reliable and accurate diagnosis. This study retrospectively analyzed data of identified BSI pathogens and compared the performance of the different diagnostic technologies used in terms of accuracy, sensitivity, turnaround time (TAT) and cost.

Methods: Currently, culture followed by analytical profile index biochemical strips (API), (BioMerieux) are used as the conventional standard diagnostics in Kenyan public hospitals and labs. We compared the results of this standard to that of the BioFire FilmArray (FA) (BioFire Diagnostics) and MicroScan WalkAway-40 plus System (MS) (Beckman Coulter) used in diagnosis of BSI. The FA technology was able to identify 150/152 bacterial and yeast isolates with an overall accuracy of 99.04% (95% CI: 96.59-99.88%), sensitivity of 98.68% (95% CI: 95.33-99.84%), mean TAT of 8 hours 40 minutes per eight samples and running cost per sample of USD 140.11. The MS identified 150/152 isolates with an overall accuracy of 98.56% (95% CI: 95.86-99.70%), sensitivity of 98.68% (95% CI: 95.30-99.84%), mean TAT per sample was 42 hours and running cost per sample of USD 28.05. API detected 150/152 isolates, with an overall accuracy of 99.04% (95%

Open Peer Review

Approval Status

	1	2
version 2 (revision) 28 Sep 2022		
version 1 12 Oct 2020	view	view

1. **Ciira Kiiyukia** , Mount Kenya University (MKU), Thika, Kenya
2. **Josette Raymond** , Bicêtre Hospital, Kremlin Bicetre, France

Any reports and responses or comments on the article can be found at the end of the article.

CI: 96.59-99.88%), sensitivity of 98.68% (95% CI: 95.33-99.84%) and the mean TAT per sample was 53 and 103 hours for bacterial and yeast samples, respectively, with a running cost per sample of USD 28.05.

Conclusions: *The findings in this paper suggest that the FA and MS platforms should be able to perform adequately in Kenya referral hospitals and medical clinics as a rapid diagnostic tool.*

Keywords

Bloodstream infection, FilmArray, MicroScan, Resistance genes

Corresponding author: Ronald Kirera (rironkire3@yahoo.com)

Author roles: **Kirera R:** Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Validation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; **Kipkirui E:** Writing – Review & Editing; **Koech M:** Writing – Review & Editing; **Ombogo A:** Data Curation; **Ndonye J:** Writing – Review & Editing; **Kirui M:** Writing – Original Draft Preparation; **Philip CO:** Writing – Review & Editing; **Kipkemoi N:** Writing – Review & Editing; **Odundo E:** Writing – Review & Editing; **Flynn AF:** Data Curation, Formal Analysis, Funding Acquisition, Project Administration, Resources, Software, Supervision, Writing – Review & Editing; **Hulseberg C:** Data Curation, Formal Analysis, Funding Acquisition, Project Administration, Resources, Supervision, Writing – Review & Editing; **Walson J:** Writing – Review & Editing; **Nganga J:** Supervision, Writing – Review & Editing; **Kariuki D:** Supervision, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: Funding for this study was provided through HJF/DEID contract number W81XWH-16-C-0170.

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Copyright: © 2020 Kirera R *et al.* This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Kirera R, Kipkirui E, Koech M *et al.* **Identification of selected primary bloodstream infection pathogens in patients attending Kisii level five and Homa Bay county hospitals [version 1; peer review: 1 approved with reservations, 1 not approved]** F1000Research 2020, 9:1228 <https://doi.org/10.12688/f1000research.26300.1>

First published: 12 Oct 2020, 9:1228 <https://doi.org/10.12688/f1000research.26300.1>

Introduction

Bacteremia accounts for a large number of hospital admissions and results in high morbidity and mortality¹. In sub-Saharan Africa, there is limited information on bloodstream infections (BSI)^{2,3}, which can be partly attributed to the paucity of studies conducted in developing countries lacking high throughput BSI diagnostic technology. The availability of such equipment would facilitate widespread BSI detection in patients, help close this critical knowledge gap, and potentially save lives^{4,5}.

Blood culture and analytical profile index (API, BioMerieux) strip analysis has been the conventional standard for bacteremia diagnosis in many hospitals throughout the world, including Kenya^{6,7}. Using this technique has been a challenge because it is a labor intensive process that requires experienced laboratory technologists and has a reportedly lower level of accuracy than other techniques such as conventional cultures²⁻⁶. To address this issue, diagnostic platforms such as the BioFire FilmArray (FA) and MicroScan WalkAway 40 plus (MS) are now widely used in Europe and the United States²⁻⁸.

The FA is a sophisticated closed-automated polymerase chain reaction (PCR) system that utilizes specific commercial pouches such as FA blood culture ID panel to identify BSI causative agents and antimicrobial resistance markers within 1 hour of a positive blood culture⁹. This platform can identify 24 causative agents of BSI (eight gram-positives, 11 gram-negatives, and give yeast species) and three antimicrobial resistance genes: *mecA* for methicillin, *vanA/B* for vancomycin and *bla_{KPC}* for carbapenem by nested multiplex PCR⁵⁻⁸. The MS system can provide identification of bacteria within 16 to 20 hours, phenotypic antimicrobial profile (AST) and extended-spectrum beta lactamase (ESBL) using negative combo panel type 66 for gram negatives and positive combo panel type 39 for gram positives^{10,11} and identification of yeast within 4 hours using a rapid yeast panel (Beckman Coulter, United States).

The use of conventional methods requires considerably long turnaround time (TAT) from 12–72 hours. In potentially life-threatening cases of BSI, the microbial cause of infection must be identified as quickly as possible to ensure proper treatment and management of the disease. The newly employed methods FA® and MS® have never been used before in Kisii and Homa Bay hospitals.

In this paper, we compared the accuracy, sensitivity, turnaround time (TAT) and cost of new technologies against the conventional API strip technique based on past data from blood culture isolates. Based on our findings, we will identify whether these automated platforms would be capable of providing a rapid diagnosis of BSI in Kenya hospitals.

Methods

Study sites

Stored blood culture samples received from Kisii Teaching and Referral Hospital and Homa Bay County Referral hospital

were analyzed at Microbiology Hub Kericho. These collection sites were selected because they do not have the capacity to identify BSI pathogens to the species level. Kisii Teaching and Referral Hospital is a public hospital located in Kitutu Chache Constituency, Kisii County. It is located in Kisii town Central Business, District Hospital Road, and serves a population of over 1 million. Homa Bay County Referral Hospital is a government health center located in Homa Bay Township Sub-location, Homa-Bay Location, Asego Division, and Rangwe Constituency in Homa Bay County. It has a population of over 1 million. The common diseases in these areas are malaria, upper respiratory tract infections, typhoid, pneumonia, tuberculosis and HIV¹².

Study design

This study analyzed BSI isolates data tested using FA, MS technologies and culture followed by API strip analysis. A total of 152 isolates data (122 blood culture isolates and 30 control isolates) were analyzed. The study focused on the identification of BSI, accuracy, sensitivity, TAT as well as the cost of the items. Isolate analysis was performed at the Microbiology Hub Kericho (MHK), a United States Army Medical Research Directorate-Africa (USAMRD-A) facility working in collaboration with Kenya Medical Research Institute (KEMRI). The MHK performs surveillance and clinical research diagnosis of enteric pathogens causing acute diarrhea across Kenya in addition to screening blood culture samples for BSI agents.

Sample size determination

Formula $n = Z^2 \times P(1-P)/d^2$, n = Sample size, Prevalence (p) = 10.4%

95% confidence interval (z) = 1.96

Precision d^2 = 0.05

$n = 1.96^2 \times 0.104(1-0.104)/0.05^2$

Calculated sample size (n) = 143 isolates.

The prevalence was taken from the study by Maze *et al.* (2018)¹³ “The epidemiology of febrile illness in sub-Saharan Africa: implications for diagnosis and management”. The prevalence rate is based on East Africa data which is part of Kenya, the ranges in prevalence is between 10-20% in Kenya.

Blood culture

Blood samples were collected into BACTEC Plus Aerobic/F, Peds Plus Aerobic/F, Anaerobic/F and Lytic/10 Anaerobic/F vials (BD, United States) and incubated using the BacTec 9050 instrument (BD, United States) for 5 days to account for slow-growing pathogens. A positive signal was indicated by an increased fluorescence caused by the carbon dioxide released by an organism reacting with the vial dye. Positive blood culture samples were removed and processed to identify the organism. Samples were processed directly using the FA without need for prior subculture. As for the MS and the API strip method, samples were first gram-stained and

sub-cultured on MacConkey agar, Blood agar plate, Sabouraud Dextrose agar, Hektoen enteric agar and Tryptic soy agar (Becton Dickson).

Microbial identification of the positive blood culture samples

For identification by FA, samples were tested per the manufacturer's instructions. First, the blood culture identification panel was inserted in the loading chamber, then hydration solution was added to the sample and then the panel was placed into the FA. The results were checked after 1 hour.

Pure colonies were used for the MS identification procedure. An inoculum of 0.5 McFarland standard equivalents was prepared by selecting 1 to 3 discrete colonies from pure culture on MacConkey agar (MAC) or blood agar plate (BAP) or Sabouraud dextrose agar (SDA) and suspended in 3 ml of the MS inoculum water (Beckman Coulter). From the solution, 100 µl was transferred and mixed with 25 ml of the MS inoculum water with pluronic and then poured into the sterile inoculator D set tray. The solution (140 µl) was transferred into a gram-negative or a gram-positive panel (Beckman Coulter), and then loaded into the MS and results checked after 18–24 hours and 4 hours for yeast organisms.

For manual biochemical analysis method, the API strips (BioMerieux, United States) and media (MacConkey agar, blood agar, Hektoen enteric agar, triple sugar irons and Sabouraud dextrose agar plates) were brought to room temperature. After this, 5 mL of deionized water was added to the tray along with the strips. The API ampules or equivalent suspension medium was inoculated with a single colony. The inoculation of wells for gram negative, gram positive and yeast organisms was done as per manufacturer's instruction. The incubation box was closed and incubated at 36°C for 18–24 hours for bacterial while for the yeast it was incubated at 29°C for 48 to 72 hours. A positive signal was indicated by a colorimetric change that was interpreted using the API guidelines.

Statistical analysis

Overall accuracy was calculated as the (number of individual isolate identified using evaluated technique) / (total number of same isolates identified) x 100%, sensitivity values and the 95% confidence intervals (CI) for both of these

metrics were analyzed using the Graphpad Prism 8.2.1 software. The TAT was defined as the time taken from sample preparation to identification¹⁴. The average cost per samples included consumable reagents and disposable supplies and was defined as the total cost of each assay per sample run.

The indeterminate results were resolved by comparing the two techniques FA and MS, where the two techniques agreed was taken as a true positive, the discordant results were repeated using the API technique (gold standard).

Ethics approval and consent to participate

Ethical review for this work was obtained from the Kenya Medical Research Institute Scientific and Ethical review Unit-Scientific Steering Committee (KEMRI SERU-SSC) #3686 and Walter Reed Army Institute Research (WRAIR) Institutional Review Boards (IRBs) #2513. Consent was not sought for this study since it was determined that there was no interaction with human subjects.

Results

The sensitivity and accuracy of the FA, MS, and API

The overall accuracy and sensitivity of each platform is shown in [Table 1](#). For the FA, the calculated accuracy was 99.04% (95% CI, 96.59-99.88%). Out of the total 152 isolates identified, FA technology was able to correctly identify 150 isolates resulting in a calculated sensitivity of 98.68% (95% CI: 95.33-99.84%). Similar to the accuracy computation for the FA instrument, the accuracy of the MS instrument was determined based on the number of isolates correctly identified by the MS out of the total number of isolates correctly identified. This yielded an overall accuracy of 98.56% (95% CI: 95.86-99.70%). The MS technology identified 149 true isolates, which produced a calculated sensitivity of 98.68% (95% CI: 95.30-99.84%). The API strip analysis identified 150 isolates with an accuracy of 99.04% (95% CI: 96.59-99.88%) with no significant difference in overall accuracy to the FA and MS. The sensitivity of API method was 98.68% (95% CI: 95.33-99.84%).

Pathogen identification by FA, MS and API

Next, we decided to breakdown which microbes that each platform correctly identified ([Table 2](#)). The FA and API were able to identify 150/152 BSI pathogens. Interestingly, the FA

Table 1. Comparison of accuracy and sensitivity of API, FA and MS. The accuracy and sensitivity for the evaluated three techniques is shown above. The bold values listed are the calculated accuracy or sensitivity means for each method. Shown in parentheses are the 95% CI values.

Parameter Evaluated	API	FA	MS
Accuracy	99.04% (96.59 - 99.88%)	99.04% (96.59 to 99.88%)	98.56% (95.86 - 99.70%)
Sensitivity	98.68% (95.33% - 99.84%)	98.68% (95.33% to 99.84%).	98.68% (95.30% - 99.84%)

FA, FilmArray; MS, MicroScan; API, Analytical Profile Index.

Table 2. Breakdown of pathogen identification by the FA, MS and API. The accuracy broken down by microorganism was calculated for each platform. The total number of isolates identified followed by accuracy percentage of FA, MS and API is listed above. For the FA, the "n/a" indicates that the isolates could not be identified beyond the family level (*Enterobacteriaceae*). Those rows with a dash mark (-) indicate those identified at specific genus level (*Salmonella*) and not group level (*Enterobacteriaceae*).

Organisms	FA %	FA Accuracy	MS	% MS Accuracy	API	% API Accuracy
<i>Staphylococcus aureus</i>	7	100	7	100	7	100
<i>Staphylococcus</i> spp	16	100	15	93.75	16	100
<i>Streptococcus pneumoniae</i>	7	100	7	100	7	100
<i>Streptococcus</i> spp	5	83.3	7	100	6	85.7
<i>Enterococcus faecium</i>	8	100	8	100	8	100
<i>Escherichia coli</i>	8	100	8	100	8	100
<i>Enterobacter cloacae</i>	4	100	2	50	2	50
<i>Klebsiella pneumoniae</i>	11	100	11	100	11	100
<i>Acinetobacter baumannii</i>	7	100	6	85.71	7	100
<i>Pseudomonas aeruginosa</i>	9	100	9	100	9	100
<i>Enterobacteriaceae</i>	57	100	-	-	-	-
<i>Salmonella</i> spp	n/a	n/a	57	100	57	100
<i>Klebsiella oxytoca</i>	2	100	2	100	2	100
<i>Candida albicans</i>	9	100	9	100	9	100
<i>Candida krusei</i>	1	100	1	100	1	100
<i>Candida parapsilosis</i>	1	100	1	100	1	100

FA-FilmArray, MS- MicroScan, API-Analytical Profile Index.

platform was able to identify 4/4 of *Enterobacter cloacae* isolates as opposed to API technique, which detected only 2/4. However, the FA only recognized *Staphylococcus* at the genus level. In addition, the system could not characterize *Streptococcus anginosus* and *Streptococcus bovis* at the species level as these bacteria were not in its database, and therefore, were identified as *Streptococcus* spp. The FA identified *Salmonella* isolates as *Enterobacteriaceae* while the API and the MS were able to identify these isolates as *Salmonella* spp. The MS was able to accurately identify the presence of all other isolates similar to the API method except with *Staphylococcus* spp. (93.75%) and *Acinetobacter baumannii* (85.71%), while the API method was 100% accurate for both. In addition, the MS correctly identified all other *Streptococcus* isolates besides *S. pneumoniae*, whereas the FA and API standard had accuracies of 83.3% and 85.7%, respectively. Results of identification using each technique are available (see *Underlying data*¹⁵).

The mean turn-around time for the FA, MS and API

We limited the running time for each platform to the length of a normal working day (8 hours) (Table 3). Under this

Table 3. The mean turnaround time of the FA, MS, and API. For each platform being analyzed, turnaround times were broken into processing and ID analysis. The time shown for each of these categories is the mean of multiple runs, which had eight samples each. The processing column shows the time taken to prepare the samples for culture and then selection of isolates for identification. Of note, the FA did not require gram staining or culture and selection of an isolate from a blood culture. Identification analysis was based on the time each platform required to complete their respective protocols. The p-value showed the significance of the mean difference among the techniques.

Equipment	Processing time per 8 samples (min)	ID analysis per 8 samples (min)	Total time (min)	Total number of runs
FA	40	480	520	19
MS	1620	960	2580	19
API	1620	1680	3300	19

p-value <0.0001 for mean TAT: FA vs. MS/API, MS vs. FA, and API vs. MS

FA-FilmArray, MS-MicroScan, API-Analytical Profile Index, ID-Identification.

condition, the FA could only run eight samples. We therefore established this limit to ensure an equal number of samples per run across all the techniques. The turnaround time (TAT) for the FA per sample run was 1 hour 6 minutes, with an average of 5 minutes processing time and 1 hour identification and results analysis. The average time for FA was 8 hours 40 minutes and significantly less ($p < 0.0001$) compared to the MS and API. The MS had a mean TAT of 42 hours per sample run, with 27 hours processing time and the mean TAT was significantly more ($p < 0.0001$) compared to the FA. Breaking this down, the culture process and incubation required 24 hours, which could be more depending on the bacteria and purity of culture. The API method had a mean TAT of 53 hours per sample run for bacterial isolates while for yeast was 103 Hrs. The mean TAT was significantly more ($p < 0.0001$) compared to the FA. Sample processing data are available for each technique (see *Underlying data*¹⁵).

The average cost of running one sample per technique

The total average cost of processing one sample using the FA technique was 140.11 USD (Table 4). The total average cost of running one isolate per sample using the MS instrument was 38.75 USD while API technique was 29.17 USD. Extra equipment required but not included were biosafety cabinet, incubators, autoclaves, hot plates, conical flasks, stirrers and spatulas as well as the annual preventive maintenance for this equipment. Only the costs of the consumable items needed for each method were evaluated. As expected, the cost of the items used for the API technique was lower than for those used by the MS and FA.

Discussion

In resource-limited settings, the use of conventional methods in diagnosis of bacteremia has been a challenge to most public health facilities leading to misclassification of the diagnosis of BSI^{8,16}. The automated methods FA and MS proved to be more efficient, reliable and faster in the identification of a wide range of microorganisms than API. The technologies are reliable with a short turnaround time. These positive factors outweigh the use of API strips for microbial identification, which is considered the conventional standard in Kenya for diagnosis of BSI. In comparison to the FA and MS, the API method was more labor intensive. Furthermore, fastidious bacteria might not be identified if they fail to grow on culture media but can be identified directly from blood culture using FA.

Overall, the sensitivity of FA (98.68%), MS (98.68%) and API (98.68%) were identical, with an overall accuracy of 99.04%. Moreover, the sensitivity of FA demonstrated in this study was similar to the sensitivity observed in a previous study carried out in Kizulu-Natal¹⁷. The differences in sensitivity came in inability of FA and MS to agree in terms of genus and species individual identification of BSI pathogens.

The higher accuracy by FA in individual identification of BSI pathogens could be because it is a molecular-based platform. The FA identified *Enterobacter cloacae* with a higher

Table 4. The cost breakdown running the FA, MS, and API. The average cost of running sample was broken down into biochemical reagents/media used. Reagents not used by a platform as designated N/A (non-applicable). Not included in the cost breakdown were the equipment aforementioned above. The periodic maintenance required for the automated platforms was also not included.

Materials	Cost per sample (USD)		
	API	MS	FA
API Biomeriux	4.72	N/A	N/A
MacConkey agar	0.16	0.16	N/A
Hektoen enteric agar	0.32	N/A	N/A
Triple sugar iron agar	0.14	N/A	N/A
Blood agar base	0.14	0.14	N/A
Dish Petri CS-100 15X100m	1.05	N/A	N/A
Gram stain kit	0.22	0.22	N/A
Polyester tipped swabs	0.25	0.25	N/A
Sheep blood agar	0.24	0.24	N/A
3ml inoculum water	N/A	2.66	N/A
25ml inoculum water with pluronic	N/A	2.92	N/A
Inoculator D sets	N/A	1.88	N/A
Panel lid	N/A	0.71	N/A
Microscan Panel (GPC/NBPC)	N/A	7.64	N/A
Kovacs reagent	0.71	0.71	N/A
0.8% Sulfanilic acid (Nit 1)	0.49	0.49	N/A
0.5% N-N-Dimethyl-Alpha-Naphthylamine(Nit 2)	0.63	0.63	N/A
40% Potassium hydroxide (Vp1)	0.82	0.82	N/A
Alpha naphthol (Vp2)	0.54	0.54	N/A
10% Ferric chloride (TDA)	0.59	0.59	N/A
Peptidase reagent	0.49	0.49	N/A
NaOH	0.53	0.53	N/A
Oxidase reagent	0.52	0.52	N/A
Blood culture bottle	6.98	6.98	6.98
Blood culture identification pouch	N/A	N/A	124.58
Inoculating needle	0.12	0.12	N/A
Needles and syringes	0.3	0.3	0.3
Biohazard bag	0.2	0.2	0.2
Microscope slides	0.32	0.32	N/A
Sharps containers small	3.95	3.95	3.95
Lens cleaning paper	0.08	0.08	N/A

Materials	Cost per sample (USD)		
	API	MS	FA
Bleach	1.44	1.44	1.44
Mineral oil	0.24	0.24	N/A
Oil Immersion	0.24	0.24	N/A
Absolute Ethanol	2.17	2.17	2.17
Pipette tips	0.08	0.08	N/A
Gloves	0.49	0.49	0.49
Total	29.17	38.75	140.11

FA-FilmArray, MS-MicroScan, API-Analytical Profile Index.

accuracy than the other two methods, which could not identify the two isolates. This is probably because the FA identified two isolates as *Enterobacter cloacae* complex, which neither of the other methods could identify. However, the accuracy of FA was limited when identifying *Streptococcus* spp. where the accuracy was 83.3%, the organisms in question (*Streptococcus anginosus* and *Streptococcus bovis*) are not available in the FA database and are not common causes of BSI². We believe that these organisms were actually skin contaminants. Still, the overall accuracy demonstrated by the FA is in line with previous paper evaluating the diagnostic capabilities of the system¹⁸.

The MS was able to accurately identify the presence of BSI bacteria with similar accuracy to the API method, except for the identification of *Staphylococcus* spp. where the accuracy was 93.75% and *Acinetobacter baumannii* with an accuracy of 85.71% for MS. The MS surpassed the API strip method in the identification of *Streptococcus* spp. where the accuracy was (100%) compared to API method (85.71%). These issues with MS in identifying *Staphylococcus* spp. and *Acinetobacter baumannii* is in line with previous studies, where the MS misidentified *Acinetobacter baumannii*^{19,20}. For this study, the misidentified *Streptococcus* spp. were actually *Staphylococcus* spp.

In past studies, the API strip analysis had a lower accuracy identifying microorganisms such as *Citrobacter species*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Enterobacter species* than automated platforms²¹. Interestingly, this did not occur with this study, and could partly be because the lab technician performing the assay had extensive clinical microbiology experience. Microbiology labs typically address this lower accuracy by adding biochemical tests such as oxidase and catalase to increase accuracy. We, however, did not incorporate these assays into the API strip analysis.

The mean TAT difference per run of eight samples among the technologies was significant at $p < 0.0001$. The FA technology required 8 hours 48 minutes per eight samples compared to the MS, which required 42 hours and the API method,

which required 53 hours for bacterial species and 103 hours for yeast. The major factor contributing this difference was time needed to prepare the isolates, which require gram-staining then culturing for 24/48 hours prior to identification by MS or API²¹. It should be noted that the MS has higher throughput and can process 40 or more panels in one run. In addition, the API method can test more samples and is only dependent on availability of incubators, reagents and the experience of the technician. The shorter TAT for FA is a very attractive feature for under-developed areas with poor infrastructure and inaccessible areas where field clinical/research activities are undertaken and do not necessarily require a high-throughput machine. Though not a metric evaluated in this study, the FA requires considerably less training and skill compared to the other methods, which help to balance its throughput limitations.

The average cost of testing one sample using FA was noticeably higher than the cost of the MS and API methods. This was expected as the FA test kits cost more than the MS panels and the API reagents. While the FA is more expensive, it is able to identify co-infection in one sample, which would require separate runs for the MS and API⁵.

Of note, the FA is able to identify resistant genes such as methicillin resistance common with *Staphylococcus aureus*, vancomycin resistance common with *Enterococcus* spp. and carbapenem resistance common with *Klebsiella pneumoniae* and other *Enterobacteriaceae*⁸. While the MS has no capability to identify antimicrobial resistant genes commonly associated with BSI, it is able to perform phenotypic drug sensitivity. In fact, the MS has a wider range of antimicrobial testing capabilities with regularly updated software database in line with CLSI guidelines.

Conclusion

While the evaluated methods were similar in accuracy and sensitivity, there were appreciable differences in TAT and cost. The FA cost more, but had a quicker TAT compared to the MS and API methods. This is a significant concern when using the machine in areas with limited financial resources. However, the FA requires minimal training prior to use and is able to identify co-infections. Furthermore, the FA requires a small space, and therefore, the cost of the FA panels should not be considered a major drawback since early detection of BSI has shown to reduce medical costs, hospital stays, and help guide the clinicians on the best treatment approach⁵, which lower overall economic costs.

Recommendation

The FA and MS have not been evaluated at Kenya hospitals and further evaluation using a larger sample size is recommended. However, these preliminary results clearly suggest that both the FA and MS platforms are valuable tools in rapid identification of BSI. Each technology has its advantages and disadvantages, which must be considered. Still, implementation of either platform could result in reduction of hospital stays, lower cost, better patient management and more appropriate use of antibiotics by clinicians.

Data availability

Underlying data

Figshare: IDENTI~1.DOC. <https://doi.org/10.6084/m9.figshare.12948533.v4>¹⁵.

This project contains the following underlying data:

- Identification of Selected Primary Bloodstream Infection Pathogens in Patients Attending Kisii Level Five and Homa Bay County Hospitals- FA.xlsx. (Data obtained using Film Array.)
- Identification of Selected Primary Bloodstream Infection Pathogens in Patients Attending Kisii Level Five and Homa Bay County Hospitals-MS.xlsx. (Data obtained using Microscan.)
- Identification of Selected Primary Bloodstream Infection Pathogens in Patients Attending Kisii Level Five and Homa Bay County Hospitals-Api.xlsx. (Data obtained using analytical profile index.)
- Identification of Selected Primary Bloodstream Infection Pathogens in Patients Attending Kisii Level Five and Homa Bay County Hospitals-FA raw data.xlsx. (Pathogen count data obtained using Film Array.)
- Identification of Selected Primary Bloodstream Infection Pathogens in Patients Attending Kisii Level Five and Homa Bay County Hospitals-MS raw data.xlsx. (Pathogen count data obtained using Microscan.)
- Identification of Selected Primary Bloodstream Infection Pathogens in Patients Attending Kisii Level Five

and Homa Bay County Hospitals-Api raw data.xlsx. (Pathogen count data obtained using analytical profile index.)

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](#) (CC-BY 4.0).

Acknowledgements

We acknowledge the role of United States Army Medical Research Directorate-Africa, Kenya, the Microbiology Hub – Kericho, and Kenya Medical Research Institute for facilitating this study. Ethics committees from both WRAIR and KEMRI-SERU played a critical role in ensuring that this study is feasible and meets the required standards and invaluable gratitude also goes to Walter Reed Project-Kericho Regulatory office, Michael Obonyo, Mary Leelgo and Judith Bosuben for unremitting support in their guidance, our thanks also goes to Benson Singa for the support during regulatory process and Rukia Kibaya for continued review and guidance.

Author contributions

Ronald Kirera was responsible for conceptualization, study design, data analysis, and drafting of the manuscript. Daniel Kariuki, Joseph Nganga, Judd L. Walson, Christine Hulseberg and Alexander Flynn contributed in the manuscript review. Elizabeth Odundo, Erick Kipkirui, Cliff Odhiambo, Nancy Kipkemoi, Abigail Ombogo, Janet Ndonge, Mary Kirui, and Margaret Koech contributed in data analysis and manuscript review.

References

1. Dagne M, Yismaw G, Gizachew M, *et al.*: **Bacterial profile and antimicrobial susceptibility pattern in septicemia suspected patients attending Gondar University Hospital, Northwest Ethiopia.** *BMC Res Notes*. 2013; **6**(1): 283. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
2. Altun O, Almuhayawi M, Ullberg M, *et al.*: **Clinical evaluation of the Filmarray blood culture identification panel in identification of bacteria and yeasts from positive blood culture bottles.** *J Clin Microbiol*. 2013; **51**(12): 4130–6. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
3. Akoua-Koffi C, Tia H, Plo JK, *et al.*: **Epidemiology of community-onset bloodstream infections in Bouaké, central Côte d'Ivoire.** *New Microbes New Infect*. 2015; **7**: 100–4. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
4. Viscoli C: **Bloodstream Infections: The peak of the iceberg.** *Virulence*. 2016; **7**(3): 248–51. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
5. Ray STJ, Drew RJ, Hardiman F, *et al.*: **Rapid Identification of Microorganisms by FilmArray Blood Culture Identification Panel Improves Clinical Management in Children.** *Pediatr Infect Dis J*. 2016; **35**(5): e134–8. [PubMed Abstract](#) | [Publisher Full Text](#)
6. Berkley JA, Lowe BS, Mwangi I, *et al.*: **Bacteremia among Children Admitted to a Rural Hospital in Kenya.** *N Engl J Med*. 2005; **352**(1): 39–47. [PubMed Abstract](#) | [Publisher Full Text](#)
7. Prakash KP, Arora V, Geethanjali PP: **Bloodstream bacterial pathogens and their antibiotic resistance pattern in Dhahira region, Oman.** *Oman Med J*. 2011; **26**(4): 240–7. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
8. Blaschke AJ, Heyrend C, Byington CL, *et al.*: **Rapid Identification of Pathogens from Positive Blood Cultures by Multiplex PCR using the FilmArray System.** *Diagn Microbiol Infect Dis*. 2013; **74**(4): 349–55. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
9. Altun O, Almuhayawi M, Ullberg M, *et al.*: **Clinical evaluation of the Filmarray blood culture identification panel in identification of bacteria and yeasts from positive blood culture bottles.** *J Clin Microbiol*. 2013; **51**(12): 4130–6. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
10. Snyder JW, Munier GK, Johnson CL: **Direct comparison of the BD phoenix system with the MicroScan WalkAway system for identification and antimicrobial susceptibility testing of Enterobacteriaceae and nonfermentative gram-negative organisms.** *J Clin Microbiol*. 2008; **46**(7): 2327–33. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
11. St-Germain GG, Beauchesne D: **Evaluation of the MicroScan Rapid Yeast Identification panel.** *J Clin Microbiol*. 1991; **29**(10): 2296–9. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
12. Integrated FC, Plan D: **COUNTY GOVERNMENT OF HOMA BAY ' A County of Choice ' FIRST COUNTY INTEGRATED.** 2017. [Reference Source](#)
13. Maze MJ, Bassat Q, Feasey NA, *et al.*: **The epidemiology of febrile illness in sub-Saharan Africa: implications for diagnosis and management.** *Clin Microbiol Infect*. 2018; **24**(8): 808–814. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
14. Philip CO, Koech M, Kipkemai N, *et al.*: **Evaluation of the performance of a multiplex reverse transcription polymerase chain reaction kit as a potential diagnostic and surveillance kit for rotavirus in Kenya.** *Trop Dis Travel Med Vaccines*. 2019; **5**: 12. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
15. Kirera R, Kipkirui E, Kirui M, *et al.*: **IDENTI~1.DOC.** *figshare*. Dataset. 2020. <https://www.doi.org/10.6084/m9.figshare.12948533.v4>

16. Pradhan R, Shrestha U, Gautam SC, *et al.*: **Bloodstream Infection among Children Presenting to a General Hospital Outpatient Clinic in Urban Nepal.** *PLoS One.* 2012; **7**(10): e47531.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
17. Fhooblall M, Nkwanyana F, Mlisana KP: **Evaluation of the BioFire® FilmArray® blood culture identification panel on positive blood cultures in a regional hospital laboratory in KwaZulu-Natal.** *Afr J Lab Med.* 2016; **5**(1): 411.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
18. Salimnia H, Fairfax MR, Lephart PR, *et al.*: **Evaluation of the FilmArray Blood Culture Identification Panel: Results of a Multicenter Controlled Trial.** *J Clin Microbiol.* 2016; **54**(3): 687–98.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
19. Jin WY, Jang SJ, Lee MJ, *et al.*: **Evaluation of VITEK 2, MicroScan, and Phoenix for identification of clinical isolates and reference strains.** *Diagn Microbiol Infect Dis.* 2011; **70**(4): 442–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
20. Patteet L, Goossens H, Ieven M: **Validation of the MicroScan-96 for the species identification and methicillin susceptibility testing of clinical significant coagulase-negative staphylococci.** *Eur J Clin Microbiol Infect Dis.* 2012; **31**(5): 747–51.
[PubMed Abstract](#) | [Publisher Full Text](#)
21. O'Hara CM, Tenover FC, Miller JM: **Parallel comparison of accuracy of API 20E, Vitek GNI MicroScan Walk/Away Rapid ID and Becton Dickinson Cobas Micro ID-E/NF for identification of members of the family Enterobacteriaceae and common gram-negative, non- glucose-fermenting bacilli.** *J Clin Microbiol.* 1993; **31**(12): 3165–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)

Open Peer Review

Current Peer Review Status: ? ✖

Version 1

Reviewer Report 20 May 2021

<https://doi.org/10.5256/f1000research.29032.r85225>

© 2021 Raymond J. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Josette Raymond

France Bacteriology Laboratory, Bicêtre Hospital, Kremlin Bicetre, France

The study compare three methods of identification of pathogens growth in blood culture samples: API, Film Array and MS. All the 3 methods show excellent sensitivity and accuracy. What was the specificity?

Some comments:

It should be clearly noted that due to the technology and the price, these techniques (FA and MS) cannot be used in any laboratory in Africa (or low income countries).

Unfortunately, the FA method is not able to identify the *Salmonella*. This is a real problem, since the isolated Enterobacteriaceae were mainly *Salmonella* knowing that *Salmonella* is the major pathogen in Africa.

In the discussion, the authors state that *S. anginosus* and *S. bovis* are contaminant. I do not agree since these *Streptococcus* may be responsible of endocarditis or other (abdominal) infections.

The identification of the bacteria is not enough. More data on antimicrobial susceptibilities are required since antimicrobial resistance is a major problem in Africa. So, more data are needed.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Infectious diseases (pediatric mainly) and Helicobacter infection

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 27 May 2021

Ronald Kirera

Dear reviewer,

Thank you for taking time to review our journal. We appreciate comments and suggestions.

The study compare three methods of identification of pathogens growth in blood culture samples: API, Film Array and MS. All the 3 methods show excellent sensitivity and accuracy. What was the specificity?

Response: The overall specificity was 98%. We did not include specificity in the journal because consultation with my co-authors we decided to use sensitivity and accuracy.

Some comments:

It should be clearly noted that due to the technology and the price, these techniques (FA and MS) cannot be used in any laboratory in Africa (or low income countries).

Response: In Kenya, the government has invested a lot in the health sector through county governments under devolution and universal health initiative. These technologies will be embraced in the referral hospitals and research institutions, also the non-governmental organizations and private sector have also invested much in this institutions. With the emergence of drug resistant microorganisms these technologies will help in early diagnosis and reduce on multidrug resistant.

Unfortunately, the FA method is not able to identify the Salmonella. This is a real problem, since the isolated Enterobacteriaceae were mainly Salmonella knowing that Salmonella is the major pathogen in Africa.

Response: FA BCID 1 panel is not able to identify the *Salmonella* (genus) but it identifies up to the family level, following manufacturers' recommendations and inhouse standard procedures this can be identified further to genus level using salmonella antisera. The FA

identification panel keeps on improving and the current panel (BCID2) identifies *Salmonella* at genus level using the same machine/platform. The turnaround time for FA is really helpful in early diagnosis of *Salmonella*.

In the discussion, the authors state that S. anginosus and S. bovis are contaminant. I do not agree since these Streptococcus may be responsible of endocarditis or other (abdominal) infections.

Response: Thank you for pointing this out, These microorganisms cause bacteremia taking advantage of immunocompromised patients though not common in immunocompetent individuals.

The identification of the bacteria is not enough. More data on antimicrobial susceptibilities are required since antimicrobial resistance is a major problem in Africa. So, more data are needed.

Response: We agree, in our recommendation we suggested more studies with big number. Our study was limited by timelines and resources.

Thank you,

Ronald Kirera,

Corresponding author.

Competing Interests: There is no competing interest.

Reviewer Report 23 November 2020

<https://doi.org/10.5256/f1000research.29032.r72842>

© 2020 Kiiyukia C. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Ciira Kiiyukia

Medical School, Mount Kenya University (MKU), Thika, Kenya

The evaluation of the various analytical techniques available for the BSI in Kenya was timely. The methods used and the the results obtained are reliable. However, the abstract need some revision since the section on Methods contains more about the results than methodology. This section can be split to include a section on Results.

In the abstract 3rd line from the top, the authors claim that - *This study retrospectively analyzed data of identified BSI pathogens*. Which means that the they did not isolate and identify the pathogens as described in the Methods section. It is not clear whether they used already identified pathogens

or used stored blood culture samples from Kisii Referral Hospital and identified the pathogens.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Medical microbiology-Bacteriology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 24 Nov 2020

Ronald Kirera

Dear reviewer,

Thank you for the review and taking the time to go through the paper,

The question on results and methods in the abstract section

Response: This was combined to meet the allowable minimum number in the abstract section as per journal requirement however I had to limit the explanation on results and methods to meet the required number.

On abstract 3rd line on "this study retrospectively analyzed data of identified BSI pathogens"

Response:

a) I used archived BSI isolates which I had processed/analyzed before using the same methods under analysis for comparison.

b) The explanation in the method section was to show how the isolates were processed and how the techniques work.

Thank you,
Ronald Kirera
Corresponding author.

Competing Interests: We have no competing interest.

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com

F1000Research