

RESEARCH ARTICLE

Broad Panel Respiratory Multiplex PCR (Pneumonia Panel) in improving overall survival, length of hospital stay, and antibiotic free days among patients with community acquired pneumonia - A randomized controlled trial

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ABSTRACT

Background: Broad Panel Respiratory Multiplex PCR (Pneumonia Panel) tests a panel of bacteria and viruses associated with community acquired pneumonia (CAP) which help streamline antimicrobial therapy. Recently, pneumonia panel aids clinicians in early streamlining of antimicrobials as opposed to waiting for bacterial culture results [2].

Objective: To determine whether the use of pneumonia panel improves the overall survival rate, length of hospital stay, and number of antibiotic free days among hospitalized CAP patients.

Methodology: In this RCT, adult patients admitted for CAP were randomized to perform pneumonia panel and sputum culture (pneumonia panel group) versus sputum culture only (control group). The results were relayed to the medical team and were incorporated into the medical records. Length of hospital stay, antibiotic free days in day 28, and mortality rates were the primary outcomes measured.

Results: Eighty participants completed the study. There was no significant difference in the length of hospital stay (p-value 0.073, 95% C.I.), duration of antibiotic therapy (p-value 0.332, 95% C.I.), and mortality rates (p-value 0.570, 95% C.I.) between the 2 groups.

Conclusion: Routine use of pneumonia panel does not significantly reduce length of hospital stay, duration of antibiotic therapy, and mortality rates among admitted patients with moderate to severe CAP. The benefit of pneumonia panel was seen on early detection of drug resistant pathogen resulting in early antibiotic escalation and shorter duration of antibiotic therapy. Further studies are necessary to show its benefit in the high risk population.

Introduction

Community acquired pneumonia (CAP) is one of the leading causes of morbidity and mortality among Filipinos. Based on the 2016 Clinical Practice Guidelines on the Diagnosis, Empiric Management and Prevention of Community Acquired Pneumonia in Immunocompetent Adults, patients are stratified according to their risk of disease progression. A patient's vital signs and stability of co-morbidities are considered for moderate risk pneumonia. High risk community acquired pneumonia is defined as having the clinical features of moderate risk community acquired pneumonia plus severe sepsis/septic shock or the need for mechanical ventilator. The recommended empiric broad spectrum antibiotics, are either with Beta lactam antibiotic plus a macrolide, or respiratory quinolone. Microbiologic studies of respiratory specimen (sputum, endotracheal aspirate, tracheal aspirate, bronchoalveolar lavage, etc.) for gram stain and culture and sensitivity tests are recommended for moderate to high risk CAP. Streamlining of antibiotic therapy based on microbiologic tests is recommended, given the patient has resolution of fever for more than 24 hours, less cough and resolution of respiratory distress, improving white cell count, no bacteremia, no unstable comorbidities, and no signs of organ dysfunction [1].

There is current concern of emergence and spread of bacterial resistance. Reducing the selection pressure in patients with CAP is currently a public health concern. Reducing exposure to antibiotics may be one of the objectives this study aims to tackle. The use of molecular tests may improve etiologic diagnosis and streamline antimicrobial therapy. Recently, broad-panel respiratory mPCRs have been developed which tests a large panel of bacteria and viruses associated with CAP. This can therefore aid in helping clinicians decide the initial antimicrobial as opposed to waiting for bacterial cultures which may take 2-3 days to yield results [2].

Several studies have already been done to investigate the diagnostic accuracy of the PCR based test. A study performed by Sze Hwei Lee, *et al.*, included 59 endotracheal aspirates from intubated patients using culture and sensitivity as the gold standard. There were a total of 37 concordant specimen and 10 discordant results yielding an overall agreement of 79%. The results of this test led to the de-escalation of empirical antibiotic in

16% of patients, escalation or addition of another effective antibiotic in 13%, and no change in 56% of patients [3]. In another study by Kosai, *et al.*, the researchers found that when comparing conventional culture method with the Biofire FilmArray Pneumonia panel, the latter was able to detect 84 more pathogens as compared to the 25 bacteria detected by conventional culture media out of the 57 samples included in the study. Pneumonia panel was able to detect multiple pathogens 42% of the time. This research demonstrated that the enhanced the detection rate of pathogens and antimicrobial resistance markers in lower respiratory tract specimen as compared to conventional culture methods [4].

In line with the recent COVID-19 pandemic, a randomized controlled trial was performed utilizing the use of the broad-panel respiratory mPCR test. This study included critically-ill adult patients admitted to the ICU with a confirmed SARS-Cov2 pneumonia. Patients were randomized to an intervention group where broad panel respiratory PCR was performed, as opposed to the usual standard of care at the time. This study showed that there is no significant difference between the 2 groups on the median antibiotic free days at Day 28 and cumulative antibiotic duration [5]. This was an expected result, as later on, antimicrobial use was found to not be a key component in the treatment of COVID-19 infections.

The MULTI-CAP trial is an ongoing randomized controlled trial where pneumonia patients admitted to the ICU were randomized to perform respiratory broad-panel mPCR in addition to the conventional microbiologic intervention (interventional group) or the control group where treatment is based on the standard of care for community acquired pneumonia. An

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algorithm of early antibiotic de-escalation or discontinuation is applied on the interventional arm. This include the early discontinuation of antibiotic therapy if the mPCR and conventional microbiological investigations are negative for bacteria and with a procalcitonin of less than 1. The primary outcomes to be determined in this study include the number of antibiotic free days at Day 28. The patients are to be followed up for 90 days. At the time of writing this paper, the study has yet to release preliminary data, but the researchers hypothesized that patients in the intervention group will show a significantly greater antibiotic free days as compared to the control group [2].

This study aimed to determine whether the use of pneumonia panel improves the overall survival rate, length of hospital stay, and number of antibiotic free days among hospitalized CAP patients. Specifically, the researchers aimed to determine whether there is a significant difference in antibiotic free days on Day 28, length of hospital stay in days, and overall survival rate among hospitalized patients with CAP between patient who performed pneumonia panel as compared to the standard of care treatment.

Previous studies have already determined the diagnostic accuracy of pneumonia panel as compared to sputum culture and sensitivity as a gold standard. However, there is currently no evidence to support the clinical impact of the earlier microbiologic diagnosis among patients with CAP in the local setting. At the time of writing, the cost of pneumonia panel is around 24,089.00 pesos; while a full-day course of intravenous broad spectrum antibiotics based on the latest local guidelines costs ranging from 2,727.43 to 6,192.00 pesos and up to 13,062 pesos per day if the patient has risk factors for *Pseudomonas aeruginosa*. Patients may also entail an additional 8,942.00 to 19,828.00 pesos per day if they have risk factors for methicillin-resistant *Staphylococcus aureus* (MRSA).

The added information of the diagnostic test was hypothesized to enable clinicians to use antibiotics more effectively, leading to a more streamlined use of the correct antimicrobial at an earlier stage of the admission thus decreasing the overall duration of treatment, length of hospital stay, and improving survival rates which would ultimately justify the cost of the test. Current guidelines for the management of CAP suggests the use broad spectrum antibiotics and waiting for sputum cultures before streamlining antibiotic therapy. The incorporation of pneumonia panel in the management of CAP will have a direct benefit to the patient in terms of antibiotic stewardship and morbidity/mortality such as ICU-acquired infections, thus, encouraging the use of this test through the medical community. Furthermore, the data gathered by this research can be used as a reference for future studies in this field.

Methodology

2.1 Study Participants

This is a single-center randomized controlled trial which included all adult patients aged 18 years old and above, hospitalized, and diagnosed with community acquired pneumonia within 48 hours of admission. Participants were able to submit sputum or endotracheal aspirate for both pneumonia panel and culture and sensitivity (pneumonia panel group) or sputum culture and sensitivity alone (control group). Patients with respiratory failure due to conditions other than community acquired pneumonia such as acute coronary syndrome, decompensated heart failure, renal failure, cerebrovascular infarcts or hemorrhages, severe sepsis due to infections other than pneumonia, and patients who underwent advanced cardiac life support were excluded from the study. Patients who developed respiratory failure requiring ventilatory support, due to community acquired pneumonia were still included in the study. All eligible patients within the study period of October 2023 to March 2024 were included in the study.

2.2 Ethical Consideration

This research study was reviewed and approved by the Cardinal Santos Medical Center Research Ethics Review Committee. The researcher/s observed strict adherence to ethical principles stated in the Philippine National Ethical Guidelines for Research Involving Human Participants of 2022 and will abide by the Data Privacy Act of 2012.

The participants' identifying information such as name, birth date, contact number, and address were not gathered. Participants were anonymized, and a unique identification number was generated. The researchers did not

interfere with the attending physician's management. The researchers were available for queries and were made responsible for the participants' completion or withdrawal from the study. The researcher and co-author/s do not have any conflict of interest arising from financial, familial, or proprietary considerations. The data collection form were kept in a password-protected computer and will be deleted (manner of destruction) after five (5) years.

All information gathered were only accessible to the principal investigator, co-authors, the statistician. Expenses for the Broad Panel Multiplex PCR (Pneumonia panel) were covered by Pfizer, a pharmaceutical company, after acquisition of a research grant. Therefore, there were no additional costs for the participants enrolled in the study.

2.3 Data Collection

The approval to perform the research and to collect data were acquired from the institution, institutional review board, and the ethics committee. A research grant was acquired from Pfizer which covered for the expenses of the study. Recruitment was done through referrals of attending physicians. All hospitalized patients meeting the inclusion criteria were recruited in the study. Eligible patients (or their next of kin depending of the patient's situation) were informed about the trial. The risks and benefits of the participating in the study were explained by the researchers in a private setting within the hospital premise. Permission to enroll eligible patients was obtained from the attending physician. Written informed consent were then secured.

Data collection were done through chart review, interview of a reliable source, and verified by reviewing existing medical records. Baseline information which were collected include: basic demographics, possible confounding factors such as the patient's co-morbidities, history of aspiration, recurrent pneumonia, smoking history, COPD, history of tracheostomy, history of bronchiectasis, episodes of aspirations, prior hospitalizations, and prior antibiotic history within 90 days. Imaging results of chest radiograph and Chest CT scans (if available) were gathered. Other pertinent ancillary tests that were gathered include sputum or ETA gram stains, culture and sensitivities, complete blood count, and procalcitonin.

Eligible participants were randomized by the researchers using a Web-based system and assigned either to control or to pneumonia panel group in 1:1 ratio. Randomization was performed within 24 hours following enrollment into the study. Participants included in the study were assigned either to the perform Broad Panel Respiratory Multiplex PCR (Pneumonia panel group) or standard of care (control group). Blinding was not done. The researchers, attending physicians, and participants were given access to the results of the diagnostic tests.

The standard of care group (control group) was based on the local guidelines for the standard of care of community-acquired pneumonia. Chest X-ray must have been done upon inclusion while chest CT scan maybe done under the discretion of the attending physician. Conventional microbiological investigations, such as sputum or endotracheal aspirate gram stain and culture with sensitivity test must have been performed upon inclusion in the study. All other ancillary procedures performed, empiric antibiotic therapy started, and mechanical ventilator strategies were under the discretion of the attending physician.

For the pneumonia panel group, in addition to the conventional microbiological and imaging studies, patients in this group had sputum specimen submitted for Broad Panel Respiratory Multiplex PCR (pneumonia panel) within 48 hours of admission. Sputum sample were collected by voluntary expectoration with or without sputum induction using 10ml 3% NaCl via ultrasonic nebulization, nasopharyngeal or oropharyngeal aspiration, or endotracheal/tracheal aspiration, if applicable. The results of the diagnostic test were relayed to the attending physician and incorporated into the medical record. All other ancillary procedures performed, empiric antibiotic therapy started, and mechanical ventilator strategies were under the discretion of the attending physician given the initial results.

The patients were followed up during the entire hospital stay and up to Day 28 from study enrollment. The primary outcome measured were the overall survival rate, length of hospital stay (in days), and the number of antibiotic free days at Day 28. The number of antibiotic-free days at Day 28, defined as the number of days alive without any antibiotic, neither parenteral nor enteral, from the randomization to Day 28. Patients who died before Day 28

have a value of 0. Patients who have been discharged prior to Day 28 of the study will be followed up via phone call, SMS, and e-mail.

2.4 Statistical Analysis

The researchers used SPSS version 21 for the statistical analysis of the data collected. Frequency, percentage, mean and standard deviation were calculated. Analysis of variance (ANOVA test) at 95% confidence interval or p-value <0.05 were used to determine whether the experimental arm has a significantly lower mortality rate, shorter length of hospital stay, and greater antibiotic free days at Day 28. Descriptive analysis was done for the baseline characteristics of patients admitted for community acquired pneumonia and their risk factors.

Results

There were a total of 154 patients eligible for the study who were admitted during the research period between October 2023 to March 2024. Twelve patients were excluded due to respiratory failure due to causes other than pneumonia. Twenty patients did not provide consent. A total of 118 participants were randomized, with 61 patients into the pneumonia panel group and 57 patients in the control group. In the pneumonia panel group, 16

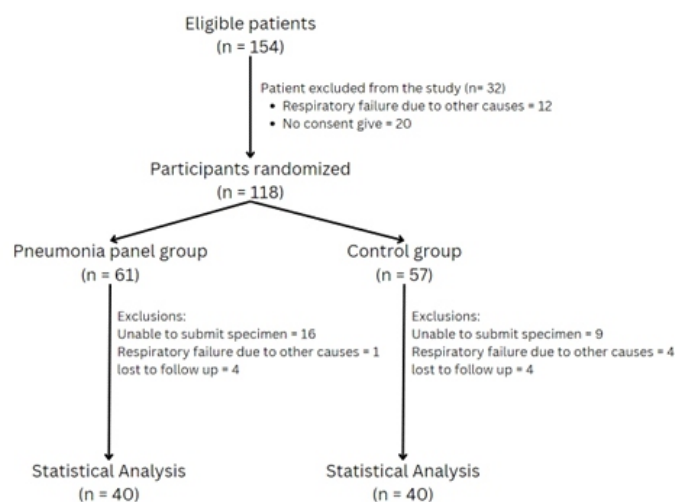


Figure 1. Participant Flowsheet

patients were not able to submit a specimen for pneumonia panel and GSCS, 4 were lost to follow up, while 1 was excluded for developing respiratory failure due to other causes. In the control group, 9 patients were not able to submit specimen for sputum GSCS, 4 were lost to follow-up, and 4 were excluded due to developing respiratory failure due to other causes. A total of 80 participants completed the study and were followed up until 28 days after enrollment. The trial was concluded after completion of the initial 6 month study period has ended and after supplies of PCR test (Pneumonia panel) were consumed.

There was no significant difference between the baseline characteristics of the two groups in age and sex. The patients in the pneumonia panel group had more hematologic co-morbidities (p-value 0.044) with 2 cases of thalassemia and 2 cases of myelodysplastic syndrome, while there were no with hematologic co-morbidities in the control group. Confounding factors including history of aspiration, smoking history, history of tracheostomy or bronchiectasis, prior hospitalization and intravenous antibiotic use within 90 days were similar between the 2 groups.

The two groups were similar in terms of diagnosis of other pneumonia during the hospitalizations. Only 2 intubated patients were included in the study (1 in the pneumonia panel group and 1 in the control group). Although not statistically significant, 10 patients required high flow nasal cannula in the pneumonia panel group compared to 5 patients in the control group (p-value 0.263). Baseline complete blood count and procalcitonin levels were also similar between the 2 groups.

Klebsiella pneumoniae was the most common pathogen detected among participants who submitted specimen for pneumonia panel at 32%, followed by *Haemophilus influenzae* (30%) and *Pseudomonas aeruginosa* (7%). Resistance genes were detected in 11 patients, the most common of which is CTX-M (15% of the pneumonia panel group). Among the 40 specimens submitted for both pneumonia panel and sputum culture in the pneumonia panel group, pneumonia panel was able to detect 59 pathogens as compared to only 37 pathogens in the sputum culture. Out of the 37 pathogens detected in sputum culture, the same pathogens were detected on pneumonia panel in 25 cases with a concordance rate of 67.5%.

In the pneumonia panel group, escalation of antibiotics within 48 hours of admission was noted among 12 patients, none of which, required another escalation of antibiotic after 48 hours of admission. Among the 12 patients where antibiotics were shifted within 48 hours of admission, resistance genes were detected in 8 patients, *Pseudomonas aeruginosa* was detected in 3 patients, and *Acinetobacter baumannii* was detected in 1. In the pneumonia panel group, 11 patients required escalation of antibiotics after 48 hours of admission as compared to only 6 in the control group.

Sputum culture showed significantly more growth (p-value 0.001, 95% C.I.) in the pneumonia panel group (72.5%) as compared to the control group (42.5%). *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* were the 2 most common pathogen detected in sputum culture for the pneumonia panel group, while *Candida albicans* was the most common pathogen detected in the control group, followed by *Klebsiella pneumoniae*.

The average length of hospital stay was similar in the 2 groups with a mean of 9.4 days in the pneumonia panel group compared to 7.25 days in the control group (p-value 0.073, 95% C.I.). Antibiotic free days were likewise not significantly different, with a mean of 15.4 days in the pneumonia panel group compared to 16.8 days in the control group (p-value 0.332, 95% C.I.). There were only 2 mortalities in the pneumonia panel group and 1 in the control group.

Although not statistically significant, 10 patients required high flow nasal cannula in the pneumonia panel group compared to 5 patients in the control group (p-value 0.263, 95% C.I.). When analyzing patients who required high flow nasal cannula, there was greater antibiotic free days in the pneumonia panel group with a mean of 12.63 days as compared to the control group at 8 days. Length of hospital stay and mortality were not significantly different.

Discussion

In this randomized controlled trial, all eligible patients within the study period were included between October 2023 to March 2024. Patients were randomized into either the pneumonia panel group or the control group with similar baseline characteristics such as age, sex and co-morbidities with the exception of hematologic conditions (thalassemia and myelodysplastic syndrome). Risk factors for *Pseudomonas aeruginosa* such as history of chronic obstructive pulmonary disease, bronchiectasis, and tracheostomy were compared and were noted to be similar between the 2 groups. (p-value = 0.083, 0.160, 0.999 respectively, 95% C.I.). Risk factors for Methicillin-resistant *Staphylococcus aureus* (MRSA) were also similar between the 2 groups which included prior hospitalization and prior IV antibiotic use within 90 days (p-value 0.323, 0.323 respectively, 95% C.I.) [1].

The length of hospital stay (p-value 0.073, 95% C.I.), duration of antibiotic therapy (p-value 0.332, 95% C.I.), and mortality rates (p-value 0.570, 95% C.I.) were shown to not be significantly different between the 2 groups. However, further analysis of the data showed that patients in the pneumonia panel group had more growth in the sputum culture as compared to the control group. More pathogenic and drug-resistant species were detected in the pneumonia panel group, which were not detected in the control group such as *Acinetobacter baumannii* and *Stenotrophomonas maltophilia*. The increase in the prevalence of multidrug-resistant Gram-negative bacteria has been shown in recent studies to substantially increase morbidity, mortality, and healthcare costs due to the ongoing spread of antimicrobial resistance [8]. Although not statistically significant, there were more patients with procalcitonin levels >0.5 in the pneumonia panel group as compared to the control group (p-value 0.135, CI 95%). This may attribute to the bias of the study and explain the higher rate of antibiotic escalation after 48 hours of admission in the pneumonia panel group (n=11) as compared to the control group (n=6).

Table 1. Baseline characteristics and Clinical Status

	Pneumonia panel group (n=40)	Control Group (n=40)	P-value
Age (mean±SD)	71.8±17.5	69.1±20.7	0.556
Sex			
Male	18(45%)	22(55%)	0.570
Female	22(55%)	18(45%)	0.570
Co-morbidities			
Asthma	4(10%)	1(2.5%)	0.486
COPD	3(7.5%)	0(0%)	0.083
Hypertension	16(40%)	21(5%)	0.303
Diabetes Mellitus	10(25%)	15(37.5%)	0.256
Chronic kidney disease	4(10%)	7(17.5%)	0.372
Heart Disease	9(22.5%)	11(27.5%)	0.570
Hematologic condition	4(10%)	0(0%)	0.044*
Neurologic condition	7(17.5%)	8(20%)	0.743
Malignancy	1(2.5%)	1(2.5%)	0.999
History of Aspiration	4(10%)	6(15%)	0.486
Smoking History			
Packyear > 10	5(12.5%)	7(17.5%)	0.534
Packyear < 10	35(87.5%)	33(82.5%)	0.534
History of Tracheostomy	1(2.5%)	1(2.5%)	0.999
History of Bronchiectasis	0(0%)	2(5%)	0.160
Prior Hospitalizations within 90 days	3(7.5%)	1(2.5%)	0.323
Prior use of IV Antibiotic within 90 days	3(7.5%)	1(2.5%)	0.323
Diagnosis other than CAP			
Sepsis (osteomyelitis, UTI)	3(7.5%)	3(7.5%)	0.999
ILD	2(5%)	1(2.5%)	0.570
Pleural effusion	5(12.5%)	2(5%)	0.183
Asthma exacerbation	3(7.5%)	0(0%)	0.083
COPD exacerbation	1(2.5%)	3(7.5%)	0.323
Covid infection	2(5%)	0(0%)	0.160
Influenza	3(7.5%)	4(10%)	0.660
Pulmonary tuberculosis	2(5%)	7(17.5%)	0.058
Decompensated heart failure	4(10%)	2(5%)	0.324
Cardiac Arrhythmia	1(2.5%)	0(0%)	0.323
Coronary artery disease	1(2.5%)	0(0%)	0.324
O2 support			
Room air	16(40%)	19(47.5%)	0.263
low flow oxygen support	13(32.5%)	15(37.5%)	0.263
HFNC/NIV	10(25%)	5(12.5%)	0.263
Invasive mechanical ventilation	1(2.5%)	1(2.5%)	0.263
Complete blood count			
Hemoglobin	12.2±2.11	12.5±1.92	0.131
Hematocrit	37.8±6.53	37.4±5.64	0.514
White blood cells	11±3.86	14.8±15.2	0.494
segmenter	76.8±6.87	74.6±17.9	0.340
lympocyte	13.1±4.54	11.9±8.25	0.411
monocyte	8.69±4.46	8.22±4.59	0.649
eosinophil	1.86±2.01	2.25±1.75	0.224
basophil	0.60±0.55	1.00±0.00	0.999
Platelet count	229±96.7	259±98.4	0.430
procalcitonin > 0.5	14(35%)	8(20%)	0.135
procalcitonin < 0.5	26(65%)	32(80%)	0.135

Table 2. Primary outcomes

	Pneumonia panel group (n=40)	Control Group (n=40)	P-value
Mortality Rate	2 (5%)	1 (2.5%)	0.570
Length of hospital stay in days (mean±SD)	9.40±5.54	7.25±4.50	0.073
Antibiotic Free Days at Day 28(mean±SD)	15.4±5.74	16.8±5.29	0.332
Patients requiring High Flow Nasal Cannula			
	Pneumonia panel (n=10)	Control (n=5)	P-value
Antibiotic free days	12.63 ± 7.5	8 ± 6.99	0.086
Length of hospital stay in days	10 ± 5.69	11.6 ± 6.31	0.443
Mortality	2	1	0.570

The faster result of the pneumonia panel prompted an earlier antibiotic escalation within 48 hours of admission in 12 patients. The early antibiotic escalation was brought about by the detection of resistance genes or pathogens known to be

resistant to the recommended initial broad spectrum antibiotic (i.e. Pseudomonas aeruginosa, Acinetobacter baumannii). None of these 12 patients required another antibiotic escalation and was discharged after completion of the antibiotic therapy.

Majority of those included in the study were moderate risk pneumonia patients with only 15 (18%) requiring high flow oxygen support and only 2 intubated patients (2.5%). Recent studies has shown that the use of high flow nasal cannula and non-invasive ventilation are recommended strategies for severe pneumonia both for acute hypercapnic and acute hypoxemic respiratory failure [7]. In this study, a subgroup analysis including only patients requiring high flow oxygen support (n=15) showed a lesser antibiotic duration in the pneumonia panel group as compared to the control group. But there was no difference in the length of hospital stay and mortality rates. These results encourage future studies focusing on patients with severe pneumonia to include patients requiring high flow oxygen support.

Limitations

The results of this study should be used as a preliminary data regarding the utilization of the Pneumonia panel given the limited sample size. Because of the small sample size, the limited power of the study has to be taken into consideration. Although baseline characteristics and risk factors were similar between the two groups, detection of more drug resistant pathogens in the pneumonia panel group, as well as more patients with procalcitonin levels >0.5 , as compared to the control group may affect the validity of the results. *Candida albicans*, which are commonly considered normal respiratory flora, was detected more frequently in the control group compared to the pneumonia panel group (p-value 0.089, 95% C.I.). More participants in the control group had no growth in sputum culture (n= 23) compared to the pneumonia panel group (n= 11). These factors should be considered as it may contribute to the bias of the results. Lastly, the choice of antimicrobial therapy, duration of treatment, as well as the decision to escalate treatment based on the pneumonia panel results were under the discretion of attending physician, thus limiting the reproducibility of the results.

Conclusions

In conclusion, among admitted patients diagnosed with moderate to severe community acquired pneumonia, the inclusion of pneumonia panel does not significantly decrease the length of hospital stay, total duration of antibiotic therapy, and mortality rates when compared to the standard of care treatment. The benefit of pneumonia panel was seen when there is early detection of drug resistant pathogen thereby resulting in early antibiotic escalation and shorter duration of antibiotic therapy. Further studies are necessary to show its benefit in the high risk population.

Recommendation

We recommend that this research be expanded into a multi-center study in order to improve the sample size and limit bias. Furthermore, we recommend limiting the study population to include only high-risk pneumonia (i.e. intubated patients and requiring high flow oxygen support). as the benefits of pneumonia panel are seen when there is early detection of drug resistant pathogens.

References

1. Joint Statement of the Philippine Society for Microbiology and Infectious Diseases, Philippine College of Chest Physicians, Philippine Academy of Family Physicians, Philippine College of Radiology (2016) "Philippine Clinical Practice Guidelines on the Diagnosis, Empiric Management, and Prevention of Community-acquired Pneumonia (CAP) in Immunocompetent Adults. <https://www.psmid.org/philippine-clinical-practice-guidelines-on-the-diagnosis-empiric-management-and-prevention-of-community-acquired-pneumonia-cap-in-immunocompetent-adults-2016/>.
2. Voiriot G, *et al.* (2021) Combined use of a broad-panel respiratory multiplex PCR and procalcitonin to reduce duration of antibiotics exposure in patients with severe community-acquired pneumonia (MULTI-CAP): A multicentre, parallel-group, open-label, individual randomised trial conducted in French intensive care units, *BMJ Open*, 11(8). doi:10.1136/bmjopen-2020-048187.
3. Lee SH, Ruan SY, Pan SC, Lee TF, Chien JY, & Hsueh PR. (2019) Performance of a multiplex PCR pneumonia panel for the identification of respiratory pathogens and the main determinants of resistance from the lower respiratory tract specimens of adult patients in Intensive Care Units. *Journal of Microbiology, Immunology and Infection*, 52(6):920-928. doi:10.1016/j.jmii.2019.10.009.
4. Kosai K, *et al.* (2022) BioFire FilmArray pneumonia panel enhances detection of pathogens and antimicrobial resistance in lower respiratory tract specimens, *Annals of Clinical Microbiology and Antimicrobials*, 21(1). doi:10.1186/s12941-022-00512-8.
5. Song, Fartoukh M, Nseir S, Mégarbane B, Cohen Y, Lafarge A, Contou D, Voiriot G. (2023) Respiratory multiplex PCR and procalcitonin to reduce antibiotic exposure in severe SARS-COV-2 pneumonia: A multicentre randomized controlled trial. *Clinical Microbiology and Infection*, 29(6):734-743. doi:10.1016/j.cmi.2023.01.009 W.-J., Hui, C. K., Hull, J. H., Biring, S. S., McGarvey, L., Mazzone, S. B., & Chung, K. F. (2021). Confronting covid-19-associated cough and the post-covid syndrome: Role of viral neurotropism, neuroinflammation, and neuroimmune responses. *The Lancet Respiratory Medicine*, 9(5):533–544. [http://doi.org/10.1016/s2213-2600\(21\)00125-9](http://doi.org/10.1016/s2213-2600(21)00125-9).
6. Bouadma L, Luyt C-E, Tubach F, Cracco C, Alvarez A, Schwebel C, Wolff M. (2010) Use of Procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial): A multicentre randomised controlled trial. *The Lancet*, 375(9713):463-474. doi:10.1016/s0140-6736(09)61879-1.
7. Cutuli SL, *et al.* (2021) Noninvasive ventilation and high-flow oxygen therapy for severe community-acquired pneumonia, *Current Opinion in Infectious Diseases*, 34(2):142–150. doi:10.1097/qco.0000000000000715.
8. Martin-Loeches I. and Torres A. (2021) New guidelines for severe community-acquired pneumonia, *Current Opinion in Pulmonary Medicine*, 27(3):210–215. doi:10.1097/mcp.0000000000000760.