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ORIGINAL ARTICLE

Transforming Bacterial Lower Respiratory Tract Infection Diagnosis: A Study on the Efficiency of the FilmArray Pneumonia Panel

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Background: Lower respiratory tract infections (LRTIs) significantly contribute to global morbidity and mortality. Conventional bacterial LRTIs diagnosis relies on microbiological methods, which are time-consuming. The Biofire® FilmArray® Pneumonia Panel (FAPP) offers a faster and more accurate detection of respiratory pathogens but shows conflicting results with conventional cultures. **Aim:** We assessed the agreement between bacterial organisms and resistance genes identified using FAPP and standard culture techniques. **Methods:** This single-center retrospective study analyzed 400 patient samples, comparing the positive predictive value (PPV), negative predictive value (NPV), sensitivity, and specificity with conventional cultures. The prevalence of bacterial organisms and resistance markers in FAPP and cultures was estimated. **Results:** In 400 samples, 692 bacterial targets and 216 resistance markers were detected using FAPP. FAPP detection was 3.9 times higher than bacterial culture. The overall PPV, NPV, sensitivity, and specificity were 23.55%, 99.76%, 92.61%, and 90.92%, respectively. Multiple pathogens were found in 177 samples (46.3%) with FAPP. **Conclusion:** FAPP provides rapid and sensitive detection of respiratory bacterial infections. However, results should be interpreted with the clinical context. Further studies are needed to clarify its clinical impact and cost-effectiveness.

Key words: FAPP, lower respiratory tract infections, bacterial lower respiratory tract infections diagnosis, rapid diagnosis

INTRODUCTION

Lower respiratory tract infections (LRTIs) represent a significant global health concern with a substantial contribution to morbidity and mortality rates worldwide.[1,2] Among these infections, bacterial pneumonia (PN) stands out as a major contributor underscoring the urgent need for timely and accurate diagnostic tools, to facilitate the appropriate management and improve patient outcomes.[3,4]

The conventional approach for diagnosing bacterial LRTIs primarily involves microbiological methods, which are effective but can be time-consuming and often unable to provide the timely results necessary for prompt clinical decision-making.[5] This research challenge prompted the exploration of more advanced diagnostic tools, such as the FilmArray Pneumonia Panel (FAPP).[6] FAPP is an automated multiplex polymerase chain reaction (PCR) test capable of rapidly detecting 27 bacteria and viruses, along with seven genetic markers of antibiotic resistance, as fast as approximately 1–2 h.[6] It employs a semiquantitative system to estimate the analyzed sample's bacterial load.[6]

This study aimed to evaluate the effectiveness of FAPP in diagnosing and managing bacterial LRTIs, particularly focusing on its sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) in comparison to conventional microbiological methods.[6]

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MATERIALS AND METHODS

Patient selection and sample collection

The present, retrospective, observational study was conducted at Tri-Service General Hospital, in a single-center setting with the approval of the Institutional Review Board of TSGH (Approval number: C202305073, Date of Approval: 2023/06/17). The study was conducted in accordance with the Declaration of Helsinki. Before the commencement of the study, participants will be informed that their test results will be utilized for scientific research purposes and will not entail the disclosure of personal privacy. Participants provided their agreement through the act of signing the consent form. It is important to emphasize that informed consent was procured from all participants included in this study. Participants included individuals aged ≥18 years who took the FAPP test between December 2022 and June 2023. In accordance with the local protocol, FAPP testing was initiated when indications of LRTI were present. At least two indicators of LRTI, including fever, hypoxemia, radiological findings consistent with LRTI, increased lower respiratory tract (LRT) secretion, and elevated acute-phase reactants were considered.[7,8]

A comprehensive approach was employed to conduct both conventional semiquantitative cultures (CC) and biochemical assessments, including C-reactive protein (CRP) levels, for all patients.[7,8] Between December 2022 and May 2023, 509 samples from 461 patients were screened for eligibility, of which 400 samples from 400 patients qualified. The exclusion criteria were the following: (1) patients under 18 years of age, (2) unavailable clinical information, (3) repeated samples from the same patient, and (4) patients who did not meet the eligibility criteria outlined above.[9] Data pertaining to demographics, clinical conditions, outcomes, and antimicrobial therapy were collected from the electronic medical records by attending physicians.[7,8] No antibiotic stewardship programs have been implemented.[7,8] Although consensus protocols for antimicrobial therapy were established during the study period, the prescription of antimicrobials was left to the discretion of physicians.

BioFire FilmArray pneumonia panel (FAPP)

FAPP is an automated multiplex PCR system that targets 27 PN-related pathogens. A semiquantitative system was used to estimate the number of bacteria in the analyzed sample at the intervals of 104, 105, 106, or >107 copies of the bacterial genome per milliliter of sample.[8] LRT specimens were stored in a frozen (– 80°C) environment and were analyzed on the BioFire FilmArray pneumonia panel (FAPP). Testing was performed by the qualified personnel in accordance with the manufacturer's instructions in a single research laboratory.[9]

Microbiological testing

Tracheal aspirates and sputum samples were subjected to conventional culture-based procedures and FA-PP.[7,8] The conventional culture method was performed as the part of standard of care testing at the Clinical Microbiology Laboratory of the Tri-Service General Hospital.[9] The samples were inoculated onto blood, chocolate, and McConkey agar (BioMérieux, Marcy l'Étoile, France) and incubated in a CO_2 environment for a maximum period of 3 days. The microorganisms that emerged in cultures were subsequently identified using MALDI-TOF MS (Maldi Biotyper, Bruker Daltonics, Bremen, Germany).

Statistical analysis

A database was built and analyzed by the authors. Both qualitative (positive vs. negative results) and quantitative (according to the number of copies/mL of bacterial DNA returned by the FA-PP assay) positive and negative percent agreements between the comparison methods (PPV and NPV, respectively) were estimated. Logistic regression models providing odds ratios and 5% confidence intervals (CIs) were constructed to assess the association between the number of DNA copies/mL detected

Table 1: Patient characteristics

	Population characteristics (*n*=400)
Age, years, median, (IQR)	73 (64-83)
Male No. (%)	238 (59.50%)
Female No.(%)	162 (40.5%)
Age distribution	
91-100, years	42 (10.5%)
81-90, years	90 (22.5%)
71-80, years	112 (28.0%)
<=70, years	156 (39.0%)
Setting	
Intensive care unit (ICU)	192 (48.0%)
Emergency department (ED)	10 (2.5%)
Respiratory care unit	17 (4.3%)
Elevated CRP (>5mg/dL)	266 (66.5%)
Sample type	
Tracheal aspiration	324 (81.0%)
Sputum	76 (19.0%)
LRTI related diagnosis	
Community acquired pneumonia (CAP)	62 (15.6%)
Hospital acquired pneumonia (HAP)	32 (8.0%)
Ventilator associated pneumonia (VAP)	17 (4.3%)
SARS-COV2 infection pneumonia	20 (5.0%)
Undetermined	70 (17.5%)

by FA-PP and the probability of obtaining a positive culture. Differences between the variables were assessed by the ANOVA test. Two-sided exact *P* values were reported and a $P < 0.05$ was considered statistically significant. Statistical analyses were performed using the SPSS software version 20.0 (IBM Corporation, 1 New Orchard Road, Armonk, New York, 10504, United States).[7,8]

RESULTS

Patient population

Four hundred patients were enrolled in this study. The mean age was 73.04 years (range, 22–100 years) and most of the participants were male (59.50%). A total of 192 patients (48%) were admitted to the intensive care unit.[8] The percentage of patients with elevated CRP levels was 93%. For LRTI-related diagnoses, 62 patients had community-acquired pneumonia (CAP), 32 had hospital-acquired pneumonia (HAP), and 17 had ventilator-associated pneumonia (VAP). Patient characteristics are described in Table 1.[10]

FAPP and conventional culture results

A total of 400 FAPP respiratory samples from an equal number of patients were analyzed in parallel for standard culture and the inflammatory index of CRP, respectively.[9,11,12]

The distribution of FAPP sample types included 324 (81.0%) tracheal aspirates and 76 (19.0%) sputum samples. FAPP was used to detect 692 bacterial targets and 216 antimicrobial resistance markers. FAPP analysis revealed that the *Acinetobacter calcoaceticus–Acinetobacter baumannii* complex, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* were the most frequently detected bacteria, with occurrence frequencies of 115, 127, and 103, respectively. For the number of samples in which multiple pathogens were detected by the FAPP, single bacterial pathogens were detected in 153 samples, two bacterial pathogens were detected in 80 samples, and three or more bacterial pathogens were detected in 101 samples.

Based on the culture results, 42 acinetobacter-associated bacteria, 33 *P. aeruginosa,* and 36 *K. pneumoniae* strains were detected. Overall, the FAPP identified approximately 3.9 fold more bacterial organisms than the culture method (692 vs. 176).

Regarding the concordance of bacterial detection results between the FAPP and CC methods, the overall PPV of the PN panel was 23.55% (95% CI, 20.4–26.8%); NPV was 99.76% (95% CI, 99.6–99.9%); sensitivity was 92.61% (95% CI, 88.2–96.5%); and specificity was 90.92% (95% CI, 90.2–91.7%)[7] [Table 2].

The bacterial and antimicrobial resistance identified in FAPP is presented in Table 3.

Table 2: Performance summary of the FAPP compared to those of the conventional culture (CC)

Pathogen target	FAPP Positive (No.)	FAPP Negative (No.)	Culture Positive (No.)	Culture Negative (No.)	TP	TN	FP	FN	PPV (TP/TP+FP)	NPV (TN/TN+FN)	SEN (TP/TP+FN)	SPE (TN/TN+FP)
ACB complex	115	285	42	358	37	280	78	5	32.17%	98.25%	88.10%	78.21%
K. aerogenes	13	387	2	398	2	387	11	0	15.38%	100.00%	100.00%	97.24%
E. cloacae cpx	37	363	4	396	4	363	33	0	10.81%	100.00%	100.00%	91.67%
E. coli	51	349	7	393	6	348	45	1	11.76%	99.71%	85.71%	88.55%
H. influenzae	35	365	2	398	2	365	33	0	5.71%	100.00%	100.00%	91.71%
K. oxytoca	11	389	4	396	3	388	8	1	27.27%	99.74%	75.00%	97.98%
K. pneumoniae	127	273	36	364	33	270	94	3	25.98%	98.90%	91.67%	74.18%
M. catarrhalis	12	388	0	400	0	388	12	0	0.00%	100.00%	N/A	97.00%
Proteus spp.	20	380	3	397	3	380	17	0	15.00%	100.00%	100.00%	95.72%
P. aeruginosa	103	297	33	367	32	296	71	1	31.07%	99.66%	96.97%	80.65%
S. marcescens	32	368	7	393	6	367	26	1	18.75%	99.73%	85.71%	93.38%
S. aureus	97	303	35	365	34	302	63	1	35.05%	99.67%	97.14%	82.74%
S. agalactiae	32	368	1	399	1	368	31	0	3.13%	100.00%	100.00%	92.23%
S. pneumoniae	6	394	0	400	0	394	6	0	0.00%	100.00%	N/A	98.50%
S. pyogenes	1	399	0	400	0	399	1	0	0.00%	100.00%	N/A	99.75%
Total	692	5308	176	5824	163	5295	529	13	23.55%	99.76%	92.61%	90.92%

ACB complex: Acinetobacter calcoaceticus-baumannii complex. PPV: Positive predictive value. NPV: Negative predictive value. TP: True positive (FAPP and culture positive), FP: false positive (FAPP positive and culture negative). FN: False negative (FAPP negative and culture positive). TN: True negative (FAPP and culture negative). SEN: Sensitivity. SPE: Specificity

Table 3: Antimicrobial resistance markers (AMR) concordance between the FAPP and the conventional culture (CC)

Antimicrobial resistance markers (AMR)	FAPP total	FAPP *S. aureus* or ESBL-producing Enterobacterales(+)	FAPP *S. aureus* or ESBL-producing Enterobacterales(-)	CC S. aureus or ESBL-producing Enterobacterales(+)	CC *S. aureus* or ESBL-producing Enterobacterales(-)
mecA/C & MREJ (FAPN)	30	29	1	14	16
KPC (FAPN)	16	16	0	9	7
NDM (FAPN)	36	36	0	20	16
Oxa-48-like (FAPN)	6	6	0	3	3
VIM (FAPN)	16	15	1	5	11
IMP (FAPN)	38	38	0	16	21
CTX-M (FAPN)	74	74	0	42	32
Total	216	214	2	109	106

ESBL: Extended-spectrum beta-lactamases

Table 4: Summary of semiquantitative values of bacteria measured by the FAPP in the conventional culture (CC) positive samples

Pathogen target	C(+) with FAPP 10^4 copies/mL (No.)	C(+) with FAPP 10^5 copies/mL (No.)	C(+) with FAPP 10^6 copies/mL (No.)	C(+) with FAPP 10^7 copies/mL (No.)	C(+) total (No.)
ACB complex	4	8	6	19	42
K. aerogenes	1	0	1	0	2
E. cloacae cpx	0	1	1	2	4
E. coli	0	2	0	4	7
H. influenzae	0	0	0	2	2
K. oxytoca	0	1	0	2	4
K. pneumoniae	3	3	9	18	36
M. catarrhalis	0	0	0	0	0
Proteus spp.	0	1	1	1	3
P. aeruginosa	2	4	6	20	33
S. marcescens	0	1	3	2	7
S. aureus	1	4	9	20	35
S. agalactiae	0	0	0	1	1
S. pneumoniae	0	0	0	0	0
S. pyogenes	0	0	0	0	0
Total	11	25	36	91	176

ACB complex: Acinetobacter calcoaceticus-baumannii complex. C(+): Conventional culture positive samples

When considering PN type, *P. aeruginosa*, *K. pneumoniae*, and *Staphylococcus aureus* are the most common organisms associated with CAP and HAP [Figure 1].[10]

We also summarized the comparison between semiquantitative values of the bacteria measured using FAPP and positive conventional culture yield. In the positive culture yield samples, semi-quantitative values determined by FAPP ranged from ≥107 copies/mL (91 bacteria), 106 copies/mL (36 bacteria), 105 copies/mL (25 bacteria), and 104 copies/mL (11 bacteria)[8] [Table 4]. Positive culture results included 42 acinetobacter-associated bacteria, 33 *P. aeruginosa,* and 36 *K. pneumonia*, which were the predominately detected bacteria.

DISCUSSION

This study evaluated the FAPP in a medical center setting.[9] Our results confirmed that the FAPP can rapidly and effectively detect a variety of pathogens in LRT specimens.[7] Specifically, FAPP detected a high proportion of bacterial pathogens in our samples (83.5%), which likely reflects our inclusion criteria.[9] FAPP exhibited an approximately 3–4 fold increase in the identification of individual on-panel bacterial targets compared with the culture method (692 vs. 176).[12]

Regarding the concordance of bacterial detection results between the FAPP and CC methods, FAPP showed high sensitivity, specificity, and NPV. Notably, lower PPVs were

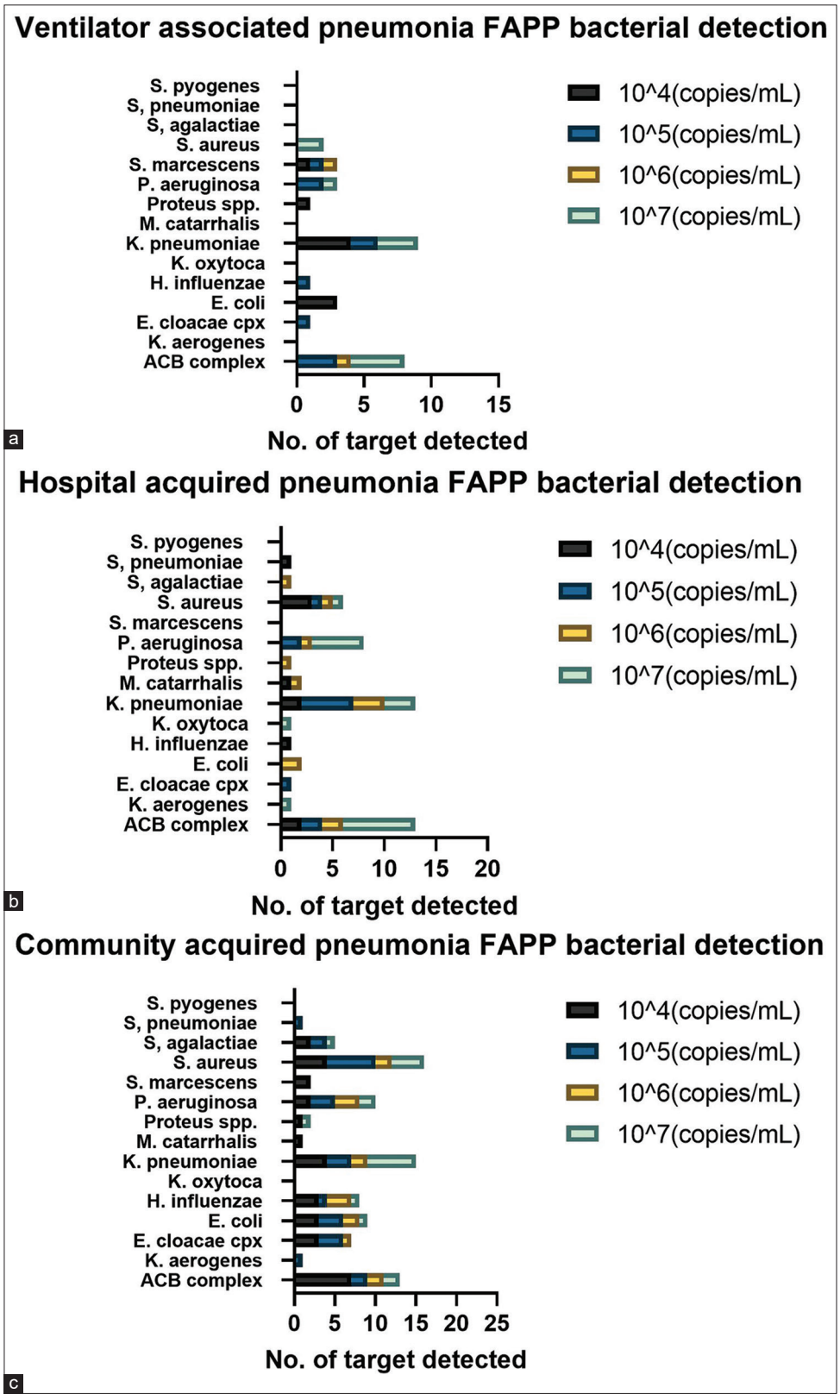

Figure 1: Number of FilmArray Pneumonia Panel (FAPP) pathogen detection among patients with ventilator-associated pneumonia (a), Hospital-acquired pneumonia (b), and Community-acquired pneumonia (c)

recorded in our than compared to previous studies.[7-12] Several factors may contribute to this observed discrepancy. First, the heterogeneity of bacterial populations, influenced by patient condition, environmental factors, and infection type, can impact detection consistency, with FAPP frequently identifying nonpathogenic species, complicating clinical interpretation. Second, FAPP detects genetic material from both viable and nonviable bacteria, which may result in false positives, as the presence of bacterial DNA does not necessarily indicate an active infection. It may also identify the colonizing bacteria, particularly in patients with chronic respiratory conditions, leading to an overestimation of clinically relevant pathogens. Third, recent antibiotic use (within 7 days) may inhibit bacterial growth in cultures, whereas FAPP continues to detect nonviable bacterial DNA, potentially inflating infection rates. Finally, in the low-prevalence settings, FAPP's high-sensitivity nature increases the likelihood of detecting clinically insignificant bacteria, further diminishing PPV.[10]

Detection using culture methods depends on the pathogen viability. Therefore, the detection of nonviable bacteria by FAPP could be one of the causes of the discordant results in bacterial detection between FAPP and culture methods. It is also possible that FAPP detected bacteria that were low in abundance or noneasily culturable because of fastidious growth characteristics. Therefore, the results of molecular assays should be interpreted carefully when used for patient management, considering the differences in characteristics between molecular assays and culture methods.

There are several strengths in our study. First, it is representative of a real-world population since it includes medical center patients from the various sources of clinical symptoms of LRTIs, including different types of PN.[10] Second, our patients and samples were stratified according to PN type, including CAP, HAP, VAP, and other LRTI. A detailed bacterial detection report of the concordance between the FAPP and CC methods was reported in detail.

However, there are some limitations of this study. First, the retrospective and observational design could not account for all potential confounders that may have influenced the study outcomes, including the clinical rationale for diagnostic and therapeutic decision-making. Second, we did not collect all the samples submitted to our laboratory during the study period.

CONCLUSION

This study supports the claim that FAPP provides the rapid diagnosis of respiratory bacterial infections with high sensitivity and specificity.[9] FAPP could detect more bacteria than standard culture methods in lower respiratory samples. However, for optimal patient care and antimicrobial stewardship,[8] FAPP results should always be interpreted in conjunction with the patient's clinical status and other diagnostic information.[10] Further studies are necessary to clarify its clinical impact on patient management and cost-effectiveness.[7]

Data availability statement

The data that support the findings of this study are available from the corresponding author, Hung-Sheng Shang, upon reasonable request.

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Conflicts of interest

There are no conflicts of interest.

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