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Pneumologia

# BioFire® FilmArray® Pneumonia Panel versus bacterial culture in adult community acquired pneumonia: treatment implications

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**Abstract**

**English:**

***Background:*** *Severe community-acquired pneumonia (sCAP) is a growing burden on public health, associated with high morbidity and mortality. The diversity of aetiological agents requires that current guidelines consider the potential benefit of using rapid molecular techniques for microbial diagnosis as part of sCAP management.*
***Objective:*** *This study aimed to assess the diagnostic performance of BioFire® FilmArray® Pneumonia Panel (BFPP) versus standard-of-care (SOC) culture for rapidly detecting respiratory pathogens and genetic markers among patients with sCAP.*
***Methods:*** *The study was conducted on 236 patients with sCAP; lower respiratory tract (LRT) specimens were investigated by both BFPP and SOC, and the results were compared regarding the diagnostic performance, their related resistance genes and their effect on patient outcomes.*
***Results:*** *BFPP showed an overall sensitivity of 81.97% (95% confidence interval [CI]: 73.98–88.34) and an overall specificity of 94.44% (95% CI: 93.59–95.21) over SOC. The 214 resistance genes detected by BFPP enabled rapid initiation of targeted antimicrobial therapy.*
***Conclusion:*** *BFPP can enhance rapid microbiological diagnosis of patients with sCAP for early implementation of precision antimicrobial therapy, improving both morbidity and mortality. However, BFPP does not detect fungal pathogens, which is an important limitation in some clinical situations.*

**Keywords**

*sCAP • BioFire • Pneumonia Panel • VITEK-2 • antibiotic resistance*

**Abbreviations:** BFPP, BioFire® FilmArray® Pneumonia Panel; BSC, biological safety cabinet; FAIV, FilmArray injection vial; LRT, lower respiratory tract; PCR, polymerase chain reaction; sCAP, severe community-acquired pneumonia

# BioFire® FilmArray® Pneumonia Panel versus cultura bacteriană în pneumonia comunitară la adulți: implicații terapeutice

**Rezumat**

**Romanian:**

***Background:*** *Pneumonia comunitară severă (sCAP) reprezintă o povară tot mai mare pentru sănătatea publică, fiind asociată cu o morbiditate și mortalitate ridicate. Diversitatea agenților etiologici determină ghidurile actuale să ia în considerare potențialul beneficiu al utilizării tehnicilor moleculare rapide pentru diagnosticul microbiologic, ca parte a managementului sCAP.*
***Obiectiv:*** *Acest studiu a avut ca scop evaluarea performanței diagnostice a testului BioFire® FilmArray® Pneumonia Panel (BFPP) comparativ cu metoda standard de cultură bacteriană (SOC), pentru detectarea rapidă a agenților patogeni respiratori și a markerilor genetici la pacienții cu sCAP.*
***Metode:*** *Studiul a inclus 236 de pacienți cu sCAP; probele din tractul respirator inferior (LRT) au fost analizate atât prin BFPP, cât și prin SOC, iar rezultatele au fost comparate în ceea ce privește performanța diagnostică, genele de rezistență detectate și impactul asupra evoluției clinice a pacienților.*

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***Rezultate:*** *BFPP a demonstrat o sensibilitate globală de 81,97% (interval de încredere [IC] 95%: 73,98–88,34) și o specificitate globală de 94,44% (IC 95%: 93,59–95,21) comparativ cu SOC. Cele 214 gene de rezistență identificate prin BFPP au permis inițierea rapidă a unei terapii antimicrobiene specifice.*
***Concluzie:*** *BFPP poate îmbunătăți diagnosticul microbiologic rapid al pacienților cu sCAP, facilitând aplicarea timpurie a unei terapii antimicrobiene de precizie și reducând morbiditatea și mortalitatea. Totuși, BFPP nu detectează agenții patogeni fungici, ceea ce reprezintă o limitare importantă în anumite situații clinice.*

**Cuvinte-cheie**

*sCAP • BioFire • Pneumonia Panel • VITEK-2 • rezistență la antibiotice*

## Introduction

Community-acquired pneumonia (CAP) is a prevalent respiratory infectious disease with high morbidity and mortality and is the second most common cause of hospitalisation (1). Severe community-acquired pneumonia (sCAP) is a recognised term describing intensive care unit (ICU)-admitted patients with CAP who may require organ support. Observational studies have reported extremely high mortality in this group (2–4). Early administration of empirical antibiotics is essential, as it is the cornerstone of pneumonia therapy, covering suspected causative agents for 48–72 hr until culture-based diagnostic results are available (5). This approach entails accepting the risk of associated adverse outcomes, including drug toxicity, increased risk of antibiotic-resistant infections and related costs such as superinfection pneumonia and *Clostridioides difficile* infection (6, 7). More promising diagnostic tests have been developed to replace conventional bacterial culture, which involves multiple steps and typically requires 2–3 days to yield actionable results. Moreover, several studies have demonstrated that culture is suboptimal in detecting the causative pathogen in approximately half of cases (2, 8). Various studies have evaluated the cost-effectiveness of BioFire® FilmArray® Pneumonia Panel (BFPP), a multiplex polymerase chain reaction test that rapidly and reliably identifies pathogens and resistance genes in lower respiratory tract (LRT) specimens from patients with severe pneumonia. These studies focused on its role in guiding appropriate antibiotic therapy, minimising risk and reducing length of hospital stay (3, 4, 9). There has been great regional variation in the uptake of multiplex molecular diagnostics for pneumonia. Recent ERS/ESICM/ESCMID/ALAT guidelines from Europe strongly recommended the use of molecular panels in sCAP to increase diagnostic yield and decisions regarding stewards (1). Multicentre studies from North America have supported widespread assay implementation like BFPP, with evidence on earlier antibiotic optimisation and outcomes improvement (2, 3). Conversely, uptake across several Asian and Middle Eastern countries has been limited more by economic factors, infrastructural barriers (4, 5) and emerging evidence on cost-effectiveness in settings with a high burden of ICUs. This spread underscores such an imperative need to appraise a diagnostic tool like BFPP across various healthcare systems. This study aims to evaluate the effectiveness of BFPP compared with standard of care (SOC) in managing sCAP.

## Materials and methods

### *Study design*

A prospective study was conducted at Port Said University, Ain Shams University Hospitals and Ain Shams University Specialized Hospital from February 2024 to November 2024. Participants were older than 18 years and were randomly selected from patients hospitalised with sCAP in the ICU, diagnosed on clinical and radiological grounds according to the ATS/IDSA 2019 guideline criteria (10). Patients who presented with radiological features inconsistent with pneumonia and immunosuppressed individuals due to any cause, including malignancies, were excluded from the study.

### *Ethical considerations*

After providing written informed consent, all patients underwent a full medical history assessment and clinical examination upon admission. The study was approved by the Ethical Committee of the Faculty of Medicine at Port Said University (MED [4/2/2024], S.No. 141, CHS_002).

### *Data collection*

In all participants, mini-bronchoalveolar lavage (mini-BAL) specimens were collected and submitted to the microbiology laboratory for both BFPP and SOC testing.
Antibiotic selection was guided by the results of the BFPP. For patients with negative BFPP results, empirical antimicrobial therapy was initiated based on the ATS/IDSA 2019 guideline recommendations (10), and modifications were made following

**Table 1.** Targets of the BioFire pneumonia panel

| Bacteria | Atypical bacteria | Viruses | Antimicrobial resistance genes |
|---|---|---|---|
| Strept_agalactiae | Chlamydia_P | Adenovirus | IMP |
| Strept Pneumoniae | Legionella_P | Coronavirus | KPC |
| Strept_Pyogenes | Mycoplasma_P | Human_Metapneumovirus | mecA_C_and_MREJ |
| Moraxella_catarrhalis | | Human_Rhinovirus_Enterovirus | NDM |
| Proteus | | INFLUENZA_B | OXA_48_like |
| Pseudomonas aeruginosa | | INFLUENZA_A | VIM |
| Serratia_marcescens | | MERS_CoV | IMP |
| Staph_aureus | | Parainfluenza | KPC |
| E._Coli | | RSV | IMP |
| H_influenzae | | | |
| Klebsiella_aerogenes | | | |
| Klebsiella_oxytoca | | | |
| Klebsiella_Pneumoniae | | | |
| Acinetobacter calcoaceticus baumannii_complec | | | |
| Enterobacter cloacae complex | | | |

IMP, Imipenemase metallo-β-lactamase; KPC, Klebsiella pneumoniae carbapenemase; NDM, New Delhi metallo-β-lactamase; VIM, Verona integron-encoded metallo-β-lactamase.

the standard sensitivity testing results. Hospital length of stay (LOS), ICU LOS, duration of mechanical ventilation and patient outcomes (discharge or mortality) were recorded.

***BFPP***

LRT specimens were evaluated using the BioFire® FilmArray® 2.0 system BioFire Diagnostics, LLC (Biomérieux) system with the BFPP, a multiplex PCR test with an approximate turnaround time of 60–75 min. Qualified laboratory technicians conducted the testing in accordance with the manufacturer's instructions and institution-specific laboratory protocols to ensure proper handling of respiratory samples and preservation of quality. All initial specimens were processed in a biological safety cabinet (BSC) and then transferred into a FilmArray injection vial (FAIV) containing sample buffer. Subsequently, the mixture was injected into the BFPP test pouch. Technicians then inserted the inoculated pouches into the FilmArray instrument for analysis. Each specimen was processed individually, and the BSC was surface disinfected prior to handling subsequent samples (11, 12).

The BFPP test pouch includes all necessary reagents for specimen lysis, nucleic acid extraction, reverse transcription, amplification and detection of genomic sequences specific to each of the 33 panel targets (Table 1). Additionally, the test pouch contains two internal controls that assess proper function of the pouch and enables calculation of the semi-quantitative results. The user hydrated the BioFire pouch using the manufacturer-supplied hydration solution, followed by loading the sample mixture (respiratory specimen and buffer) and inserting the pouch into the BioFire instrument. The user then scanned the pouch, inserted it into the BioFire FilmArray® 2.0 and initiated the run. Each BFPP pouch includes two process controls (an Ribonucleic acid (RNA) process control and a quantified standard material control), both of which must yield positive results for the run to be considered valid. Runs that failed the internal control criteria were repeated using a new test pouch (13).

***SOC testing***

Specimens were Gram-stained and cultured according to established clinical laboratory protocols. Acceptable samples were concentrated using Cytospin and assessed via conventional Gram staining before inoculation. Bacterial cultures were prepared by inoculating portions of the specimen onto various selective and differential media including blood agar, chocolate agar and MacConkey agar using the streak plate method with a 0.001-mL calibrated loop. Blood agar and chocolate agar plates were incubated at 35°C, while MacConkey agar was incubated at 35°C in a 5% $CO_2$ atmosphere. Bacterial growth on each plate was evaluated daily. The VITEK® 2 system (bioMérieux, Marcy l'Étoile, Lyon, France) was used per the manufacturer's instructions to identify bacterial isolates and determine antibiotic susceptibility breakpoints (4, 12, 14). There were made no specific tests for identifying viruses due to unavailability.

***Blinding***

Laboratory personnel performing BFPP and SOC culture were blinded to clinical data to avoid bias.

***Colonisation versus infection***

When BFPP detected organisms were not identified by SOC, clinical judgement relied on clinical data, radiological evidence and laboratory biomarkers.

When BFPP discovered organisms not recognised by SOC culture, the results were evaluated based on clinical correlation. This included a multidisciplinary team (pulmonologists and microbiologists) review of the patient's clinical presentation (symptoms, signs), radiological findings (new infiltrates on Chest X-ray (CXR) or Computed tomography (CT) and laboratory biomarkers (e.g. procalcitonin >0.5 ng/mL or C-reactive protein [CRP] >50 mg/L). A result was considered a true infection if the clinical context was strong to support it.

***Statistical analysis***

Statistical analysis was performed using SPSS software (version 25; SPSS Inc., Chicago, IL, USA). Quantitative data were reported as mean ± standard deviation (SD), while categorical data were expressed as frequency and percentage. The correlation between BFPP and SOC testing was evaluated using positive percent agreement (PPA), negative percent agreement (NPA) and overall percent agreement (OPA), with 95% confidence intervals (CIs) calculated by the modified Wald method in GraphPad Prism® (version 10.2.0; GraphPad, San Diego, CA, USA).

In cases of LRT infections, conventional culture methods alone are inadequate; additional molecular techniques are required to detect viral pathogens and unculturable bacteria. Therefore, the terms PPA, NPA and OPA are preferred over sensitivity, specificity and accuracy, respectively (4, 15). The formulas used were as follows (15):

PPA = (true positives/[true positives + false negatives]) × 100%

NPA = (true negatives/[true negatives + false positives]) × 100%

OPA = ([true positives + true negatives]/[true positives + true negatives + false positives + false negatives]) × 100%

## Results

***Subject characteristics***

The study included 236 mini-BAL samples collected from 236 subjects who were admitted to the ICUs of Ain Shams University and Ain Shams University Specialized Hospitals with a diagnosis of CAP. The majority of participants were male (63.6%), with a mean age of 62.89 ± 18.61 years. Most were current smokers (59.3%) and had various comorbidities. Table 2 presents demographic characteristics, comorbidity distribution, hospital and ICU LOS, duration of mechanical ventilation and clinical outcomes.

**Table 2.** Characteristic data of participating subjects

| | | Mean | SD |
|---|---|---|---|
| Age (years) | | 62.89 | 18.61 |
| Age category (F/%) | | | |
| 18–35 (years) | | 33 | 14.0 |
| 36–50 (years) | | 31 | 13.1 |
| 51–65 (years) | | 42 | 17.8 |
| >65 (years) | | 130 | 55.1 |
| Sex (F/%) | Male | 150 | 63.6 |
| | Female | 86 | 36.4 |
| Smoking status (F/%) | | | |
| Current smoker | | 140 | 59.3 |
| Ex-smoker | | 16 | 6.8 |
| Non-smoker | | 80 | 33.9 |
| SI (Pack.year) | | 17.94 | 18.36 |
| Comorbidities (F/%) | | | |
| DM | | 127 | 53.81 |
| HTN | | 110 | 46.6 |
| IHD | | 85 | 36.0 |
| Chr_Resp_Dis | | 37 | 15.68 |
| CKD | | 36 | 15.25 |
| Others | | 55 | 23.3 |
| Antimicrobial use before hospitalisation (F/%) | | 184 | 77.96 |
| Hosp_LOS (days) | | 23.49 | 32.32 |
| ICU_LOS (days) | | 16.95 | 21.91 |
| MV_Dur (days) | | 5.95 | 14.82 |
| Outcome (F/%) | Discharged | 176 | 74.6 |
| | In-hospital mortality | 60 | 25.4 |
| 30-day mortality (F/%) | | 43 | 18.22 |

CKD, chronic kidney disease; CRP, C-reactive protein; diff, differential count; DM, diabetes mellitus; F/%, frequency/percentage; HTN, hypertension; ICU, intensive care unit; IHD, ischaemic heart disease; LOS, length of stay; MV, mechanical ventilation; SD, standard deviation; SI, smoking index; TLC, total leucocytic count.

***An overview of the BFPP findings compared with the conventional culture procedure***

Mini-BAL samples were collected from 236 subjects for microbiological evaluation using both the BFPP and SOC culture methods. BFPP detected bacteria exclusively in 60.59% (143/236) of samples, identifying multiple bacterial species in 30.51% (72/236) and a single bacterial species in 30.08% (71/236). Viruses were exclusively detected in 25% (59/236) of samples, while both bacteria and viruses were co-detected in 72.03% (170/236).

By contrast, culture identified a single bacterium in 30.08% (71/236) and multiple bacteria in 10.17% (24/236) of samples. BFPP detected atypical bacteria in 2.12% (5/236), whereas

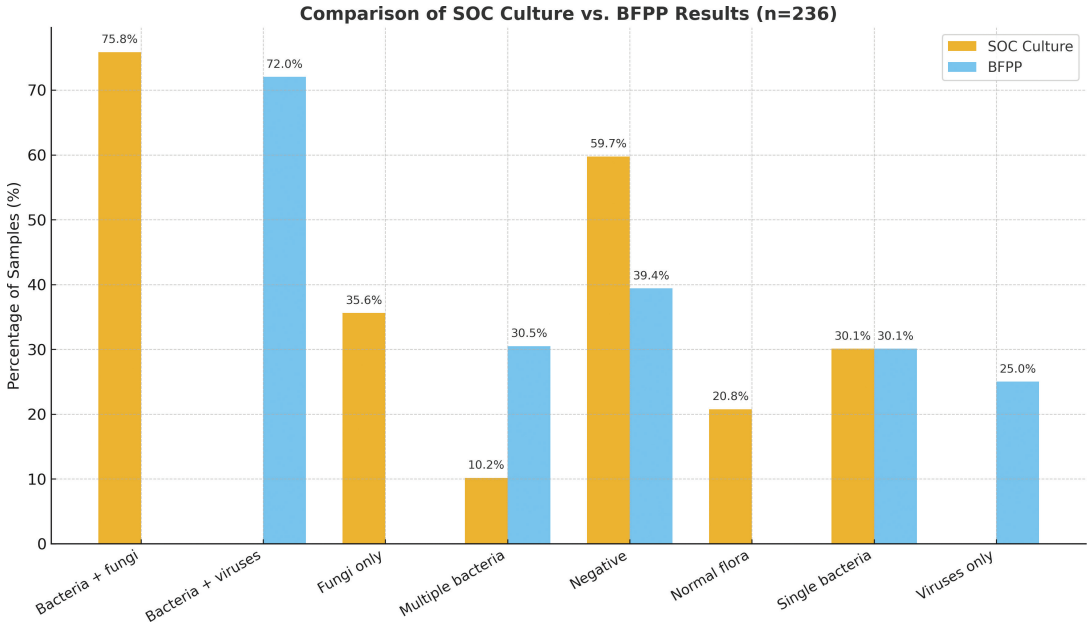


**Figure 1.** Overview of BFPP results in comparison to the standard culture method. BFPP, BioFire® FilmArray® pneumonia panel; SOC, standard of care.

SOC culture identified fungal species alone in 35.59% (84/236) and co-occurring bacteria and fungi in 75.85% (179/236). Normal flora was reported in 20.76% (49/236) of SOC samples. Negative results were observed in 39.41% (93/236) of BFPP tests and 59.75% (141/236) of SOC cultures. The distribution of single and co-detections of respiratory pathogens identified by both methods is illustrated in Figure 1.

Notably, several bacterial pathogens were detected exclusively by BFPP, that is, not identified by culture such as *Streptococcus agalactiae*, *Streptococcus pyogenes*, *Moraxella catarrhalis*, *Serratia marcescens* and *Klebsiella aerogenes*. In addition, certain clinically significant pathogens were detected only once by SOC supreme detection culture (true positives), but were detected more frequently by BFPP (suggesting potential false positives), including *Streptococcus pneumoniae, Proteus* spp., *Haemophilus influenzae, Klebsiella oxytoca* and *Enterobacter cloacae complex* (Table 3, Figure 2).

The most frequently detected bacteria (organism/236 samples) by BFPP and SOC methods, respectively, were *Klebsiella pneumoniae* group (61 vs 49), *Pseudomonas aeruginosa* (49 vs 25), *Escherichia coli* (43 vs 25), *Staphylococcus aureus* (32 vs 10) and *Acinetobacter baumannii complex* (27 vs 9) (Figure 2). The most frequently identified viruses by BFPP included *human rhinovirus/enterovirus* (9.32%), followed by *Influenza A virus* (5.93%), *human metapneumovirus* (2.97%) and *Influenza B virus* (2.54%) (Figure 3).

***Performance of BFPP in comparison to the culture method***

Compared with traditional culture methods, the BFPP demonstrated an overall sensitivity of 81.97% (95% CI: 73.98–88.34). The overall specificity was 94.44% (95% CI: 93.59–95.21), and the OPA was 93.98% (95% CI: 93.11–94.77). The (PPA, equivalent to sensitivity) for individual bacterial targets ranged from 73.5% to 100%, while the (NPA, equivalent to specificity) ranged from 86.6% to 99.6%. The OPA for these targets ranged from 83.9% to 99.6%. The performance characteristics of BFPP and standard culture methods in detecting respiratory pathogens are summarised in Table 3.

***Antimicrobial resistance genes***

A total of 214 antimicrobial resistance (*AMR*) genes were detected using the BFPP. The most frequently identified were genes associated with carbapenemase-producing bacilli, including 60 NDM, 42 OXA-48, 9 VIM, 2 KPC and 2 IMP genes ($n$ = 115). These were followed by extended-spectrum β-lactamase (ESBL) genes, predominantly Cefotaximase-M-type β-lactamase (CTX-M) ($n$ = 75), and methicillin-resistant *Staphylococcus aureus* (MRSA)-associated genes, specifically mecA/Cassette (or right-extremity) (C-MREJ) ($n$ = 24) (Table 4).

Comparing between the resistance gene profiles detected by BFPP and the phenotypic resistance profiles determined by VITEK® 2 for common pathogens revealed: in 87.75%

**Table 3.** Qualitative detection of bacterial targets between the BioFire PN Panel and SOC culture

| | Specimens (no of BFPP detections/no of standard culture detections) | | | | | | |
|---|---|---|---|---|---|---|---|
| | (+/+) True Positive | (±) False Positive | (−/+) False Negative | (−/−) True Negative | PPA%. [95% CI] | NPA%. [95% CI] | OPA%. [95% CI] |
| *Strept_agalactiae* | 0 | 13 | 0 | 223 | NA | 94.49 [90.76–97.03] | 94.51 [90.76–97.03] |
| *Strept Pneumoniae* | 1 | 7 | 0 | 228 | 99.58 [97.64–99.98] | 97.02 [93.96–98.79] | 97.03 [93.98–98.80] |
| *Strept_Pyogenes* | 0 | 1 | 0 | 235 | NA | 99.58 [97.66–99.99] | 99.58 [97.67–99.99] |
| *Moraxella_catarrhalis* | 0 | 2 | 0 | 234 | NA | 99.15 [96.97–99.90] | 97.05 [94.01–98.80] |
| *Proteus* | 1 | 6 | 0 | 229 | 99.58 [97.64–99.98] | 97.41 [94.46–99.05] | 97.5 [94.48–99.1] |
| *Pseudomonas aeruginosa* | 21 | 28 | 4 | 183 | 89.41 [84.83–92.72] | 86.7 [73.61–83.92] | 86.44 [81.40–90.54] |
| *Serratia_marcescens* | 0 | 7 | 0 | 229 | 100 [98.40–100.0] | 97.03 [93.98–98.80] | 97.05 [94.01–98.80] |
| *Staph_aureus* | 10 | 22 | 0 | 204 | 95.76 [92.38–97.68] | 90.3 [85.63–93.80] | 90.68 [86.23–94.07] |
| *E._Coli* | 22 | 21 | 3 | 190 | 88 [84.83–92.72] | 90.05 [85.19–93.73] | 89.83 [85.25–93.37] |
| *H_influenzae* | 1 | 6 | 0 | 229 | 99.58 [97.64–99.98] | 97.45 [94.53–99.06] | 97.46 [94.55–99.06] |
| *Klebsiella_aerogenes* | 0 | 5 | 0 | 231 | 100 [98.40–100.0] | 97.88 [95.13–99.31] | 97.89 [95.15–99.31] |
| *Klebsiella_oxytoca* | 1 | 4 | 0 | 231 | 99.58 [97.64–99.98] | 98.30 [95.70–99.53] | 98.31 [95.72–99.54] |
| *Klebsiella_pneumoniae* | 36 | 25 | 13 | 162 | 73.47 [58.92–85.05] | 86.63 [80.90–91.16] | 83.90 [78.58–88.35] |
| *Acinetobacter calcoaceticus baumannii_complec* | 7 | 20 | 2 | 207 | 96.19 [92.91–97.98] | 91.2 [83.87–92.02] | 90.68 [86.23–94.07] |
| *Enterobacter cloacae complex* | 1 | 16 | 0 | 219 | 99.58 [97.64–99.98] | 93.19 [89.18–96.06] | 93.22 [89.22–96.08] |
| *Total bacterial pathogens* | 100 | 177 | 22 | 3,006 | 81.97 [73.98–88.34] | 94.44 [93.59–95.21] | 93.98 [93.11–94.77] |

BFPP, BioFire® FilmArray® pneumonia panel; CI, confidence interval; NA, not applicable; NPA, negative percent agreement; OPA, overall percent agreement; PN, Pneumonia; PPA, positive percent agreement; SOC, standard of care.

of *P. aeruginosa* isolates, the carbapenemase genes detected by BFPP (NDM, OXA-48, etc.) were concordant with phenotypic carbapenem resistance. Similarly, all mecA/MREJ-positive *S. aureus* isolates were confirmed as *MRSA* by culture-based methods.

Regarding the timing outcome of antibiotic changes, patients with BFPP-guided therapy had modifications (escalation or de-escalation) on average 45.2 hr earlier than those whose antibiotics were adjusted based only on standard culture and susceptibility testing.

### *Antimicrobial utilisation before hospital admission*

A total of 77.96% (184/236) of participants used antibiotics before symptom deterioration and hospital presentation; 48.37% of them used azithromycin (89/184) and 32.61% used

**Table 4.** Frequency and percentage of resistance genes

| | | Frequency | Percent (%) |
|---|---|---|---|
| Carbapenemase producing Gram negative bacilli | VIM | 9 | 3.81 |
| | IMP | 2 | 0.85 |
| | KPC | 2 | 0.85 |
| | NDM | 60 | 25.42 |
| | OXA-48 like | 42 | 17.8 |
| | Total carbapenamase producers | 115 | 48.73 |
| ESBL producing bacteria | CTX_M | 75 | 31.78 |
| Methicillin resistant *Staphylococcus aureus* | mecA_C_and_MREJ | 24 | 10.17 |
| | Total | 214 | 90.68 |

ESBL, extended-spectrum beta lactamase.

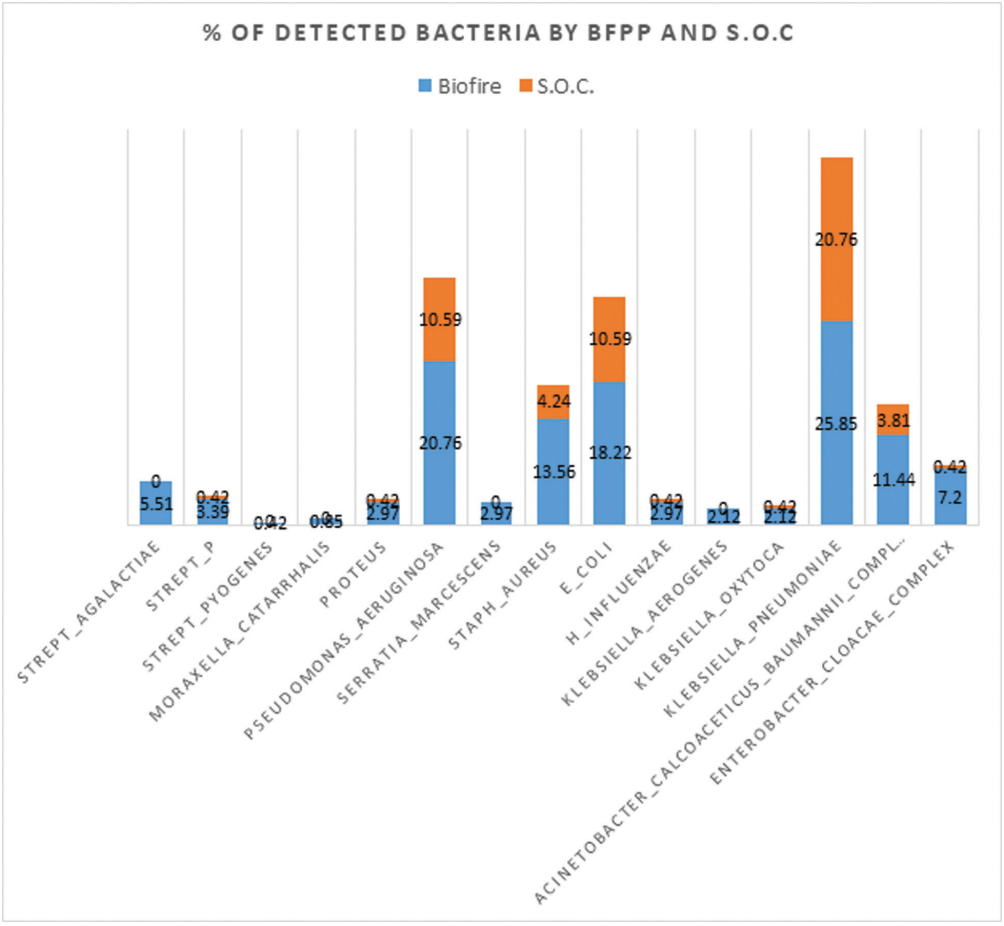


**Figure 2.** Percentages of detected bacteria by BFPP and SOC. BFPP, BioFire® FilmArray® pneumonia panel; SOC, standard of care.

amoxicillin/clavulanic acid (60/184), while 19.02% (35/184) were using levofloxacin. Duration of use ranged from 3 days to 10 days, at an average of 6.5 days.

***Comorbidities and association with infecting organisms***

Comorbid diseases associated with participating pneumonia subjects as diabetes mellitus (DM) (53.81%), chronic respiratory diseases (15.68%) and chronic kidney disease (CKD) (15.25%) are known to be risk factors for pneumonia with Gram-negative bacteria, especially *P. aeruginosa, K. pneumoniae*, *E. coli, A. baumannii* and *Gram-positive cocci*, especially *S. aureus.*

DM represents 53.81% of the total study subjects, while patients with DM constitute 22% of patients having *K. pneumoniae* in their BFPP results, 18.9% of *Pseudomonas aeronginosa*, 11.8% of *E. coli*, 13.4% of *A. baumannii* and 11% of *S. aureus*. Patients with DM also constitute 2.4% of VIM, 1.6% of IMP, 7.1% of mecA_C_and_MREJ, 22.8% of NDM, 14.2% of OXA_48_like and 27.6% of CTX_M resistance genes detected in BFPP test results.

Patients with chronic respiratory disease (15.68% of all participants) form 21.6% of patients having *K. pneumoniae* in their BFPP results, 35.1% of *P. aeronginosa,* 10.8% of *E. coli*, 5.4% of *A. baumannii* and 21.6% of *S. aureus*. Chronic respiratory disease constitutes also 8.1% of VIM, 2.7% of KPC, 10.8% of mecA_C_and_MREJ, 24.3% of NDM, 13.5% of OXA_48_like and 27.0% of CTX_M resistance genes.

Patients with CKD (15.25% of all pneumonia subjects) comprise 30.6% of patients having *K. pneumoniae* in their BFPP results, 13.9% of *P. aeronginosa*, 30.6% of *E. coli,* 16.7% of *A. baumannii* and 5.6% of *S. aureus*. CKD constitutes also 2.8% of VIM, 2.8% of mecA_C_and_MREJ, 33.3% of NDM, 22.2% of OXA_48_like and 27.8% of CTX_M resistance genes.

The association of different comorbid diseases with the BFPP-resulting bacteria and resistant genes is presented in Tables 5 and 6.

***Impact of BFPP on antimicrobial stewardship***

The average time from ICU admission to Bronchoalveolar lavage (BAL) collection, which was 6.2 ± 3.4 hr, and the

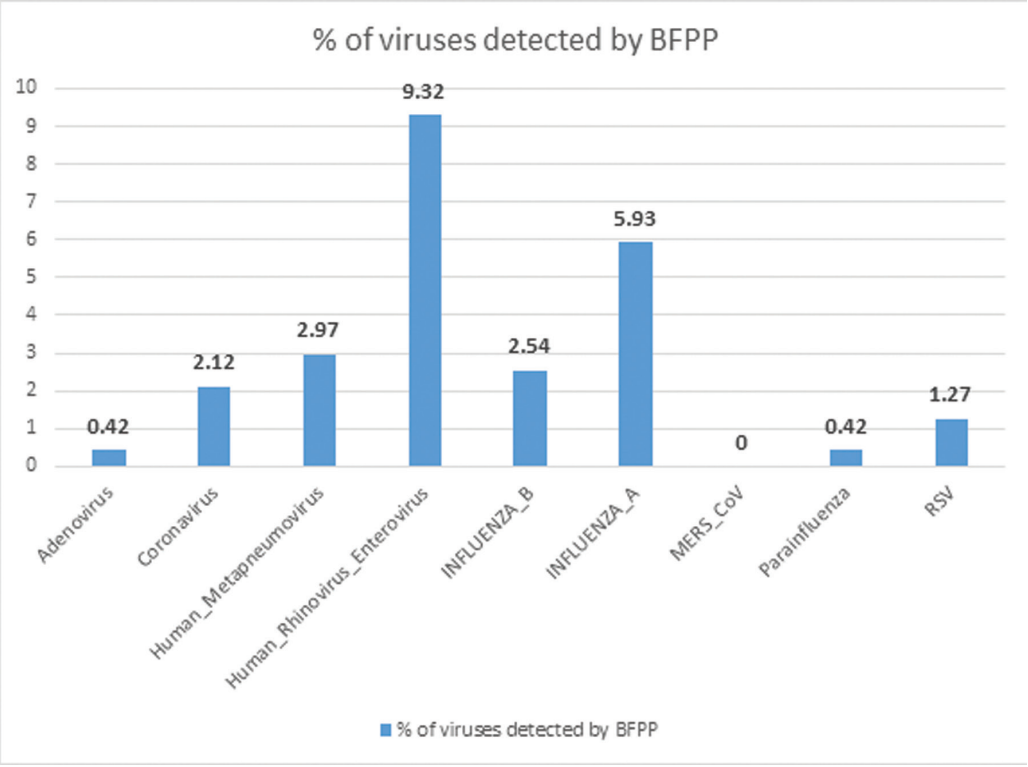


**Figure 3.** Percentages of viruses detected by BFPP. BFPP, BioFire® FilmArray® pneumonia panel.

average time to availability of BFPP results was 2.1 ± 0.5 hr after BAL collection. These timelines allowed early identification of pathogens and resistance genes, contributing to antibiotic modification decisions.

*S. aureus* was detected in 32 specimens by BFPP, of which 10 (31.25%) were positive for *S. aureus* in the corresponding SOC cultures. The mecA_C_and_MREJ resistance gene was detected in 24 BFPP samples with *S. aureus* results indicating *MRSA*. These samples proved *MRSA* in SOC cultures, which agrees with the BFPP results.

*P. aeruginosa* was detected in 49 (20.76%) specimens by BFPP, of which 25 (10.59%) were positive for *P. aeruginosa* in the corresponding SOC cultures. The carbapenemase resistance gene was detected in 43 (87.75%) BFPP samples with *P. aeruginosa* results. These samples proved to be resistant to carbapenems in SOC cultures, which agrees with the BFPP results.

Finally, viruses were detected exclusively in 59/236 patients (25%) and in combination with bacteria in 170/236 (72.03%) of BFPP results, among which BFPP detected influenza A virus in 14 samples (5.93%) and influenza B virus in 6 samples (2.54%), while no specific physician order for an influenza virus test had been made. This allowed rapid initiation of antiviral therapy such as oseltamivir, as well as implementing specific infection control measures such as droplet isolation.

In the patients whose antibiotics were guided by BFPP results, the mean time to escalation or de-escalation was 9.4 ± 2.7 hr from ICU admission, compared with 54.6 ± 12.1 hr in the group that depended only on culture.

Normal flora (e.g., Candida spp., Coagulase-negative Staphylococci, Viridans group Streptococci), which are not targeted by the BFPP panel, was reported in 20.76% (49/236) of SOC samples.

## Discussion

Given the variation in respiratory pathogens linked to the aetiology of sCAP, the development of quick and accurate molecular diagnostics to identify the causative organisms and enhance treatment outcomes has become necessary. This study aimed to evaluate the efficacy and utility of BFPP compared with conventional culture techniques in identifying respiratory pathogens, sCAP-causing bacteria and the associated antibiotic-resistance genes.

**Table 5**. Comorbid disease association with infecting organisms

| | DM | Chronic respiratory disease | CKD | HTN | IHD | Other diseases |
|---|---|---|---|---|---|---|
| *Klebsiella pneumoniae* | 22 | 21.6 | 30.6 | 10.2 | 28.2 | 25.5 |
| *Pseudomonas aeronginosa* | 18.9 | 35.1 | 13.9 | 11.4 | 20 | 29.1 |
| *E. coli* | 11.8 | 10.8 | 30.6 | 5.1 | 20 | 14.5 |
| *Acinetobacter baumannii* | 13.4 | 5.4 | 16.7 | 8.9 | 20 | 16.4 |
| *Enterobacter_cloacae*_complex | 4.7 | 10.8 | 11.1 | 3 | 7.1 | 9.1 |
| *Staphylococcus aureus* | 11 | 21 | 5.6 | 5.1 | 15.3 | 18.2 |
| BF_Strept_agalactiae | 7.1 | 8.1 | 8.3 | 2.1 | 4.7 | 5.5 |
| BF_Strept_P | 3.9 | 2.7 | 5.6 | 1.7 | 3.5 | 1.8 |
| BF_Strept_Pyogenes | 0 | 0 | 0 | 0 | 0 | 0 |
| BF_*Moraxella_catarrhalis* | 0.8 | 0 | 2.8 | 0.8 | 2.4 | 1.8 |
| BF_Proteus | 2.4 | 5.4 | 8.3 | 0.8 | 5.9 | 1.8 |
| BF_*Serratia_marcescens* | 3.9 | 5.4 | 0 | 1.7 | 4.7 | 1.8 |
| BF_H_influenzae | 4.7 | 2.7 | 2.8 | 2.1 | 2.4 | 1.8 |
| BF_*Klebsiella_aerogenes* | 0.8 | 8.1 | 11.1 | 0.4 | 2.4 | 3.6 |
| BF_*Klebsiella_oxytoca* | 2.4 | 5.4 | 2.8 | 0.4 | 3.5 | 1.8 |

BF, Bronchial fluid; CKD, chronic kidney disease; DM, diabetes mellitus; HTN, hypertension; IHD, ischaemic heart disease.

**Table 6.** Comorbid disease association with resistance genes

| | DM | HTN | IHD | Chronic respiratory disease | CKD | Others |
|---|---|---|---|---|---|---|
| VIM | 2.4 | 2.5 | 2.4 | 8.1 | 2.8 | 1.8 |
| IMP | 1.6 | 0.4 | 1.2 | 0 | 0 | 1.8 |
| KPC | 0 | 0 | 0 | 2.7 | 0 | 0 |
| mecA_C_and_MREJ | 7.1 | 3.8 | 10.6 | 10.8 | 2.8 | 10.9 |
| NDM | 22.8 | 14 | 34.1 | 24.3 | 33.3 | 30.9 |
| OXA_48_like | 14.2 | 6.8 | 22.4 | 13.5 | 22.2 | 20 |
| CTX_M | 27.6 | 13.6 | 34.1 | 27 | 27.8 | 34.5 |

CKD, chronic kidney disease; DM, diabetes mellitus; HTN, hypertension; IHD, ischaemic heart disease.

Samples of distal airway secretions were collected from 236 patients with sCAP admitted to the ICU of a large academic medical centre. Microbiological evaluation using BFPP demonstrated a significant advantage in the prompt detection of bacterial pneumonia, identifying pathogens in 60.59% of samples compared with 40.25% detected by SOC culture tests. Additionally, BFPP showed superiority in detecting polymicrobial infections (30.51% vs 10.17%) and in the identification of atypical bacteria (2.12%), which were not detected by conventional culture methods. This approach enables rapid identification of sCAP pathogens and their most relevant *AMR* genes within 2 hr in the hospital setting (11).

Interpretation of our diagnostic tests can be challenging because many of the bacteria that cause pneumonia are also common colonisers of the respiratory tract. In cases where BFPP detected organisms were not found by culture, we considered clinical correlation, radiological findings and laboratory elevated inflammatory markers (e.g. procalcitonin levels, CRP, leukocytosis) to determine the likelihood of infection versus colonisation. Specifically, polymicrobial detections with associated clinical signs of pneumonia were considered true infections, especially when supported by resistance gene detection and response to directed therapy.

Given that MRSA is one of the suspected pathogens causing sCAP (10), our results identified *S. aureus* in 32 specimens using the PN panel, of which only 10 (31.25%) were positive by SOC cultures. Furthermore, 24 samples revealed the presence of the mecA_C and mec right-extremity junction (MREJ) resistance genes, indicating MRSA), thus suggesting the need to initiate treatment with vancomycin or linezolid.

Another common organism associated with sCAP is *P. aeruginosa* (10), which was detected in 49 (20.76%) specimens via the PN panel, whereas only 25 (10.59%) were positive in the corresponding SOC cultures. BFPP detected

carbapenemase resistance genes in 43 (87.75%) of samples. These findings guided the implementation of a management plan involving antipseudomonal antibiotics other than carbapenems.

The advantage of early initiation of an optimal antibiotic management plan using a rapid molecular diagnostic tool cannot be overstated. It allows clinicians to promptly target the causative organism rather than waiting 2–3 days for culture results, which miss 50%–60% of cases with negative outcomes from SOC.

In the past decade, the prevalence of respiratory viruses in sCAP has increased (16–18). A European systematic review and meta-analysis reported a 20%–25% prevalence of respiratory viruses in CAP cases (19, 20), comparable to studies from the US (16) and Asia (18). In another success for BFPP, the tool detected viral pathogens alone in 25% of samples and co-detected bacteria and viruses in 72.03% of sample detection capabilities unavailable with traditional culture methods.

According to our data, rhinovirus and influenza viruses were the most commonly detected viruses (9.32% and 9.57%, respectively), aligning with previous studies (9, 21). Most international guidelines recommend antiviral treatment for viral sCAP, with studies showing reduced mortality in patients treated with oseltamivir or zanamivir compared with untreated patients (22, 23).

By contrast, SOC cultures uniquely detected single fungal species in 35.59% of samples and co-occurring bacteria and fungi in 75.85%. Additionally, SOC detected normal flora in 20.76% (49/236) of samples, whereas BFPP did not. Therefore, BFPP is not independently recommended in cases with suspected fungal pneumonia, such as those involving immunocompromised patients and should always be complemented with fungal culture in such clinical scenarios.

In a comparable outcome, both BFPP and SOC methods equally detected single bacterial infections in 30.08% of samples. Overall, BFPP and SOC agreed on the bacterial species in 100 out of 236 cases (42.4%), consistent with findings from other studies (4, 13).

However, BFPP identified organisms in 177 of 236 samples, compared with 95 identified by traditional cultures. Therefore, initiating antibiotic therapy based on BFPP results eliminates causative organisms more effectively and increases favourable outcomes through precision medicine. Overuse of antibiotics can lead to drug toxicity and the emergence of antibiotic-resistant bacteria such as *C. difficile* and superinfection pneumonia. These issues also have societal implications, including higher healthcare costs (6, 7).

Notably, BFPP identified bacteria undetected by SOC, such as *S. agalactiae, S. pneumoniae, S. pyogenes, M. catarrhalis, K. aerogenes and S. marcescens.* In such cases, relying solely on SOC for antibiotic escalation or de-escalation may compromise outcomes in critically ill patients with sCAP.

Compared with standard culture methods, BFPP demonstrated an overall sensitivity of 81.97% and a specificity of 94.44%, closely aligning with previous findings (4, 13), and had a measurable impact on the clinical outcomes of patients with sCAP. Negative results were reported in 93 (39.41%) BFPP samples, compared with 141 (59.75%) SOC samples highlighting a 20.34% difference, enabling timely initiation of appropriate antibiotic therapy.

The most frequently detected bacteria by BFPP were *K. pneumoniae* group, *P. aeruginosa, E. coli, S. aureus* and *A. baumannii complex*, all of which are theoretically targeted by recommended initial treatment strategies for sCAP (10).

BFPP also enabled early identification of resistance genes, facilitating personalised antibiotic selection. It helped avoid unnecessary empirical coverage for *MRSA* or *P. aeruginosa* in patients without risk factors. BFPP identified 214 resistance-associated genes, including 115 for bacilli-producing carbapenems, 75 for ESBL (CTX-M) and 24 for MRSA.

According to the WHO, a third of respondents in various countries used antibiotics without prescriptions, and over 40% did so without medical advice (13). This trend was reflected in this study: 77.96% (184/236) of patients had already started antibiotics before hospital presentation, highlighting the need for rapid diagnostics like BFPP to determine individualised treatment plans within 2 hr.

A very high proportion of patients had received antibiotics before admission (77.96%). This most probably suppressed the yield of conventional cultures and thereby introduced bias in comparative performance towards the molecular BFPP assay which does not have sensitivity to prior antibiotic exposure. Such a high rate of pre-admission antibiotic use is also indicative of a real-world clinical scenario in which rapid diagnostics would be most valuable since they can provide results that are actionable even when cultures might be negative. Niederman and Torres (24) described sCAP as the most lethal form of CAP, with mortality reaching 40%. A Spanish study also reported 38% in-hospital mortality among a large sCAP cohort (25).

In this study, using BFPP as part of the management strategy is associated with reduced mortality to 25.4% (60/236), likely due to the tool's ability to identify pathogens and resistance genes within 2 hr. This observed improvement in outcomes is likely multifactorial, but the ability of BFPP to rapidly identify pathogens and resistance genes is a potential contributing factor. So, we emphasise the observational nature of this finding.

Among the 66 patients with sCAP with negative BFPP results who were treated empirically according to guidelines (10), 46 (69.69%) were discharged after improvement and 20 (30.30%)

died in-hospital. By contrast, of the 170 patients who received antibiotics based on BFPP results, 130 (76.47%) improved and were discharged, while 40 (23.53%) died.

In terms of hospital stay duration, patients whose antibiotic therapy was guided by BFPP had an average hospital stay of 22.61 ± 28.14 days. By contrast, those who received empirical antibiotics due to negative BFPP results had an average stay of 24.84 ± 37.98 days.

This study was conducted without a formal cost-effectiveness analysis, but reduced time to appropriate therapy, hospital LOS and mortality observed during this study does throw light on the fact that the total cost savings can be achieved in spite of the BFPP panel being more expensive. A future health-economic study is warranted to formally evaluate the cost–benefit ratio of implementing BFPP in our setting.

## Limitations

The limitations of this study include: (1) single-country setting, which may reduce generalisability; (2) absence of quantitative culture or semi-quantitative BFPP data; due to unavailability; (3) BFPP does not detect fungal pathogens, which reduces its utility in suspected fungal pneumonia; (4) no additional viral testing beyond BFPP was available due to resource limitations; (5) 78% prior antibiotic use may have reduced SOC culture sensitivity and (6) no cost-effectiveness analysis was performed.

## Conclusion

BFPP is a rapid and effective tool for the early detection of respiratory pathogens in patients with sCAP. Its implementation may facilitate earlier, more personalised and more effective antimicrobial management compared with standard empirical strategies. Further larger multicentre trials and formal cost-effectiveness studies are needed to confirm these findings and to solidify its role in routine clinical practice.

## Consent to Participate

Informed consent was obtained from all individual participants included in the study.

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The authors have no relevant financial or non-financial interests to disclose.

## Authors' Contributions

- Samir Mohamed Mahmoud Fahyim: Shared in collection of the data and practical work, shared in the revision of the article.
- Hesham Atef AbdelHalim: Study conception, literature search, study design, collection and analysis of the data, practical work, shared in writing, shared in the revision of the article.
- Heba Helmy AboElNaga Study conception, literature search, study design, writing, shared in the revision of the article.
- Rania Talaat Abdel Haleem: Shared in the revision of the article.
- El Shaimaa Sabry Mohammed Hassan: Shared in the revision of the article.

All authors read and approved the final manuscript.

## Ethics Approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of the Faculty of Medicine- Port Said University (MED (4/2/2024) s.no. (141) CHS_002).

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