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The Clinical Impact of the Film Array (Bio Fire) Respiratory Panel Utilization on the Outcomes of Pediatric Patients with Acute Viral Respiratory Infections in Two Private Tertiary Hospitals in Cebu

Shajed Julasiri[1*], Jonathan Lim[2] & Karen Joy Kimseng[1]

[1]*Senior Pediatric resident in Chong Hua Hospital Mandaue*
[2]*Pediatric Rheumatologist and the Research Head Chong Hua Hospital Mandaue*

[*]Corresponding author: Shajed Julasiri MD, Senior Pediatric resident in Chong Hua Hospital Mandaue.

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Abstract

Background: *Acute respiratory tract infections (ARI) are the most prevalent illness in people of all ages, and they are a leading cause of hospitalization and death. Molecular testing methods have significantly expanded the ability to diagnose respiratory infections. Rapid viral testing aims to prompt the diagnosis of viral infections that could lead to faster hospital discharge, lower healthcare resource use and clinicians are guided on the judicious use of antibiotics, as well as greater isolation precautions. The objective of this study was to determine the clinical impact of the Film Array (Biofire) Respiratory Panel utilization on the outcomes of pediatric patients with acute viral respiratory infection.*

Methodology: *This is a cross-sectional analytic study, conducted in two private tertiary hospitals. Study population includes admitted patients aged 1-18 years old with acute respiratory infection and then divided into two groups: exposure group (with Biofire taken) and non-exposure group (without Biofire taken). Retrospective chart review was done on the admitted patients and analyzed using descriptive and inferential statistics.*

Keywords: Acute Respiratory Infections, Biofire, Outcome, Length of Hospital Stay

Introduction

Background of The Study

Acute respiratory tract infections (ARI) are the most prevalent illness in people of all ages, and they are a leading cause of hospitalization and death [1]. Clinical symptoms, laboratory evaluations, and imaging are frequently insufficient to identify the underlying pathogen [2]. The common cold, otitis media, pharyngitis, acute bronchiolitis, and pneumonia are the most prevalent respiratory illnesses among individuals seeking medical care accounting for the bulk of antibiotic prescriptions [3]. ARIs are also responsible for children's high antibiotic use, despite the fact that the majority of ARIs are viral in nature [4]. In pediatric outpatients, viral acute respiratory infections place a tremendous strain on emergency departments and patients' families [5]. Molecular testing methods have significantly expanded the ability to diagnose respiratory infections [6]. The Film Array Respiratory Panel was initially introduced in 2011 to detect respiratory viruses. In 2012, it was upgraded to include four bacterial strains and 19 viruses with an overall sensitivity and specificity of 97.4% and 99.4%, respectively [8, 9]. A number of studies have shown that identifying a specific respiratory pathogen can improve a patient's chances of being discharged successfully [14]. These studies also noted that the BioFire Film Array did not affect the length of stay in a hospital [15]. Specific viral pathogens are promptly identified, clinicians are guided on the judicious use of antibiotics, which in turn will prevent the development of antibiotic resistance [18].

Significance of the Study

By establishing the advantages of utilizing the Biofire respiratory panel to determine the specific viral etiology of acute respiratory infections, physicians may be able to prevent unnecessary antibiotic administration, promote cost-effective treatment techniques, improve clinical decision-making abilities, increase accuracy of patient diagnoses, decrease hospital stays and improve resources allocation.

Research Question

Among pediatric patients with acute viral respiratory infections in two tertiary private hospitals, what is the clinical impact of the utilization of the Film Array (Biofire) respiratory panel on their outcomes?

Review of Literature

Acute respiratory infections (ARI) are the most common illness among people of all ages and genders [1]. The clinical signs of respiratory tract infections frequently have no or few correlations with the bacteria that is causing the infection. However, distinguishing between bacterial and viral causes is critical for effective treatment [2]. Antibiotic-resistant microbial infections are associated with increased morbidity, mortality, and a significant economic burden [3]. Viral infections can be diagnosed using a variety of methods. Polymerase chain reaction (PCR)-based assays have recently been introduced and numerous studies have demonstrated that panels that can identify a wide range of viral infections significantly improve diagnostic output [4]. Acute viral respiratory infections in pediatric outpatients are a huge burden on emergency departments and patients' families, especially during influenza seasons, accounting for roughly 20% of all deaths in pre-school children worldwide, with pneumonia accounting for 90% of these deaths [5]. Past epidemiologic studies used routine diagnostic methods such as culture to detect viral and bacterial respiratory pathogens [6]. Molecular respiratory panel (MRP) assays are gaining popularity as a result of its ability to detect numerous diseases with excellent sensitivity and specificity as well as demonstrated cost reductions [7].

The BIOFIRE® Respiratory 2.1 plus Panel tests for 19 viruses and four bacteria cause respiratory tract infections with an overall sensitivity and specificity of 97.4% and 99.4%, respectively [9]. It integrates sample preparation, amplification, detection and analysis into one simple system that requires just 2 minutes of hands-on time, with a total run time of about an hour [9].

Even when viral infection is a strong possibility, empiric antibiotic treatment is frequently started, leading to unnecessary antibiotic use. Reducing the use of antibiotics has an effect on reducing side effects and aids in efforts by the public health sector to address rising antibiotic resistance [11-13]. In a retrospective study by Rogers, et al., they stated that healthcare providers may be more confident in discharge after they have identified a specific pathogen associated with the patient's illness [14]. One such study by Andrews et al. performed in adult patients compared the Bio Fire Film Array to routine laboratory-based PCR and serology tests and found no evidence of an association between Film Array testing and length of hospital stay . They attributed their length of stay results to a delay in initiation of the Film Array nasal swab by clinical staff due to the lack of hospital procedures [15]. Although the introduction of real time polymerase chain reaction testing into routine clinical practice has resulted in a large number of viral diagnoses. It has had little impact on patient treatment [16].

In study conducted by Lee, they demonstrated that adopting MRP assays with a quicker turnaround time can result in significant improvements for pediatric inpatients with viral acute respiratory tract infections. Rapid diagnostics can assist physician in making wise decisions on the use of antibiotics for patients with acute respiratory tract infections by promptly delivering respiratory pathogen data [18].

General Objective

The objective of this study was to determine the clinical impact of the Film Array (Bio fire) Respiratory Panel utilization on the outcomes of pediatric patients with acute viral respiratory infection

Specific Objectives

To describe the admitted pediatric patients with acute viral respiratory infection in terms of the following demographic variables:

a. Age
b. Sex
c. Month and Year Admitted
d. Influenza vaccination status
e. Residence (Urban vs. Rural)

To determine the distribution of specific pediatric viral respiratory pathogen based on:

a. Age group
b. Month and Year
c. Influenza vaccination status
d. Residence (Urban vs. Rural)

To determine how the use of the Film Array (Biofire) respiratory panel test among hospitalized pediatric patients with viral respiratory infections affected the following:

a. Admission type (Non-critical vs. Critical care unit)
b. Antibiotic Usage
c. Length of Hospital stay
d. Status on discharge (Improved, With Oxygen dependence or Sequelae, and Expired)

Methodology

Study Design- The researcher used a cross-sectional analytic study design, using retrospective chart review of pediatric patients admitted from October 2018 to March 2022.

- **Study Setting**: The study was conducted in two tertiary private hospitals in Cebu that are both capable of performing Film Array (Biofire) respiratory panel.
- **Study Population:** The subjects were divided into exposure group (with Biofire Respiratory panel) and non-exposure group (without Biofire respiratory panel)
- **Inclusion Criteria:** Pediatric patients ages 1 month to 18 years old, diagnosed with acute viral respiratory infection, admitted in either two private tertiary hospital in Cebu and Mandaue from October 2018 to March 2022 and with negative culture growth in any specimen (Blood, CSF, Throat, Tracheal Aspirate, Urine, Wound).
- **Exclusion Criteria:** Admitted more than once in the same year in either two private tertiary hospital in Cebu and Mandaue, discharged against medical advice (DAMA) or transferred to another institution, immunocompromised patient or receiving immunosuppressive therapy, with respiratory and non-respiratory comorbidities, Bacteria identified in the Film Array (Biofire) respiratory panel 2 or 2.1 and with positive culture growth in any specimen (Blood, CSF, Throat, Tracheal Aspirate, Urine, Wound)

Limitation of the Study

The data gathered is limited to the information provided by the medical records. Three and half years of chart review is available since the respiratory film array (Biofire) was only utilized in the last quarter of 2018. Furthermore, the study population only included admitted patients for better monitoring of the course of the illness. Hence, the overall severity of the respiratory illness

reflected in the study may be worse than that of the general population during the study period.

Sample Size

Purposive sampling was used in this investigation. In computing the sample size for chi square goodness of fit test (contingency tables), the GPower version 3.19.7 was used (See Figure 1). The study had a total sample size estimate of 220 participants which was subdivided into 110 participants for the non-exposure group and 110 for the exposure group. The first 110 participants who fulfilled the inclusion and exclusion criteria on both exposure and non- exposure groups starting from March 2022 down to October 2018 were included in the study.

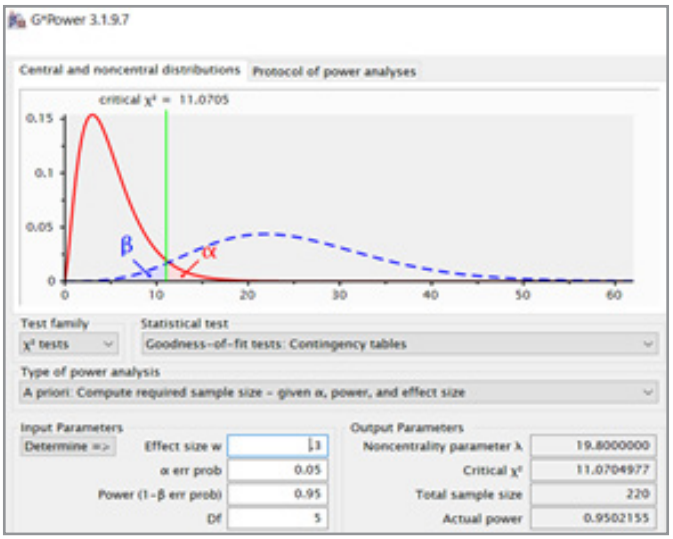

Figure 1: Sample Size computation based on G'Power 3.19.7 program

Data Collection and Analysis

Once the study was approved by the institutional review board, a letter was sent to the main laboratory to seek permission to retrieve the complete master list of the patients who underwent the Biofire Respiratory panel 2 or 2.1. Likewise, a letter to the head of the records section was sent to ask permission to review the charts of the pediatric (1 month to 18 years old) patients diagnosed with an acute viral respiratory infection. Once given approval to collect data, the researcher identified the exposure group and the non-exposure group. The patient's demographic data (age, sex, month and year admitted, influenza vaccine status, residence, admission type, antibiotic usage, length of hospital stay and status on discharge) and distribution of specific pathogens detected in Film Array (Biofire) respiratory panel were collected. These data were encoded in a master table in Microsoft Excel. Analysis of the results were conducted based on the objectives of this study. Quantitative descriptive statistics were used to describe and summarize the dataset obtained in the study.

The chi-square test of independent was conducted to determine the association between admission type, antibiotic usage, length of hospital and status in discharge as outcomes to the usage of Film Array (Biofire) Respiratory panel and those who didn't underwent the test.

Ethical Considerations

After securing the approval from the Chong Hua hospitals' Institutional Review Board (IRB), the study commenced. The primary investigator acknowledged that the study population consists of vulnerable pediatric patients. Due diligence in upholding the subject's rights including privacy and patient confidentiality was implemented. Informed consent was obtained from the parents and/or legal guardians for the study. The data were collected through review of charts and anonymity of the subject identifiers throughout the study was ensured. Any electronically encoded study participant information was password protected with access only to the study investigator. All soft copies will be deleted and hard copies will be shredded after five years from the time of submission to Chong Hua Hospital IRB.

Results and Interpretation of Data

A total of 220 participants were included and analyzed in this study. The results are reflected as follows:

The majority of the pediatric patients with acute viral respiratory infections are 1-5 years old from both the exposure group (n=77, 70.0%) and non-exposure group (n=70, 63.6%) as shown in table 1 below.

Table 1: Frequency of acute respiratory viral infections per age group

	Exposure Group		Non- Exposure Group	
AGE GROUP	f	%	f	%
<1-year-old	16	14.5%	19	17.3%
1-5 years old	77	70%	70	63.6%
6-10 years old	11	10%	7	6.4%
11-18 years old	6	5.5%	14	12.7%

In terms of gender, there are more females than males for both exposure group (n=71, 64.5%) and non-exposure group (n=66, 60.0%) as reflected in table 2 below.

Table 2: Sex distribution of the study participants

	Exposure Group		Non- Exposure Group	
SEX	f	%	f	%
Male	39	35.5%	44	40.0%
Female	71	64.5%	66	60.0%

Table 3 below shows in terms of distribution of admitted patients per month with acute viral respiratory infection from October 2018 to March 2022, majority of the pediatric patients with acute viral respiratory infections were admitted in the month of July (n=31, 28.2%) for the exposed group. While the majority of the non- exposed group were admitted in the month of October (n=34, 30.9%).

Table 3: Frequency distribution of patients per month from October 2018 to March 2022.

	Exposure Group		Non- Exposure Group	
Month Admitted	f	%	f	%
January	5	4.5%	3	2.7%
February	1	0.9%	10	9.1%
March	0	0%	13	11.8%
April	0	0%	6	5.5%
May	4	3.6%	4	3.6%
June	11	10%	4	3.6%
July	31	28.2%	2	1.8%
August	6	5.5%	3	2.7%
September	10	9.1%	3	2.7%
October	13	11.8%	34	30.9%
November	17	15.5%	20	18.2%
December	12	10.9%	8	7.3%

Many of the respondents under the exposed group were admitted in year 2021 (n=100, 90.0%). On one hand, most of the respondents under the non-exposure group were admitted in year 2018 (n=47 42.7%) as shown in table 4 below.

Table 4: Distribution of study participants by year of admission.

	Exposure Group		Non- Exposure Group	
Year admitted	f	%	f	%
2018	0	0%	47	42.7%
2019	0	0%	33	30%
2020	6	5.5%	18	16.4%
2021	100	90.9%	12	10.9%
2022	4	3.6%	0%	0%

As shown in table 5 below is the distribution of the ARI participants per locality. Majority of the sampled pediatric patients for both exposure group (n=92, 83.6%) and non-exposure group (n=75, 68.2%) are residing in an urban locality.

Table 5: Distribution of the study participants per locality.

	Exposure Group		Non- Exposure Group	
Locality	f	%	f	%
Urban	92	83.6%	75	68.2%
Rural	18	16.4%	35	31.8%

In terms of influenza vaccination status, a greater number of sampled pediatric
patients for both exposure group (n=81, 73.6%) and non- exposure group (n=90, 81.8%) are not vaccinated as shown in Table 6.

Table 6: Distribution of the study participants by influenza vaccination status.

	Exposure Group		Non- Exposure Group	
Influenza Vaccination	f	%	f	%
Vaccinated	29	26.4%	20	18.2%
Unvaccinated	81	73.6%	90	81.8%

For single viral pathogen detected, human rhinovirus/enterovirus had the highest frequency (n=27, 29%), while Coronavirus HKU1 (n=1, 1.1%) and Parainfluenza virus (n=1, 1.1%) had the lowest frequency. For viral pathogens that are co detected with others, human rhinovirus/enterovirus co detected with influenza B had the highest frequency (n=4, 23.5%) as shown in the table 7.

Table 7: Frequency and Percentage of Specific Viral Pathogen (via Single Detection and Codetection)

SINGLE DETECTION	Frequency	Percentage
Coronavirus HKU 1	1	1.1%
Human Metapneumovirus	14	15.1%
Human Rhinovirus/Enterovirus	27	29%
Influenza A	7	7.5%
Influenza B	22	23.7%
Parainfluenza Virus 1	1	1.1%
Parainfluenza Virus 3	4	4.3%
Respiratory Syncytial Virus	8	8.6%
Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)	9	9.7%
Total	93	100%
CODETECTION	**Frequency**	**Percentage**
Adenovirus, human metapneumovirus	2	11.8%
Human Metapneumovirus, Human Rhinovirus/Enterovirus	3	17.6%
Human Metapneumovirus, Human Rhinovirus/Enterovirus, Influenza B	1	5.9%
Human Rhinovirus/Enterovirus, Adenovirus	1	5.9%
Human Rhinovirus/Enterovirus, Chlamydia pneumoniae	1	5.9%
Human Rhinovirus/Enterovirus, Influenza A	2	11.8%
Human Rhinovirus/Enterovirus, Influenza B	4	23.5%
Human Rhinovirus/Enterovirus, Parainfluenza Virus 1	1	5.9%
Parainfluenza virus 4, Human Rhinovirus/Enterovirus	1	5.9%
Respiratory Syncytial Virus, Human Rhinovirus/Enterovirus	1	5.9%
Total	**17**	**100%**
Grand Total	**110**	**100%**

These are the viral pathogens that are frequently detected among the sampled pediatric patients by age group. For the patient whose age is less than a year, only the viral pathogen coronavirus HKU 1 was detected. While the rest of the single viral pathogens were frequently detected among the 1-5 years old age group. For co-detected viral pathogens, they are more frequently detected between the ages from 1-5 years old (n=13, 76.5%) as reflected in the table 8 below.

Table 8: Distribution of single viral pathogen detection by age group

AGE GROUP								
	< 1 year old		1-5 years old		6-10 years old		11-18 years old	
	f	%	f	%	f	%	f	%
Coronavirus HKU 1	1	100.0%	0	0.0%	0	0.0%	0	0.0%
Human Metapneumovirus	1	7.1%	10	71.4%	3	21.4%	0	0.0%
Human Rhinovirus/Enterovirus	8	29.6%	17	63.0%	1	3.7%	1	3.7%
Influenza A	0	0.0%	6	85.7%	0	0.0%	1	14.3%
Influenza B	3	13.6%	15	68.2%	3	13.6%	1	4.5%
Parainfluenza Virus 1	0	0.0%	1	100.0%	0	0.0%	0	0.0%

Parainfluenza Virus 3	0	0.0%	4	100.0%	0	0.0%	0	0.0%
Respiratory Synctial Virus	2	25.0%	5	62.5%	1	12.5%	0	0.0%
Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)	0	0.0%	4	44.4%	2	22.2%	3	33.3%
Codetection	3	17.6%	13	76.5%	1	5.9%	0	0.0%

In terms of gender, Coronavirus HKU 1 was detected in one female pediatric patient. The frequency of detection for Human Metapneumovirus and Parainfluenza Virus 3 viral pathogens are equal among male and female pediatric patients. While the rest of the single detected virus are more frequent among male pediatric patients. For co-detected viral pathogens, it is more frequently detected among female pediatric patients than among males as shown in table 9 below.

Table 9: Distribution of single viral pathogen detection by sex group

SEX				
VIRAL ETIOLOGY	**Male**		**Female**	
	f	%	f	%
Coronavirus HKU 1	0	0%	1	100.0%
Human Metapneumovirus	7	50.0%	7	50.0%
Human Rhinovirus/Enterovirus	19	70.4%	8	29.6%
Influenza A	5	71.4%	2	28.6%
Influenza B	16	72.7%	6	27.3%
Parainfluenza Virus 1	1	100%	0	0%
Parainfluenza Virus 3	2	50.0%	2	50.0%
Respiratory Syncytial Virus	6	75.0%	2	25.0%
Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)	7	77.8%	2	22.2%
Codetection	8	47.1%	9	52.9%

For the distribution of single pathogen detection by month as shown in table10 below, Coronavirus HKU 1 and Parainfluenza Virus 1 were noted to be the single pathogens detected for the month of January (n=1, 100%) and July (n=1, 11%), respectively. Human Metapneumovirus was most frequently detected in the month of October (n=4, 28.6%) and November (n=4, 28.6%) while Human Rhinovirus/Enterovirus was most frequently detected in the month of October (n=6, 22.2%). The viral pathogen Influenza A was most frequently detected in the month of November (n=3, 60%) while Influenza B was most frequently detected in the month of July (n=18, 81.8%). Majority of the cases of pediatric patients detected with Parainfluenza Virus 3 is in the month of May (n=2, 50%). Respiratory Syncytial Virus it was detected in patients admitted in the month of November (n=3, 37.5%) while detection of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2 was common in the months of August (n=4, 44.4%) and September (n=4, 44.4%). Furthermore, viral pathogens with codetection, was were commonly detected in the months of July (n=3, 17.6%) and December (n=3, 17.6%).

Table 10: Distribution of single viral pathogen detection by month admitted

	Jan f (%)	**Feb f(%)**	**Mar f(%)**	**Apr f(%)**	**May f(%)**	**June f(%)**	**Jul f(%)**	**Aug f(%)**	**Sept f(%)**	**Oct f(%)**	**Nov f(%)**	**Dec f(%)**
Coronavirus HKU 1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Human Metapneumovirus	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (14.3%)	0 (0%)	2 (14.3%)	4 (28.6%)	4 (28.6%)	2 (14.3%)
Human Rhinovirus/Enterovirus	2 (7.4%)	0 (0%)	0 (0%)	0 (0%)	2 (7.4%)	4 (14.8%)	3 (11.1%)	1 (3.7%)	2 (7.4%)	6 (22%)	3 (7.4%)	5 (18.5%)
Influenza A	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (20%)	0 (0%)	0 (0%)	1 (20%)	3 (60%)	0 (0%)
Influenza B	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4 (18.2%)	18 (81.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Parainfluenza Virus 1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (11%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Parainfluenza Virus 3	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (50%)	1 (25%)	1 (25%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Respiratory Syncytial Virus	1 (12.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (25%)	3 (37.5%)	2 (25 %)
Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)	1 (11.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4 (44.4%)	4 (44.4%)	0 (0%)	0 (0%)	0 (0%)
Codetection	0 (0%)	1 (5.9%)	0 (0%)	0 (0%)	0 (0%)	2 (11.8%)	3 (17.6%)	1 (5.9%)	2 (11.8%)	0 (0.0%)	5 (29.4%)	3 (17.6%)

(n=3, 17.6%) and December (n=3, 17.6%).

In terms of year admitted, all the viral pathogens, including with codetection, were commonly detected in year 2021, except for Coronavirus HKU 1, wherein the single case was in year 2022 as shown in table 11 below.

Table 11: Distribution of single viral pathogen detection by year admitted

YEAR ADMITTED								
	2019		2020		2021		2022	
	f	%	f	%	f	%	f	%
Coronavirus HKU 1	0	0.0%	0	0.0%	0	0.0%	1	100.0%
Human Metapneumovirus	0	0.0%	0	0.0%	14	100.0%	0	0.0%
Human Rhinovirus/Enterovirus	0	0.0%	1	3.7%	24	88.9%	2	7.4%
Influenza A	0	0.0%	0	0.0%	7	100.0%	0	0.0%
Influenza B	0	0.0%	0	0.0%	22	100.0%	0	0.0%
Parainfluenza Virus 1	0	0.0%	0	0.0%	1	100.0%	0	0.0%
Parainfluenza Virus 3	0	0.0%	0	0.0%	4	100.0%	0	0.0%
Respiratory Synctial Virus	0	0.0%	4	50.0%	4	50.0%	0	0.0%
Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)	0	0.0%	0	0.0%	8	88.9%	1	11.1%
Codetection	0	0.0%	1	5.9%	16	94.1%	1	100.0%

In terms of locality, all the viral pathogens, including with codetection, were all more frequently detected among pediatric patients living in urban areas, except for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) which was more frequently detected among pediatric patients living in a rural locality (n=8, 88.9%) as shown in table 12 below.

Table 12: Distribution of single viral pathogen detection by locality.

LOCALITY				
Virus Isolated	Urban		Rural	
	f	%	f	%
Coronavirus HKU 1	1	100%	0	0%
Human Metapneumovirus	10	71.4%	4	28.6%
Human Rhinovirus/Enterovirus	22	81.5%	5	18.5%
Influenza A	6	85.7%	1	14.3%
Influenza B	20	90.9	2	9.1%
Parainfluenza Virus 1	1	100%	0	0%
Parainfluenza Virus 3	4	100%	0	0%
Respiratory Syncytial Virus	5	62.5%	3	37.5%
Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)	1	11.1%	8	88.9%
Codetection	12	70.6%	5	29.4%

In terms of influenza vaccination status, the viral pathogens Coronavirus HKU 1, Human Metapneumovirus, Human Rhinovirus/Enterovirus, Influenza A, Parainfluenza Virus 1, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) were more frequently detected among pediatric patients who were non-vaccinated than those who had vaccination. On the other hand, the viral pathogens Influenza B, Respiratory Syncytial Virus were more frequently detected among pediatric patients who had influenza vaccination relative to those who were not vaccinated. Frequency of detection among vaccinated versus unvaccinated is equal for the viral pathogen Parainfluenza Virus 3. Viral pathogens with codetection are more frequently detected among non-vaccinated pediatric patients as reflected in table 13 below.

Table 13: Distribution of single viral pathogen detection in terms of influenza vaccination

INFLUENZA VACCINATION STATUS				
Virus Isolated	**VACCINATED**		**NOT VACCINATED**	
	f	**%**	**f**	**%**
Coronavirus HKU 1	0	0%	1	100%
Human Metapneumovirus	4	28.6%	10	71.4%
Human Rhinovirus/Enterovirus	7	25.9%	20	74.1%
Influenza A	1	14.3%	6	85.7%
Influenza B	18	81.8%	4	18.2%
Parainfluenza Virus 1	0	0%	1	100%
Parainfluenza Virus 3	2	50.0%	2	50.0%
Respiratory Syncytial Virus	5	62.5%	3	37.5%
Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)	4	44.4%	5	55.6%
Codetection	3	17.6%	14	82.4%
Codetection	12	70.6%	5	29.4%

The outcome among hospitalized pediatric patients, who underwent the Film Array (Biofire) respiratory panel were analyzed. For admission type and status on discharged, it was not subjected to statistical treatment because all the data gathered regarding admission type are in majority, pediatric patients admitted in non-critical set-up while for status on discharge, all data sampled were pediatric patients with "improved" status when they were discharged. No long-term sequelae or mortality were documented in these pediatric patients.

The bar graph below (figure 2) contains the data bearing on the contingency between the kind of group (exposure group versus non-exposure group) and antibiotic usage (1-7 days, 8-14 days, no antibiotic use). Examining the pattern of the frequencies, it can be noted that there is a greater frequency of pediatric patients under non-exposure group who had antibiotic usage for 1-7 days and 8-14 days than pediatric patients under the exposure group (utilized Biofire). On one hand, there is a greater frequency of pediatric patients under the exposure group (utilized Biofire) who had no antibiotic use relative to the pediatric patients under the non-exposure group.

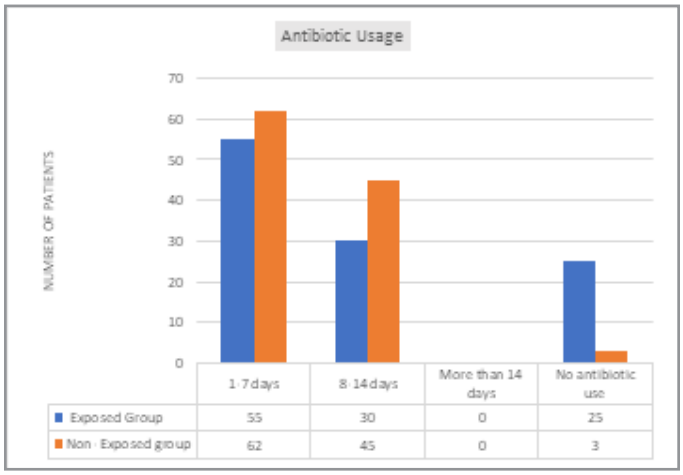

Figure 2: Bar graph shows the antibiotic usage in both study group participants

The chi-square results show that the type of group differs significantly in terms of antibiotic usage (x2=20.71, P =.001). The p-value (two-tailed) is smaller than the standard alpha value of 0.05, so the null hypothesis that the conditions are independent of each other should be rejected. This means that there is significant association in antibiotic use (no usage of antibiotic) between pediatric patients, who underwent Film Array (Biofire) respiratory panel (exposure group) versus pediatric patients, who did not undergo Film Array (Biofire) respiratory panel (non-exposure group).

Figure 3 below showed the data bearing on the contingency between the two of group (exposed and non-exposed group) and length of hospital stay (1-3 days, 4-7 days, and more than 7 days). Examining the pattern of the frequencies, it can be noted that there is a greater frequency of pediatric patients under the non-exposure group who had a longer length of hospital stay (4-7 days and more than 7 days). On one hand, there is a greater frequency of pediatric patients under the exposure group (utilized Biofire) who had a shorter length of hospital stay (1-3 days) than pediatric patients under the non-exposure group as shown in figure 3.

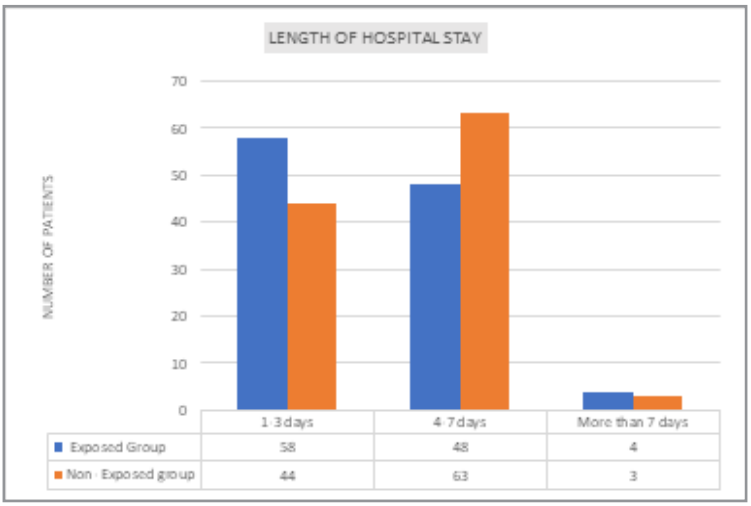

Figure 3: Bar graph show the duration of the length of hospital stay

The chi-square results show that the type of group differs significantly in terms of length of hospital stay (x2=14.09, P=.029). The p-value (two-tailed) is smaller than the standard alpha value of 0.05, so the null hypothesis that the conditions are independent of each other should be rejected. This also implies that there is significant association in shorter hospital stay of pediatric patients who underwent Film Array (Biofire) respiratory panel versus pediatric patients who did not undergo the test.

Discussion

In both developed and developing countries, acute respiratory tract infection is the most common cause for hospitalization in children. Early epidemiologic studies documenting that children are at particular risk for viral respiratory infection have other findings such as higher frequency of illnesses in females and peak of illness is during autumn and spring season [1]. Immune status of children is different from adults, and the amount of maternal antibodies attenuate distinctly, which would make children susceptible to respiratory viral infections. In this present study, it demonstrated that the most common age group hospitalized are ages 1-5-year-old, female children and those that resided in urban locality.

The adoption of preventive measures, including as personal and home hygiene, sanitation, and sufficient ventilation, may be done throughout the peak of the ARI season if parents or other caregivers of children are aware of the seasonal variations of infections [5]. Keeping the hands clean frequently, avoiding crowded public spaces, and getting an annual flu shot are additional preventive steps. Our data demonstrated that the most children admitted are in the month of July and October which is the rainy season in tropical countries. In addition, most patient who underwent the Film Array (Biofire) respiratory panel were tested in the latter years with majority during July 2021, when there was an increase number of SARS-CoV-2 cases. On the other hand, those who didn't undergo the test were admitted in the early years when the Film Array (Biofire) was not yet familiar to most pediatricians. Moreover, majority of SARS-CoV-2 cases were detected in the months of August and September 2021 when there was spike of delta variant cases in the area.

Majority in both groups were not given the influenza vaccine. This could be explained as the study population only included admitted patients. Therefore, it is expected that the unvaccinated would present a more severe course requiring admission.

Although ARIs are linked to a wide variety of infections, regardless of the underlying cause, the clinical symptoms are usually similar. Therefore, identification of the potential causal agents is a must for effective therapy, and virus detection can minimize the unnecessary and excessive use of antibiotics. The present study demonstrated that the most commonly detected viruses out of all the ARI cases are the human rhinovirus and enterovirus. Our analysis found that the infection was strongly associated with the cause of hospitalization.

Although ARIs are linked to a wide variety of infections, regardless of the underlying cause, the clinical symptoms are usually similar. Therefore, identification of the potential causal agents is a must for effective therapy, and virus detection can minimize the unnecessary and excessive use of antibiotics. The present study demonstrated that the most commonly detected viruses out of all the ARI cases are the human rhinovirus and enterovirus. At the host level, the outcome of dual infection is commonly superinfection. Co-infections can also alter the epidemiology of viral infections. It is postulated that the sequence of infections, the time interval between viral exposure and the route of infections affect the pathogenicity of the co-infection [21]. Our data demonstrated the most common viruses with co-detection that can cause hospitalization in children are human rhinovirus and influenza B. Moreover, the profile of children with viral co-detection are majority is a female, age 1-5 years old, residing in urban locality with no history of influenza vaccination. This is most likely due to the fact that the younger age group living in the more populated urban locality and without influenza vaccination are more prone to be get ARI requiring admission. Our data also further demonstrated that most children with viral co-detection respiratory panel results are admitted in the months of July and December. This follows the pattern of more viral infection during the rainy seasons.

The study showed that, compared to patients who were not evaluated using the respiratory panel, children's medical management changed significantly when the results of a Film Array (Biofire)

Respiratory panel were provided. These adjustments included a reduction in the use of antibiotics and a shorter hospital stay.

In contrast to patients who used a Film Array respiratory panel, a tendency toward shorter lengths of stay was observed in our study. Patients with severe respiratory issues and chronic illnesses were not included in the trial. A previous study found that positive respiratory viral testing correlates with decreased hospital length of stay in certain pediatric inpatient populations who had complicated medical histories, suggesting that the usefulness of Film Array respiratory panel testing for reducing length of stay may not necessarily depend on the patient's underlying clinical picture as demonstrated in our analysis [4].

In a previous study conducted by Rehder et al [20]. isolation of two or more respiratory viral pathogens is associated with moderate or severe illness and death in children cared for in the hospital setting but larger prospective studies are needed to clarify patients at greatest risk and to evaluate interactions between specific viruses. Just as certain individual viruses may be more virulent, it is possible that specific virus combinations may be associated with worse clinical outcomes. But in our study, this was not associated with the severity of illness because most of cases included in the study were all admitted in non-critical set up and discharged improved with no mortality documented.

Conclusion

Acute respiratory tract infection is a clinical diagnosis and most infections are caused by viruses. The most commonly affected age group are children ages 1-5 years old with human rhinovirus and enterovirus as the most common viral pathogens detected especially during the months of July and October. Use of a respiratory panel to assess disease severity for the individual patient could be used for clinical decision making in the management of children with ARIs.

The Respiratory panel test is not routinely available in many hospitals in detecting respiratory infection before the pandemic because of its cost and its restricted use in patients with high-risk of complications or with an unexpected disease course. But with the advent of the Sars-Cov-2 pandemic, the respiratory panel was routinely used to rule out Sars-Cov-2 infection as part of the respiratory virus.

In conclusion, the use of Film Array (Biofire) respiratory panels improved patient care by assisting clinical judgement regarding the usage of antibiotics as well as the length of hospitalization.

The Film Array (Biofire) respiratory panel is useful in assisting clinical judgement regarding the usage of antibiotic as well as the length of hospitalization among children affected by acute respiratory infections.

Declarations

Ethical Approval and Consent to Participate: It was approved by the Chong Hua hospital institutional review board last November 25, 2021. Informed consent was obtained from all the parent and/or legal guardian for the study and it was attached to their individual chart during the time of their admission. All methods were carried out in accordance with relevant institutional guidelines and regulations.

Consent for publication: Not Applicable.

Availability of Data and Materials: The availability of the data and material is through per request from the corresponding author who is Dr. Shajed Julasiri and you can send a request the data from this study through.

Conflict of Interest: None of the authors have a conflict to disclose.

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Contributors Statement: Dr. Julasiri designed the project, presented the ideas and the computational framework, gathered and analyzed the data. Dr. Julasiri with the help of Dr. Lim. carried out the implementation. Dr. Julasiri performed the calculations. Dr. Lim and Dr. Kimseng verified the analytical methods. Dr. Julasiri wrote the manuscript with input by Dr. Lim and Dr. Kimseng. All authors conceived the study and were in charge of overall direction and planning.

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Results

A total of 220 samples were included. Majority of patients in both groups were female, aged 1-5 years old, lived in an urban locality and with no influenza vaccination. The most single common virus detected was hRV/hEV(n=29%), while the most common codetection virus is hRV/hEV with influenza B (n=23.5%). For those who underwent the test, patients were frequently admitted in the year 2021 (n=90%) and month of July (n=28.2%). Utilization of the respiratory panel was associated with significant changes in medical management including decreased antibiotic usage (P=0.001) and shorter length of hospital stay (P=0.029), compared to those patients who didn't undergo the test.

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