Review Article

Etiological and Epidemiological characteristics of influenza-like illness (ILI) among pediatric patients admitted in a Tertiary Hospital from 2021-2024 in Quezon City, Metro Manila Philippines: A Retrospective Study

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ABSTRACT

Objective: To determine the epidemiologic characteristics and etiology of Influenza like illness (ILI) cases among children aged 0-18 years admitted at a hospital in Quezon City, Philippines.

Methods: A retrospective cross sectional analytical study was conducted through review of medical records of 682 patients aged 0-18 years hospitalized as a case of ILI from January 2021 to August 2024. All enrolled patients had nasopharyngeal samples tested using BIOFIRE® COVID-19 multiplex PCR. The etiology and epidemiologic characteristics of the cases were described. The association between etiologic, epidemiologic and clinical characteristics of ILI with the occurrence of complications was determined using univariate analysis and multiple logistic regression with level of significance set at alpha < 0.05.

Results: The commonest pathogens were Human Rhinovirus (38%), Influenza A (23%), and Adenovirus (21%). The most common complication was pneumonia (36.8%). Among clinical factors, longer duration from onset of ILI to hospitalization was a significant risk factor for pneumonia on univariate and multivariate analysis. Among etiologic agents, identification of Human metapneumovirus and Respiratory Syncytial Virus were significant risk factors for pneumonia on univariate analysis but only SARS-CoV-2 was a significant risk factor for pneumonia on multivariate analysis

Conclusion: This is the first multiyear study on the epidemiology and etiology of ILI among hospitalized pediatric patients in the Philippines with etiologies confirmed by multiplex PCR. Human metapneumovirus and SARS-CoV-2 have emerged as significant risk factors for pneumonia as a complication of ILI. Up-to-date information through surveillance on the etiology and epidemiology of ILI provides evidence for crafting better public health programs for the Philippines.

Keywords: Respiratory tract infections, Philippines, hospitalization, risk factors, Influenza (human)

INTRODUCTION

While there is no precise annual estimate for worldwide cases of influenza-like illness (ILI), the World Health Organization (WHO) provides figures for seasonal influenza, the most significant cause of ILI. Globally, the WHO estimates around 3-5 million cases of severe influenza yearly resulting in up to 650,000 deaths.[1,2] Most cases of ILI are self-limiting[3] but posing risks of complications, particularly in high-risk groups like children.[4] The WHO defines ILI as one of the acute respiratory infections characterized by fever more than or equal to 38 degrees Celsius accompanied by cough with onset within the last 10 days.[5] It may be accompanied by other constitutional

symptoms such as sore throat, myalgia, vomiting and diarrhea.[3] Previous studies on the etiology and epidemiology of ILI showed that the virologic etiology varies greatly among geographic locales, age groups, seasons, and years.[3,6]

In the 2020 Philippine Health Statistics of the Department of Health, acute respiratory infections was the leading cause of morbidity for all ages with a morbidity rate of (1,700/100,000 population.[7] However, local studies on the etiology and epidemiology of ILI among pediatric patients, both in the community and hospital settings are lacking. An influenza surveillance system was established in the country in June 2005 and has just begun to screen for other etiologic agents of ILI in 2024.[8] The mean annual outpatient incidence rate of influenza has been estimated as 5.4 per 1,000 individuals, with particularly high incidence (22.6 per 1,000) in children less than 5 years old.[9] A study done by Cheng et. al, 2020 noted that the annual estimated influenza-attributable excess mortality rates in the Philippines from 2006 to 2015 was second highest for children less than 5 years (2.14 per 100,000 individuals).[10]

St. Luke's Medical Center (SLMC), Quezon City is a tertiary level private hospital that runs a pediatrics department, neonatal and intensive care units. Prior to 2021, there was no diagnostic testing used in this hospital to identify the specific viruses causing ILI except for Influenza A and B lateral flow test which was started in 2007. In 2021, during the COVID-19 pandemic, BIOFIRE® COVID-19 multiplex PCR test became available at SLMC to detect *SARS-CoV-2* and 14 other pathogens[11] thus providing clinicians a diagnostic test to identify the etiology of ILI.

To better understand the problem of ILI in the Philippines, we determined the epidemiologic characteristics and etiology of ILI cases among children aged 0-18 years admitted at SLMC from January 2021 to August 2024 and the association between etiologic, epidemiologic and clinical characteristics of ILI with the presence of complications.

METHODS

Medical records of patients aged 0-18 years who satisfied the WHO definition of ILI and were hospitalized at SLMC from January 2021 to August 2024 were reviewed. Data on the patient's sex, age, vaccination status, body mass index, concomitant medical problems, number of days from onset of ILI to hospitalization, etiology of ILI based on results of BIOFIRE® COVID-19 multiplex PCR test, presence of complications[12], and outcome were collected. Data were analyzed using Excel version 16.55 2021 (Microsoft, United States of America and SPSS v27 2020 (IBM, New York, USA).

Epidemiologic and etiologic characteristics of hospitalized ILI cases were analyzed using frequency and percentage for categorical data and mean, standard deviation, and range for continuous data. Determination of the association between etiologic, epidemiologic and clinical characteristics of ILI with the presence of complications were analyzed using univariate and multivariate statistics. Chi square test and logistic regression were used in the univariate analysis. Odds ratio and the 95% confidence interval were calculated. Variables that

were statistically significant in the univariate analysis were included in the multiple logistic regression. Level of significance was set at alpha $\leq$ 0.05.

RESULTS

Characteristics of patients with ILI

A total of 682 patients were included in the study. All patients had nasopharyngeal samples tested using Biofire® COVID-19 multiplex PCR. There were more male patients 390 (57.2%) compared to female patients 292 (42.8%). Mean patient age was 5.75 $\pm$ 4.14 years. Most patients had updated immunizations in accordance with the government's National Immunization Program (Table 1).

Five-hundred forty-six (80.1%) of patients had a body mass index of <18.5. Three hundred thirty-nine (49.7%) of patients were brought to the hospital 2 to 4 days from onset of ILI. Less than 5% of cases had concomitant medical problems. Mean duration of hospital stay was 2.7 $\pm$ 1.7 days. All patients were discharged improved (Table1).

Table 1. Demographic and clinical characteristics of pediatric cases of ILI, St. Luke's Medical Center, Quezon City, Philippines, January 2021 to August 2024, n=682

Demographic and clinical characteristics	number (Percent)
Sex	
1.1.1 Male	390 (57.2%)
1.1.2 Female	292 (42.8%)
Age in years (Mean +-SD)	5.75 + 4.14
Less than 6 months old	31 (4.5%)
6 months to 1 year old	130 (19.1%)
2 years to 6 years old	307 (45%)
7 years to 12 years old	178 (26.1%)
13 years to 18 years old	36 (5.3%)
Vaccination status	
Diphtheria, Tetanus, Pertussis	682 (100%)
Haemophilus influenzae	682 (100%)
Hepatitis B	682 (100%)
Polio	675 (99%)
Measles Mumps Rubella Varicella vaccine	675 (99%)
Influenza vaccine	596 (87.4%)
BMI (Asia Pacific Classification)	
<18.5	546 (80.1%)
18.5-22.9	103 (15.1%)
23-24.9	20 (2.9%)
>25	13 (1.9%)
Top 5 concomitant medical problems	
Acute Gastroenteritis	21 (3.1%)
Urinary Tract Infection	16 (2.3%)
Dengue	13 (1.9%)
Acute Exudative Tonsillopharyngitis	9 (1.3%)
Acute Nasopharyngitis	3 (0.4%)
Number of days from onset of ILI to hospitalization	
0-1	112 (16.4%)
2-4	339 (49.7%)

5-7	212 (31.1%)
8-10	19 (2.8%)
Presence of complications of ILI:	
Pneumonia	251 (36.8%)
Exacerbation of Bronchial asthma	45 (6.6%)
Neurologic complications	
Febrile seizures	33 (4.8%)
Otitis Media	12 (1.8%)
Secondary bacterial infection	
S pneumoniae	11 (1.6%)
Cardiac- influenza-related myocarditis and pericarditis	6 (0.9%)
Respiratory failure	2 (0.3%)
Neurologic complications	2 (0.3%)
Nonfebrile seizures	1 (0.1%)
Encephalitis, aseptic meningitis, brain abscess, bacterial meningitis, cerebral infarction, Reye syndrome, others	1 (0.1%)
Laryngotracheitis or LTB	1 (0.1%)
Plastic bronchitis	0
Secondary bacterial infection	
Staphylococcus aureus	0
Other bacterial coinfections	0
Secondary fungal infection (ex. Aspergillosis)	0
Neurologic complications	
Encephalopathy	0
Musculoskeletal complications (ex. Acute myositis)	0
Others	
Duration of hospital stay (days)	
Mean + standard deviation	2.7 + 1.7 days
0-1	202 (29.6%)
2-4	344 (50.4%)
5-7	120 (17.6%)
8-10	16 (2.3%)
Outcome	
1.9.1 Discharged	682 (100%)
1.9.2 Transferred to another hospital facility	0
1.9.3 Discharged against medical AdVise	0
1.9.4 Died	0

Etiology of ILI

The three most frequently reported etiologic agents were *Human Rhinovirus/Enterovirus* (HRV) with 259 (38%), followed by *Influenza A* (IAV) with 156 (23%), and *Adenovirus* (AdV) with 145 (21%) (Table 2). SARS-CoV-2 continued to be identified as an etiologic agent in 20 cases of ILI in 2024, the year after the WHO declared the end of Covid-19 as a global health emergency. As to etiologic agents by age group, *HRV* was the most commonly occurring etiologic agent in all age groups except in the 13-18 years age group. IAV was one of the top 3 commonest etiologic agents from 2 years and above. The proportion of *Coronavirus 19* (SARS-CoV-2) was highest in children less than 6 months of age. RSV was a common cause of ILI in children 6 years and below while *Mycoplasma pneumoniae* (*Mp*) was more frequently identified from patients 7 years and older (Table 3).

Co-detection of multiple etiologies

Co-detection of other pathogens was found in 329 (48.2%) of cases. One hundred thirty-eight patients had two pathogens detected on BIOFIRE® COVID-19 test, in which the commonest combination was *Human rhinovirus* plus *Parainfluenza virus* (PIV) (HRV+PIV) (15.9%).

Table 2. Etiological agents of ILI using BIOFIRE® COVID-19 respiratory panel among pediatric cases of ILI, St. Luke's Medical Center, Quezon City, Philippines, January 2021 to August 2024, n=682

Etiology	Number	Percent
Human Rhinovirus/Enterovirus	259	38
Influenza A	156	23
Adenovirus	145	21
Parainfluenza Virus	87	13
Respiratory Syncytial Virus	63	9
Mycoplasma pneumoniae	44	6
Human Metapneumovirus	36	5
Coronavirus 19	35	5
Coronavirus HCOV-OC43	23	3
Influenza B	11	4
Coronavirus HKU1	6	0.9
Coronavirus HCOV-NL63	6	0.9
Coronavirus 229E	3	0.4
Bordetella parapertussis	3	0.4
Bordetella pertussis	2	0.3

Note: Sum of percentages exceed 100% due to occurrence of mixed infections

Seasonal distribution of etiological agents

The detection rates of pathogens were not evenly distributed during the different seasons over the study period. During the rainy season (June to November), the most common etiologic agents detected were *Coronavirus* NL63 (HCoV-NL63), *IAV* and *Influenza B* (IBV), and RSV. In contrast, during the dry season (December to May), prevalent etiologic agents included AdV, *Bordetella parapertussis (B parapertussis), Bordetella pertussis* (*B pertussis*), *Coronavirus* 229E (HCoV-229E), *Coronavirus HKU1 (HCoV-HKU1)*, *Coronavirus OC43 (HCoV-OC43*), *Coronavirus*-19 (SARS-CoV-2). *Human metapneumovirus (HMPV)*, HRV, *Mp*, and *Parainfluenza virus 1-4 (PIV)* were evenly distributed within the year (Figure 1).

Complications of ILI

The most common complications were pneumonia 251 (36.8%), exacerbation of bronchial asthma 45 (6.6%), and febrile seizures 33 (4.8%) (Table 1).

Risk factors for development of complications of ILI

Univariate analysis of risk factors for development of complications of ILI was limited to the top 3 complications identified in this paper, namely pneumonia, exacerbation of bronchial asthma and febrile seizures since the proportion of other ILI complications was low.

Table 3. Predominant etiologic agents of ILI by age group among pediatric cases of ILI, St. Luke's Medical Center, Quezon City, Philippines, January 2021 to August 2024

ETIOLOGIC AGENT	AGE GROUP									
	Less than 6mos (n=31)		6 mos to 1 yr (n=130)		2 to 6yrs (n=307)		7 to 12yrs (n=178)		13 to 18yrs (n=36)	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Human Rhinovirus/Enterovirus	12	38.7	63	48.5	102	33.2	76	42.7	7	19.4
Influenza A	3	9.7	14	10.8	69	22.5	57	32.0	12	33.3
Adenovirus	1	3.2	20	15.4	79	25.7	40	22.5	5	13.9
PIVfluenza Virus	3	9.7	22	16.9	41	13.4	13	7.3	4	11.1
Respiratory Syncytial Virus	6	19.4	19	14.6	20	6.5	9	5.1	1	2.8
Mycoplasma Pneumoniae	2	6.5	7	5.4	14	4.6	16	9.0	5	13.9
Human Metapneumovirus	2	6.5	7	5.4	23	7.5	4	2.2		0.0
Coronavirus 19 (SARS-CoV-2)	11	35.5	15	11.5	5	1.6	2	1.1	2	5.6
Coronavirus HCOV-OC43	1	3.2	3	2.3	14	4.6	3	1.7	2	5.6
Influenza B		0.0	1	0.8	2	0.7	7	3.9	1	2.8
Coronavirus HKU1	2	6.5	1	0.8	2	0.7		0.0	1	2.8
Coronavirus HCOV-NL63			2	1.5	1	0.3	3	1.7		
Coronavirus 229E				0.0	4	1.3				
Bordetella Parapertussis			1	0.8	2	0.7				
Bordetella Pertussis					2	0.7				

The only risk factor for development of pneumonia which was statistically significant among the clinical variables was the number of days from onset of ILI to hospitalization. The odds of developing pneumonia further increased as the length of time from onset of ILI to hospitalization increased. There was no risk factor among demographic variables associated with exacerbation of bronchial asthma nor febrile seizures which reached statistical significance (Table 4)

Among the etiologic agents, only HMPV (OR 3.24, P =0.001) and RSV (OR 2.023, p =0.009) were risk factors for pneumonia among ILI cases on univariate analysis. There were no etiologic agents associated with increased risk for bronchial asthma. Though not reaching statistical significance, there were a number of bronchial asthma cases with concomitant HRV. Only SARS-CoV-2 (OR 3.685, p = 0.022) was associated with increased risk for febrile seizures (Table 4).

On multivariate analysis, only days from onset of illness.and *SARS-CoV-2* were significant risk factors for pneumonia. No demographic factor nor etiologic agent was a significant risk factor for exacerbation of bronchial asthma nor febrile seizure on multivariate analysis (Table 4).

DISCUSSION

ILI is a major cause of yearly outbreaks worldwide. (3) Although most cases of ILI are self-limiting,[3] it may be associated with complications especially among high-risk groups such as in the pediatric age group. Effective management of ILI, when initiated soonest will minimize the likelihood of developing complications;

Table 4. Univariate and Multivariate analysis of factors associated with the top 3 complications of pediatric cases of ILI, St. Luke's Medical Center, Quezon City, Philippines, January 2021 to August 2024

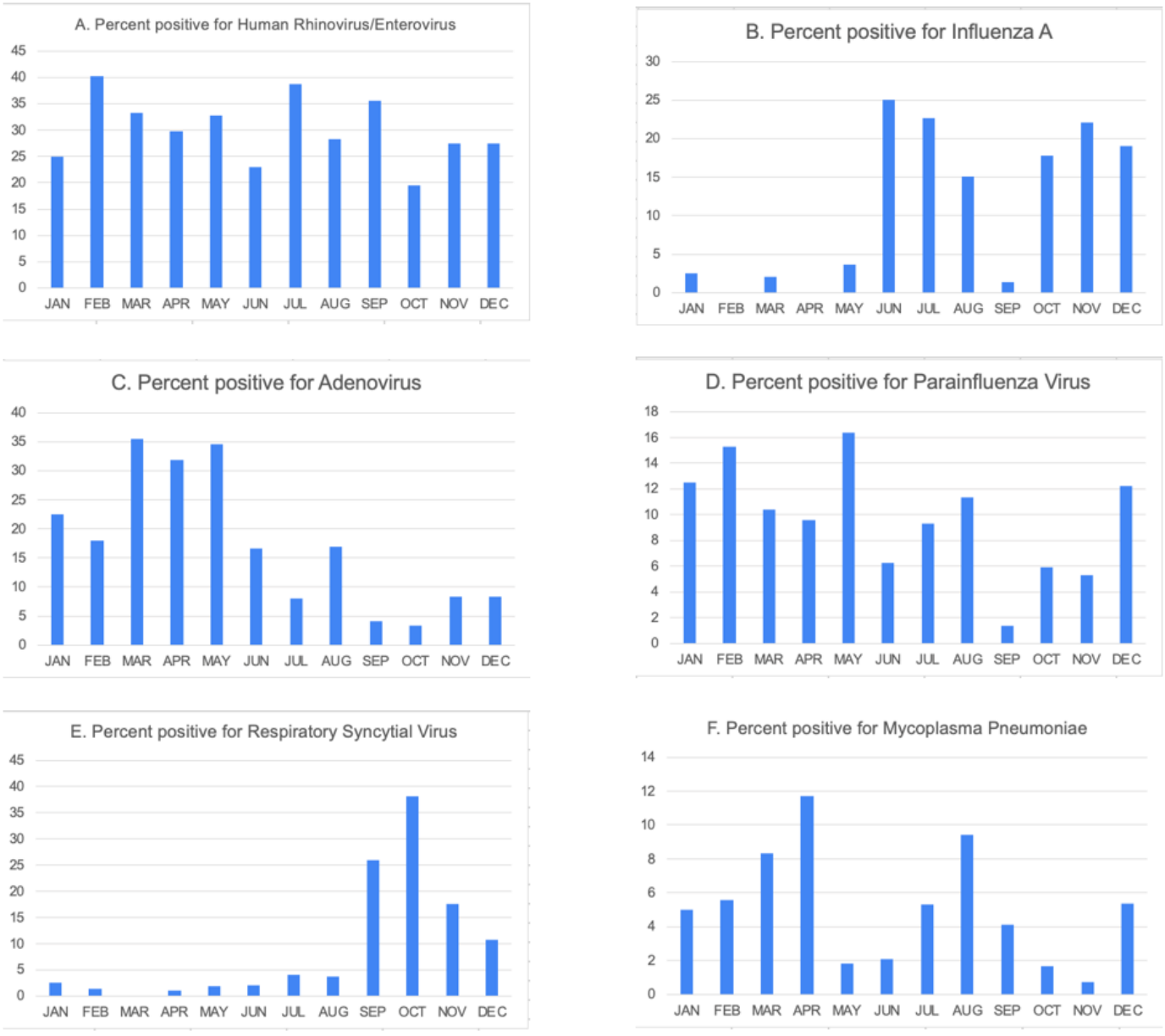
Variable	Univariate analysis OR (95% CI)			Multivariate analysis Adjusted OR (95% CI)		
	Pneumonia	Exacerbation of Bronchial Asthma	Febrile seizures	Pneumonia	Exacerbation of Bronchial Asthma	Febrile seizures
Age (<6mo)						
Age (6mo-1yo)	1.865 [0.788-4.413]	37390186.322 [0]	2.956 [0.359-24.352]			
Age (2-6yo)	1.386 [0.611-3.147]	179305359.497 [0]	2.105 [0.265-16.716]			
Age (7-12yo)	1.433 [0.610-3.369]	113894646.223 [0]	0.503 [0.048-5.291]			
Age (13-18 yo)	0.771 [0.234-2.545]	156694445.602 [0]	0.625 [0.027-14.685]			
Sex (Male)	1.158 0.835-1.606]		0.563 [0.261-1.212]			
Sex (Female)	0.874 [0.530-1.443]	0.388 [0.191-0.785]	2.121 [0.861-5.220]			
Influenza Vaccine	0.252 [0.026-2.42]	0.616 [0.206-1.840]	.000			
Polio vaccine	5.122 [0.772-33.968]	5.746 [0.520-63.483]	3.506 [0.304-40.426]			
MMRV		.000				
BMI (<18.5)	0.748 [0.455-1.228]		1.529 [0.525-4.451]			
BMI (18.5-22.9)	0.725 [0.265-1.979]	0.823 [0.306-2.216]	.000			
BMI (23-24.9)	0.279 [0.053-1.484]	.000	4.337 [0.346-54.318]			
BMI (>25)		1.025 [0.095-11.088]				
Days from onset of ILI to Hosp (0-1 days)	2.332 [1.402-3.880]		0.370 [0.164-0.836]	1.364 [1.096-1.698]	0.763 [0.504-1.155]	0.463 [0.276-0.774]
Days from onset of ILI to Hosp (2-4 days)	2.511 [1.468-4.295]	0.492 [0.227-1.068]	0.214 [0.075-0.612]			
Days from onset of ILI to Hosp (5-7 days)	3.132 [1.094-8.969]	0.386 [0.160-0.931]	.000			

Days from onset of ILI to Hosp (9-10 days)	0.195	0.679 [0.134-3.447]	0.077			
Adenovirus	0.783 [0.531-1.155]	0.161 [0.038-0.671]	0.815 [0.330-2.014]			
Bordetella parapertussis	0.858 [0.077-9.510]	0	0			
Bordetella pertussis	1.720 [0.107-27.619]	0	0			
Coronavirus 229E	0.858 [0.077-9.510]	0	0			
Coronavirus HKU1	1.726 [0.346-8.616]	0	0			
Coronavirus HCOV-NL63	0.341 [0.040-2.934]	2.873 [0.328-25.127]	0			
Coronavirus HCOV-OC43	1.6 [0.695-3.683]	0.635 [0.084-4.824]	0.891 [0.116-6.817]			
Coronavirus-19	0.209 [0.073-0.599]	0.403 [0.054-3.014]	3.685 [1.329-10.215]	4.405 [1.517-12.792]	2.645 [0.352- 19.883]	0.299 [0.106-0.848]
Human metapneumovirus	3.244 [1.612-6.525]	0	1.867 [0.542-6.434]	0.3 [0.148-0.609]	112480668.507 [0]	0.448 [0.126-1.584]
Human Rhinovirus/ Enterovirus	1.074 [0.780-1.4789]	3.563 [1.878-6.762]	0.424 [0.181-0.992]			
Influenza A	0.515 [0.345-0.768]	0.226 [0.069-0.739]	0.903 [0.384-2.123]			
Influenza B	0.640 [0.168-2.433]	1.425 [0.178-11.386]	0			
Mycoplasma pneumoniae	3.257 [1.725-6.148]	1.456 [0.497-4.268]	0			
Parainfluenza virus 1-4	1.117 [0.704-1.773]	0.651 [0.227-1.865]	2.309 [1.007-5.296]			
Respiratory Syncytial Virus	2.023 [1.201-3.408]	1.911 [0.816-4.478]	0.296 [0.040-2.203]	0.469 [0.276-0.798]	0.553 [0.235-1.299]	2.996 [0.398-22.523]

however, management decisions have to be based on etiology and epidemiologic and clinical data peculiar to the locality. Worldwide, countries including the Philippines have initiated surveillance of ILI but testing has been

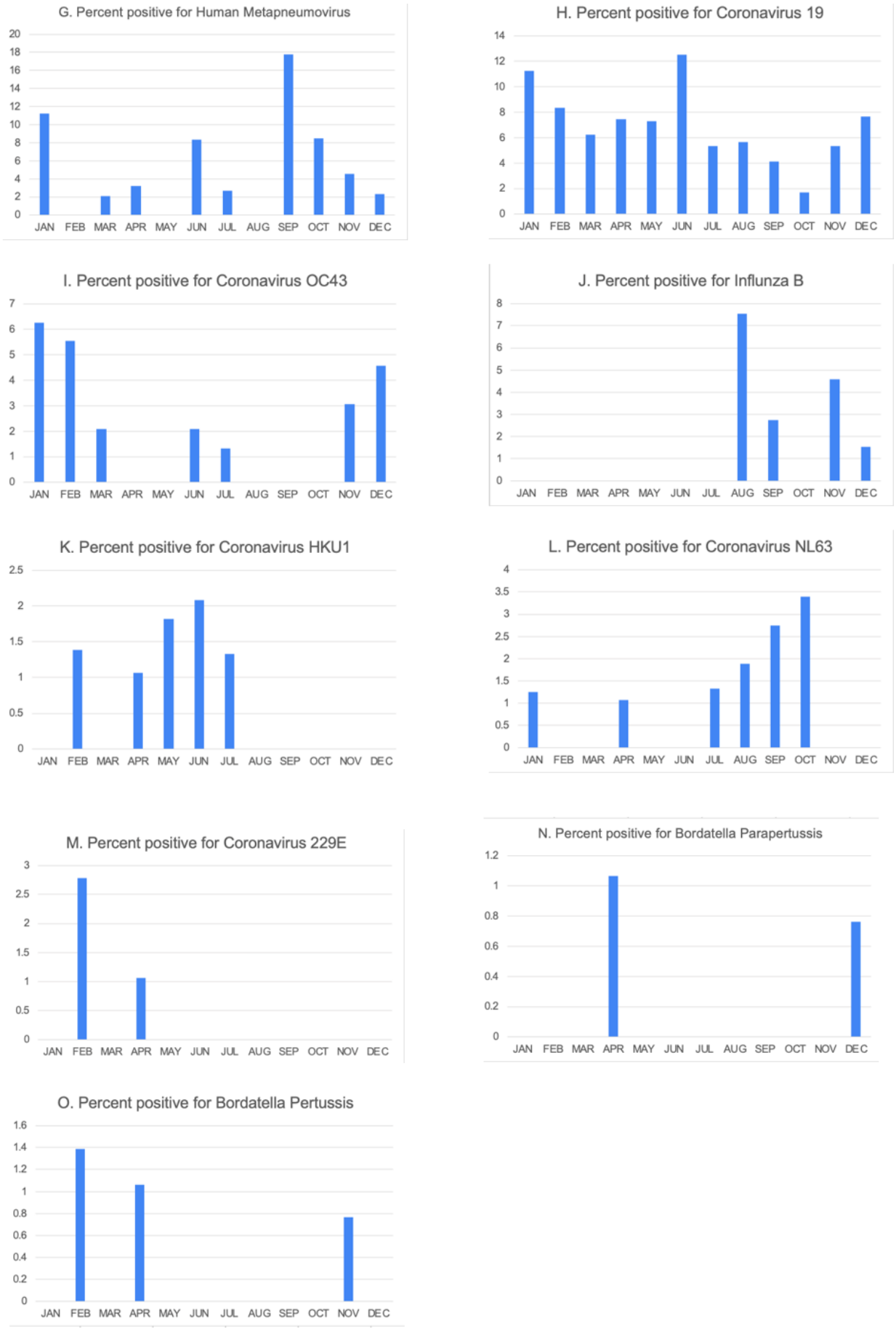
limited to detection of the *Influenza* virus. Lucero et. al. did a retrospective analysis of Philippine influenza surveillance data from 2006 to 2012 to determine seasonality and to calculate the epidemic curves and alert thresholds but surveillance was limited to *Influenza* alone.[8] The introduction of multiplex nucleic acid amplification tests in SLMC in 2021 paved the way for the rapid identification of microorganisms presenting similarly as ILI. This is the first local study on the use of BIOFIRE® COVID-19 to determine the etiology of ILI among hospitalized pediatric patients over a period of several years.

Figure 1a. Annual seasonality of etiological agents identified among pediatric ILI cases, expressed as the mean proportion positive per calendar month, St. Luke's Medical Center, Quezon City, Philippines, January 2021 to August 2024



Most admitted patients were male 57.2%. Although our statistical analysis did not show that sex was a significant variable for developing complications of ILI, there are studies which showed that males were more susceptible to respiratory tract infections and have a more severe course and higher mortality compared to females.[13] Anatomical factors may play a role in male predominance since peripheral airways are narrower during

Figure 1b. Annual seasonality of etiological agents identified among pediatric ILI cases, expressed as the mean proportion positive per calendar month, St. Luke's Medical Center, Quezon City, Philippines, January 2021 to August 2024



the first year of life among males, although some studies indicate that after the first year of life, the male predominance in respiratory tract infections may still persist due to a combination of anatomical, immunological and behavioral factors.[14]

The data showed that 80.1% of patients had a low body mass index (BMI) of <18.5. In a study by Wyrick et al, hospitalization among underweight patients was increased for those patients with respiratory infections. Low body mass index can increase the risk of infections due to impaired immune function, reduced muscle mass, altered mucosal defenses such as impaired mucociliary clearance leading to prolonged exposure to microorganisms.[15]

The most frequently reported etiologic agents in this study were HRV, IAV, AdV, HMPV and RSV which were similar to those previously reported in studies on ILI.[16,17] With respect to etiologic agents by age group, RSV was also seen predominantly in infants younger than 6 months of age; however, we additionally reported SARS-CoV-2 in this age group.[16]

HRV was the most predominant pathogen detected - 38% of the cases. Various studies showed that HRV is a major cause of lower respiratory infections and asthma exacerbations in children and adults. One study noted that children with a history of asthma or wheezing had the highest rate of rhinovirus-associated hospitalizations at 25–28/1000 children/year.[18]

IAV was one of the most frequently isolated pathogens in the study at 23%, especially during the rainy season although our statistical analysis did not show that IAV was a significant variable for developing pneumonia and other complications of ILI. This is similar to studies from other tropical countries including Senegal and Cambodia with respect to seasonality.[19,20] The seasonal patterns of the various etiologic agents of ILI described in this study is similar those of countries with tropical climates.[3,21]

As in other published studies, co-detection of multiple pathogens was found in 48.2% of our cases. Various reports have demonstrated that 2 or 3 viral species can be detected in 10-20% of children with pneumonia, and that mixed viral-bacterial infection can be found in up to 45% of cases.[3,16,22]

On univariate analysis, only HMPV and RSV were significant risk factors for pneumonia among the microorganisms tested. Discovered in 2001, HMPV is a significant cause of upper and lower respiratory tract infections, primarily in young children. It accounts for approximately 643/1000 hospitalizations per year in children less than 5 years and is more severe in children 0-5 months of age. In our study, HMPV was mostly identified in children 2-6 years of age.[23]

RSV is a significant cause of lower respiratory tract infection, hospital admissions, and mortality especially in infants less than 6 months of age. More than 95% of RSV-associated acute lower respiratory infection episodes and RSV-attributable deaths occur in low-income and middle-income countries (LMICs).[24] It is also associated with recurrent asthma and impaired lung function.[25]

There were no etiologic agents associated with increased risk for bronchial asthma among ILI cases. Though not reaching statistical significance, there were a number of bronchial asthma cases with HRV, either alone or as one of co-infecting etiologic agents. Children with asthma have reduced production of interferons (especially interferon-β and interferon-λ), which are critical for controlling viral infections, including HRV.[26] In addition, chronic airway inflammation and structural changes in asthmatic airways (e.g., thickened walls and increased mucus production) create an environment that facilitates viral infection. Also, asthmatic children often have higher levels of intercellular adhesion molecule-1 (ICAM-1), which HRV uses as a receptor to infect cells. This makes their respiratory epithelium more prone to infection.[18]

Only SARS-CoV-2 was associated with increased risk for febrile seizures among ILI cases. A study done by Han et. al in 2023 showed that 1.4% of children under five years of age with SARS-CoV-2 required hospitalization, with febrile seizures as one reason for hospital admission[27] thus, SARS-CoV-2 infection among children presenting with febrile seizures should be a consideration among patients with ILI.

On multivariate analysis, only days from onset of illness.and *SARS-CoV-2* were significant risk factors for pneumonia. Pneumonia secondary to SARS-CoV-2 results from binding of the viral spike protein to the angiotensin-converting enzyme 2 (ACE2) cellular transmembrane receptor found on the apical membranes of respiratory epithelial cells and subsequent release of viral RNA into the cell and its replication. The high concentration of ACE2 receptors in pneumocytes makes the lung more susceptible to infection by the SARS-CoV 2 virus which commonly manifests as interstitial pneumonia.[28]

In a study by Jimenez-Garcia on children hospitalized for pneumonia during the COVID-19 pandemic, 20% of 111 children was fully attributable to SARS-CoV-2 with 17% having mixed infections. Although signs and symptoms of SARS-CoV-2-associated pneumonia were generally nonspecific, children with SARS-CoV-2-associated pneumonia were frequently older, and typically presented with headache, vomiting, asthenia and had lymphopenia and thrombopenia when compared to children with non-COVID pneumonia.[29]

Having more precise information on the etiology and epidemiology of ILI may potentially result in more specific interventions to reduce the burden of ILI and its complications in the Philippines such as: administering antimicrobials for microorganisms for which these are recommended, more aggressive treatment of concomitant medical problems like bronchial asthma, immunization of children against the most common etiologic agents of ILI like IAV, IBVSARS-CoV-2, and *Bordetella pertussis,* maternal immunization with RSV vaccine,[30] dissemination of appropriate health education programs and initiation of corresponding infection control and prevention measures.

There is need for continuing surveillance of ILI cases considering that the etiology and epidemiology of ILI may change with time. Lastly, there is still much room for conducting research on ILI in order to develop strategies to address the unknown information on its prevention and control.

Study Limitations

1. This study utilized BIOFIRE® COVID-19 respiratory panel, a fully automated multiplex PCR test with a rapid turnaround time and is able to detect SARS-CoV-2 and 14 other viral and bacterial pathogens. The test may not have been able to detect other microorganisms causing ILI; however, it has been very useful in identifying etiologic agents of infections in a country like the Philippines where testing for viruses is not readily available. Its performance has been comparable to real time PCR assays and our results had been comparable to results of studies on ILI in other countries which conducted more comprehensive tests for etiology.
2. Our study was done partly at the time of the COVID-19 pandemic which may have potentially influenced the results but our study also covered the period after the COVID-19 pandemic. Except for the identification of SARS-CoV-2 as one of the etiologic agents in 5% of the enrolled cases, the other etiologic agents identified were similar to results of etiology studies on ILI in other countries, Furthermore, the continuing identification of SARS-CoV-2 from patients beyond the pandemic era also indicates that COVID-19 had already transitioned from a pandemic (widespread, rapidly spreading infection) to an endemic state (regularly occurring within a population) and therefore this virus should be integrated as part of disease control programs for respiratory viruses.

Conclusions

We retrospectively examined medical records of pediatric patients hospitalized for ILI to determine the epidemiologic characteristics and etiology of ILI cases. Data showed that ILI was a significant medical condition that can lead to complications, most notably pneumonia. Longer duration from onset of ILI to hospitalization and SARS-CoV-2 as an etiologic agent were significant risk factors for pneumonia

There is need to establish and sustain a community-based active surveillance program on ILI in the Philippines to be able to gather population-based, up-to-date data to serve as basis for planning and implementation of health programs including preparedness for future outbreaks.

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