MICROBIOLOGICAL CHARACTERISTICS OF SEVERE PNEUMONIA IN CHILDREN FROM 2 MONTH TO 24 MONTH HOSPITALIZED AT THE RESPIRATORY DEPARTMENT OF CHILDREN'S HOSPITAL 1

Nguyen Thi Thu Suong[1,2*], Tran Anh Tuan[1,2], Nguyen Thi Cam Ly[1]
[1]Medicine Vietnam National University
[2]Children's Hospital 1

ABSTRACT

Objective: *To compare some of clinical features, laboratory finding and treament of severe pneumonia caused by bacteria, virus and bacteria-virus coinfections based on PCR (Polymerase Chain Reaction) results NTA (Naso tracheal aspiration), and rapid test to finding RSV, AdV results in children from 2 months to 24 months hospitalized at the Respiratory Department of Children's Hospital 1.*

Materials and method: *A prospective, cross-sectional study with analysis of 138 severe cases of pneumonia requiring oxygen when patients were treated at Respiratory Department Children's Hospital 1 from 11/2021-8/2022, nasopharyngeal swab was tested for RSV, AdV with rapid test, collecting NTA multi-agent PCR of lower respiratory tract infections and culture as an antibiotic map for microbial pathogens,*

Results: *During the period from 11/2021 to 8/2022, 138 cases that met the criteria were included in the study. the rate of bacteria infection (+): 21%, virus (+): 6,5%, bacteria-virus coinfections: 68,8%, culture NTA (+): 24,6%, RSV (+) 31,8% and AdV (+) 5,1% were detected in nasopharyngeal swab by on rapid test. Bacteria and virus were detected in PCR NTA: S.pneumoniae 49,8%, MRSA 13,1%, H. influenza non-B 9%, M. cataharrlis 4,9%, M. pneumoniae 5,7%, C. trachomatis 13,1%, CMV 25,3%, RSV 31,8%, Parainfluenzavirus 15,2%, Adenovirus 5,1%, Influenzavirus A 0,7%, Rhinovirus 8,7%, Epstein Barr virus 3,6%, Bocavirus 20,2%. Bacterial infection mainly had fever ≥ 390 C (p=0,000204), SpO2 level < 85% mainly in virus and bacteria-virus coinfections group, severe chest constriction mainly in virus and bacteria-virus coinfections group (p=0,001), main wheeze mainly in the viral group (p=0,00125), the number > 15000TB/mm3 (p=0,047), the number of N ≥ 8000TB/mm3 and the CRP > 35 mg/L mainly in the bacteria group (p=0,021), and the group bacteria-virus coinfections. Chest X-ray focus on one side was mainly in the bacteria group, bilateral infiltrative lesions were mainly in the virus group, The virus group was treated mainly for less than 7 days and did not need to change antibiotics, respiratory support was needed NCPAP levels were higher. the bacteria-virus co-infected had more poor initial antibiotic response and longer treatment time.*

Conclusions: *Bacteria-virus coinfections accounted for a high proportion in pneumonia of children under 2 years of age in S.pneumoniae and RSV infection accounted for the highest rate, pneumonia caused by clinical virus wheezing and respiratory failure more than pneumonia caused by bacteria, bacteria-virus coinfections makes pneumonia less responsive to initial antibiotics and prolonged treatment time. The rapid test for detecting RSV and AdV in thí study has results within 15 minutes and the value is similar to PCR, support the treatment plan after admission, prevent the spread.*

Keyword: *Bacterial pneumonia, viral pneumonia, bacteria-virus coinfections pneumonia.*

Received: October 15th, 2023; Accepted: December 10th, 2023
Corresponding Author: Nguyen Thi Thu Suong
Email: nttsuong@medvnu.edu.vn
Address: Medicine Vietnam National University

I. INTRODUCTION

Pneumonia accounts for about 15% of all deaths in children under 5 years old, and most of these deaths occur in low- and middle-income countries6,10,15,16. Despite guidelines for the efficacy of antibiotic therapy and vaccine efficacy, community-acquired pneumonia remains a major cause of death in developing countries6.16. The prevalence of respiratory failure among pneumonia children requiring hospitalization was 31%2.16. Besides respiratory support, antibiotics play a crucial role in treatment. About 28.7% of pneumonia cases in children who require hospitalization show no response to initial intravenous antibiotic therapy, necessitating immediate oxygen therapy within 24 hours of admission2. Therefore, identifying the causative agent in severe pneumonia cases requiring immediate oxygen at admission holds significant importance. Viral pathogens have an increasing prevalence, sometimes leading to significant mortality rates, causing 50%-90% of lower respiratory tract infections in children under 5 years old1,3,7,14,11. Viral pneumonia presents diverse strains, with some cases exhibiting mild clinical conditions that respond well to simple treatments. However, certain viral strains contribute to severe pneumonia, increased transmission rates, and coinfections with drug-resistant bacteria. Coinfection rates of bacteria and viruses in children can reach up to 75%7. Bacterial pneumonia following viral infection can exacerbate clinical conditions. Bacterial coinfection might contribute to increased severity and mortality rates in patients1,2,16. However, clinical manifestations of bacteria-virus coinfections lack distinct characteristic symptoms to date. Hence, we conduct this study to investigate the prevalence of viral infections, coinfection rates, analyze clinical characteristics, laboratory findings, microbiological features, and treatment outcomes of severe pneumonia caused by viruses, bacteria, and bacteria-virus coinfections in children aged 2 to 24 months requiring oxygen therapy admitted to the Emergency Room, Respiratory Department of Children's Hospital 1.

II. RESEARCH SUBJECT AND METHOD

2.1. Study design

Cross-sectional descriptive prospective study.

2.2. Study population

Pediatric patients aged 2 months – 24 months diagnosed with severe pneumonia requiring oxygen therapy upon admission and treated at the Respiratory Department of Children's Hospital 1 from November 2021 to August 2022.

2.3. Sampling population:

Children aged 2 to 24 months undergoing treatment for severe pneumonia requiring oxygen therapy admitted to the Emergency room at the Respiratory Department of Children's Hospital 1 from November 2021 to August 2022.

2.4. Sampling criteria

Children admitted to the Respiratory Department of Children's Hospital 1 meet 3 criteria:

1. Age: 2 months – 24 months old.

2. Clinical symptoms: cough, shortness of breath, age-related tachypnea, chest retraction, oxygen indication (WHO 2016) :

- Central cyanosis
- $SpO_2 < 90\%$
- Unable to drink, feeding difficulties
- Rapid breathing > 70 times/ minute
- Head nodding with breathing rhythm
- Restlessness, fussiness due to lack of oxygen
- Nasal flaring.

3. Chest X-ray: showing images of tissue damage, interpreted by the head radiologist of the X-ray Department at Children's Hospital 1 who participated in the study.

2.5. Exclusion criteria

- Pediatric patients infected with covid by rapid test and or positive PCR.

- Lack of proper sample collection or failure to meet NTA standards during the study.

Children who received intravenous antibiotics within 24 hours before hospitalization

2.6. Sampling technique

Convenient sampling was employed until the required sample size was achieved.

2.7. Sample size

Apply the formula for calculating a sample size that approximates a ratio

$$n = \frac{Z^2_{(1-\alpha/2)}P(1-P)}{d^2}$$

- α is the probability of a type I error, a value of α is the threshold of error. Select α = 0.05
- Z is the normal distribution value. When α = 0.05, Z1- α/2 = 1.96
- P expected ratio. Select P = 0.5 to get the largest sample size.
- d is the allowable error (accuracy). Select d = 9%

→ n = 118.

2.8. Data collection

All pediatric patients who meet the sampling criteria will have their medical history taken and undergo clinical examinations. Laboratory tests including: hemogram, CRP, chest X-ray, and NTA will be conducted immediately after the patient receives oxygen therapy. The X-ray images will be interpreted by the chief radiologist. Disease progression, laboratory results, and changes in therapy will be continuously recorded during treatment.

NTA collection procedure: Collect 1 ml of NTA fluid for PCR testing and culture to detect RSV and Adenovirus antigens in nasal discharge using the "FUJI DRI-CHEM IMMUNO AG RSV/AdV" kit, based on the principle of immune-electrodeposition, with a sensitivity of 95% and specificity of 100% (compared to standard PCR).

2.9. Data processing

All data will be processed using SPSS 20.0.

III. RESEARCH RESULT

During the period from November 2021 to August 2022, there were 138 pediatric patients aged 2 to 24 months admitted to the Respiratory Department who met the sample selection criteria. All these patients underwent rapid testing for RSV and AdV, as well as NTA within the first 24 hours of admission.

1. General characteristics of the study population

Male patients outnumbered females, with a male-to-female ratio of 67.4% to 32.6% (2:1).

The average age was 7.39 months, ranging from the youngest at 2 months to the oldest at 23 months.

Up to 32 (23.2%) cases of premature and low birth weight and 29 cases (21%) exhibited respiratory distress after birth.

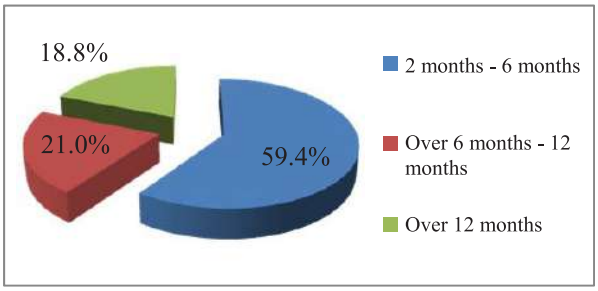

Chart 1. Age distribution (N=138)

Comment: The most common age is from 2 months - 6 months (59.4%), followed by the age over 6 months - 12 months 21%, over 12 months at least 18.8%.

2. Microbiological characteristics

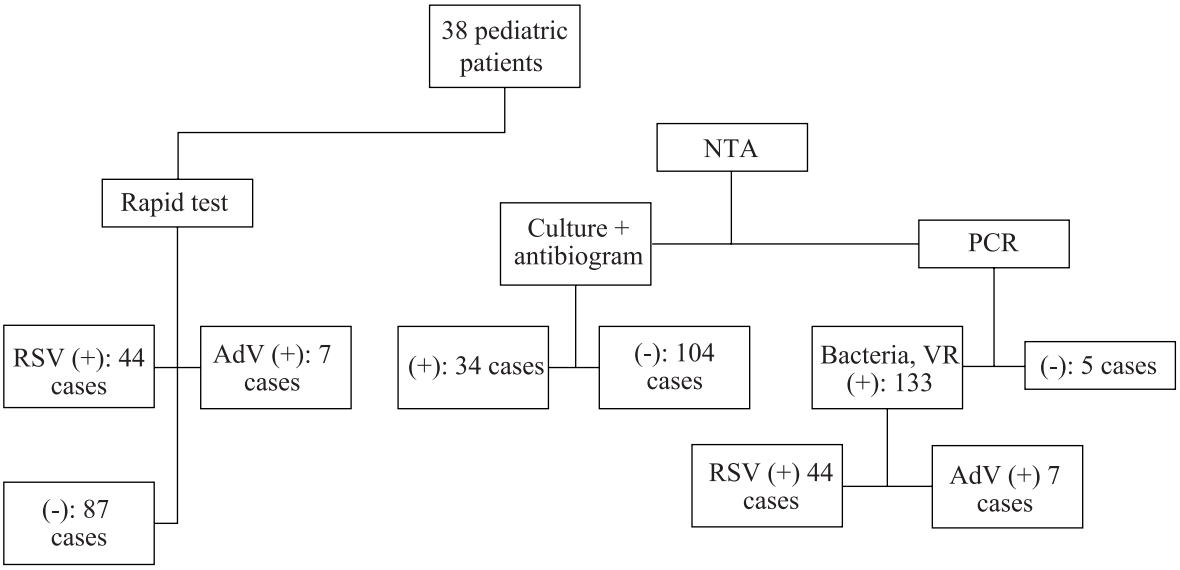

Diagram 1. The number of cases detecting agents by the results of rapid tests for RSV and AdV, PCR and NTA culture for detecting agents.

Comment: The number of RSV, AdV infections by rapid test coincides with the detection results of PCR and NTA

NTA culture: rate (+): 24.6%.

PCR: Bacteria (+): 21%, Virus (+): 6.5%, Bacteria-Virus coinfection: 68.8%, not detected: 3.7%.

Table 1. Detection rate of bacteria via NTA culture

Bacteria agents	**NTA culture (N=34)**
	TL
S. pneumoniae	13 (38,2%)
*S. aureus**	5 (14,7%)
H. influenzae non type B	1 (2,9%)
Pseudomonas	2 (5,6%)
E. coli-ESBL (+)	4 (11,8%)
E. coli -AmpC (+)	4 (11,8%)
Klebsiela-ESBL (+)	2 (5,8%)
Acinetobacter	3 (8,8%)
Acinetobacter	3 (8,8%)

Comment: Highest rate of *S. pneumoniae* on NTA culture, (*): *S. aureus* rate of 14.7%, including 3 cases of MRSA.

Table 2. Bacteria detection rate via PCR result

Bacteria agents	NTA culture (N=34)
	TL
S. pneumoniae	13 (38,2%)
*S. aureus**	5 (14,7%)
H. influenzae non type B	1 (2,9%)
Pseudomonas	2 (5,6%)
E. coli-ESBL (+)	4 (11,8%)
E. coli -AmpC (+)	4 (11,8%)
Klebsiela-ESBL (+)	2 (5,8%)
Acinetobacter	3 (8,8%)
Acinetobacter	3 (8,8%)

Comment: The highest rate of *S. pneumoniae* is 49.8%. Atypical bacteria like *M. pneumoniae* were detected but at a lower rate.

Table 3. Bacteria detection rate via PCR result

Agent type	Rate
S.pneumoniae	49,8%
MRSA	13,1%
MRSE	10,6%
S. epidermidis	4,1%
H. non-B influence	9%
M. cataharrlis	4,9%
M. pneumoniae	5,7%
C. trachomatis	13,1%
B. cepacia	3,3%
E. coli	18,8%
Klebsiela	11,3%
Acinetobacter	6,5%
Pseudomonas	6,5%

Comment: The highest rate of RSV infection, other severe pneumonia-causing viruses such as adenovirus, influenzavirus are also encountered at low rates.

3. Analysis of some clinical, subclinical characteristics and treatment outcomes in 3 bacteria, virus and bacteria - virus groups

Table 4. Rates of some clinical features of 3 pneumonia groups infected with bacteria, virus and bacteria - virus

Characteristics (N=133)		Bacteria (n=29)	Virus (n-9)	Bacteria - Virus (n=95)	Inspection χ^2
Temperature	< 39°C	5 (17,2%)	7 (77,8%)	54 (56,8%)	P=0,000204, χ^2=16,998
	≥ 39°C	24 (82,8%)	2 (22,2%)	41 (43,2%)	
SpO_2	< 85%	2 (6,9%)	6 (66,7%)	42 (44,2%)	P=0,834
	85% - 90%	11 (37,9%)	3 (33,3%)	48 (50,5%)	
	91% - 94%	16 (55,2%)	0 (0,0%)	5 (5,3%)	
Chest retractions	Experiencing chest retractions	25 (86,2%)	3 (33,3%)	48 (50,5%)	P=0,001, χ^2=13,784
	Experiencing severe chest retractions	4 (13,8%)	6 (66,7%)	47 (49,5%)	
Wheezing		4 (13,8%)	7 (77,8%)	51 (53,7%)	P=0,000125, χ^2=17,974

Comment: Bacterial infections primarily exhibited fever ≥ 39°C (p=0.000204), SpO2 levels < 85% were mainly in the viral and viral-bacterial groups, severe chest retractions were mainly in the viral and viral-bacterial groups (p=0.001), and cough was predominantly in the viral group (p=0.000125).

Table 5. Rates of subclinical characteristics of 3 pneumonia groups infected with bacteria, virus and bacteria - virus

Subclinical (N=133)		Bacteria (n=29)	Virus (n-9)	Bacteria - Virus (n=95)	Inspection χ^2
BC count	≤ 15000TB/mm^3	8 (27,6%)	8 (88,9%)	54(56,8%)	P=0,047, χ^2=6,003
	> 15000TB/mm^3	21 (72,4%)	1 (11,1%)	41(43,2%)	
N count	< 8000TB/ mm^3	8 (27,6%)	8 (88,9%)	64 (67,4%)	P=0,118
	≥ 8000TB/mm^3	21 (72,4%)	1 (11,1%)	31 (32,6%)	
CRP	≤ 35 mg/L	6 (20,7%)	7 (77,8%)	39 (41,1%)	P=0,021, χ^2=2,853
	> 35 mg/L	23 (79,3%)	2 (22,2%)	56 (58,9%)	
XQ	Bilateral infiltrate	6 (20,7%)	5 (55,6%)	43 (45,3%)	P= 0,967
	Unilateral infiltrate	65,5 (%)	1 (11,1%)	25 (26,3%)	
	Consolidation	2 (6,8%)	0 (0,0%)	10 (10,5%)	
	Upper lobar atelectasis P	2 (6,8%)	3 (33,3%)	16 (16,8)%	
	Pneumonia - pleural effusion	0 (0,0%)	0 (0,0%)	1 (1,1%)	

Comment: BC count > 15,000 cells/mm3, N count ≥ 8,000 cells/mm3 and CRP > 35 mg/L were primarily seen in the bacterial and bacterial-viral groups. Unilateral chest X-ray lesions were mainly in the bacterial group, while bilateral infiltrates were predominant in the viral group.

Table 6. Rates of treatment characteristics of 3 pneumonia groups infected with bacteria, virus and bacteria - virus

Treatment characteristics (N=133)		Bacteria (n=29)	Virus (n-9)	Bacteria - Virus (n=95)	Inspection χ^2
Treatment duration	< 7 days	8 (27,6%)	6 (66,7%)	20 (21,1%)	P=0.01, χ^2= 13,199
	7 – 14 days	15 (51,7%)	2 (22,2%)	35 (36,8%)	
	> 14 days	6 (20,7%)	1 (11,1%)	40 (42,1%)	
Antibiotic exchange	Not	13 (44,8%)	8 (88,9%)	36 (37,9%)	P=0,012, χ^2=8,788
	Have	16 (55,2%)	3 (33,3%)	59 (62,1%)	
Respiratory support	Oxy/cannula	21 (72,4%)	5(55,6%)	43 (45,3%)	P=0.050, χ^2=9.471
	NCPAP	6 (20,7%)	4 (57,1%)	48 (50,5%)	
	NKQ ventilator	2 (6,9%)	1 (11,1%)	4 (4,2%)	

Comment: The viral group is treated mainly for less than 7 days and did not require antibiotic change, however more respiratory support at NCPAP levels was needed, the bacteria - virus coinfections group had less initial antibiotic response, and the duration of treatment was longer.

IV. DISCUSSION

Our study recorded an average age of 7.39 months, ranging from the youngest at 2 months to the oldest at 23 months. The highest incidence occurred between 2 to 6 months (59.4%), followed by the age group of 6 to 12 months (21%), with the lowest proportion observed in children older than 12 months (18.8%). These findings align with literature indicating the highest incidence below 1 year old. Studies by Cao Pham Ha Giang noted the highest pneumonia rates in children under 12 months at 74.4%, while Le Minh Quy found pneumonia in under 12-month-olds at 69%. Additionally, Nguyen Thi Kim Phuong reported severe pneumonia rates of 55.2% in children under 12 months. As per BTS guidelines, hospitalization rates for pneumonia in the UK were 42.1% for children aged 0-1 year, and Sonego highlighted an increased risk of severe pneumonia in children under 5 years old (OR 2.3; 95% CI 1.4-3.9).

The rapid nasal swab test for RSV antigen detection showed a rate of 31.9% (44 cases), while the detection rate for AdV was much lower at 5.1% (7 cases). The cases detected with these two viruses correlated with the results from PCR NTA. Andrea H. L. Bruning and colleagues in 2017 evaluated the diagnostic value of rapid RSV and other virus tests, including AdV. Among 383 analyzed articles, rapid RSV tests achieved a sensitivity of 75.3% and specificity of 98.7%. The rapid antigen diagnostic test covers various viral pathogens such as RSV, parainfluenza viruses (1, 2, and 3), influenza viruses A and B, human metapneumovirus, and AdV, with a sensitivity of 80-90% and very high specificity of 80-100%. Literature has documented that RSV infections cause the highest rates of lower respiratory tract infections in neonates. Adenovirus is the second most common cause after RSV and leads to severe and prolonged pneumonia requiring respiratory support and potentially leading to contagion. There's no vaccine available for AdV, and RSV-induced cough in respiratory infections can persist. Approximately 10% of infants infected with RSV and hospitalized may later develop asthma, while AdV infections in severe pneumonia cases are responsible for 50% of cases developing postinfectious bronchiolitis obliterans (PIBO) after a 5-year follow-up. In recent years, viral infectious diseases have increasingly complicated global situations, posing frequent threats to public health and causing significant economic and social damages. Hence, researching, developing, and applying diagnostic techniques capable

of rapidly and accurately detecting disease-causing viruses are of great value for diagnosis, prognosis, and treatment.

Coinfection with bacteria is common in pediatric pneumonia, especially in children under 2 years old. In our study, 95 out of 138 cases (68.8%) were coinfections of bacteria and viruses. Virus-induced diseases have been on the rise, posing significant mortality risks even in healthy adults, the elderly, and notably in immunocompromised individuals. In children under 5 years old, lower respiratory tract infections caused by viruses account for 50%-90% of cases [1,2,7,16].

Community-acquired bacterial pneumonia and viral pneumonia may coexist. The review reported that the interaction of viral and bacterial infections doubled mortality [7,14]. Bacteria - virus coinfections in childhood community-acquired pneumonia is prevalent and contributes to the severe progression of infections, leading to increased mortality rates. The prevalence of Bacteria – virus coinfections in pneumonia can be as high as 68% of hospitalized patients. The interaction of viruses with resident and respiratory tract-invasive bacteria in the pathogenesis of pneumonia has been studied extensively. In a study involving 23 critically ill children with ventilator-associated pneumonia caused by viral lower respiratory tract infections, specifically RSV, Pacheco14 *et al.* found that 39% of respiratory aspirate samples indicated bacterial coinfection based on culture results. This was evident in children with RSV-associated pneumonia showing respiratory failure above 20%, prompting empirical antibiotic use for 24-48 hours pending culture results to reasonably exclude bacterial coinfection. Respiratory viral infections lead to secondary bacterial infections, commonly involving *S. aureus* and *S. pneumoniae* [1,2,6.15].

Madhusha GOnapaladeniya *et al.* studied the burden of severe pneumonia with RSV infection hospitalized at a care centre of the university in Colombo, Sri Lanka11, from June 2018 to August 2019, 131 children aged 3 months to 60 months were hospitalized with severe and very severe pneumonia. Nasal swab samples were collected for PCR testing, revealing an RSV infection rate of 42.6%, AdV infection rate of 13%, coinfection with *S. pneumoniae* at 50%, *S. aureus* at 25%50, and bacterial-viral coinfection at 75%. Another study by Le Minh Quy1 reported a similar coinfection rate of 71.3%.

We noted that bacterial infections mainly presented with fever ≥ 39°C (p=0.000204), SpO2 levels < 85% primarily in the viral and bacterial-viral groups, severe chest retractions mainly in the viral and bacterial-viral groups (p=0.001), and wheezing predominantly in the viral group (p=0.000125). Signs of respiratory failure included rapid breathing, decreased oxygen saturation (peripheral arterial oxygen saturation, SpO2 < 90%), and increased respiratory effort. Children with viral pneumonia may exhibit noticeable breathing difficulties, prompting caregivers to seek early medical attention, potentially resulting in a shorter duration of illness before hospitalization. Conversely, bacterial pneumonia may partially respond to initial antibiotic treatment, leading to a delayed progression to respiratory failure. In children under 5 years old, most pneumonia cases are caused by viruses. However, distinguishing between viral and bacterial infections or the possibility of coinfection with both is challenging. Excessive antibiotic use in many cases poses risks of developing resistance, medication side effects, and increased treatment costs. Indications suggesting bacterial pneumonia include sudden onset of high fever, painful swollen lymph nodes, chest X-rays showing lobar consolidation or pulmonary infiltrates predominantly affecting one side, and pleural effusion. In a study involving 98 children with pneumonia, wheezing was more prevalent in patients infected with viruses compared to those with bacterial pneumonia (43% vs. 16%)[14, 15].

In this study, leukocytosis (> 15,000 cells/mm3), neutrophil count (≥ 8,000 cells/mm3), and CRP (> 35 mg/L) were primarily observed in the bacterial and bacteria-virus coinfection groups. Unilateral lung lesions were predominantly

seen in the bacterial infection group, while bilateral infiltrates were mostly associated with viral pneumonia. Studies on leukocyte counts suggest that counts below 15,000/microL may not necessarily indicate bacterial causes, except in severe infections where leukocytes might also be reduced. Counts above 15,000/microL indicate bacterial purulent infections. Children with pneumonia caused by *M. pneumoniae*, flu, or AdV might also exhibit leukocytosis (> 15,000/microL). However, there is significant overlap and unreliable differentiation among the pathogens causing the disease. A meta-analysis of eight studies involving 1,230 patients concluded that children with bacterial pneumonia were more likely to have serum CRP concentrations > 35 mg/L - 60 mg/L (3.5mg/dL to 6 mg/dL) compared to those with non-bacterial pneumonia (OR 2.6, 95% CI 1.2-5.6) [15].

The reason for the difference in results between such studies can be explained by the fact that CRP is a nonspecific marker that can increase in both viral and bacterial infections, as well as in certain inflammatory non-infectious conditions. Coinfection and superinfection with bacteria on a background of viral pneumonia can influence quantitative CRP measurements. This scenario is quite common and therefore, using CRP alone to differentiate between viral and bacterial pneumonia is not reliable [9,15].

Chest X-rays showed no significant difference among the three groups, with bilateral infiltrates being the predominant finding. According to Tran Anh Tuan4,5, the most common lesion is alveolar infiltrates (84%), the majority of cases of bilateral lung lesions (78.2%) with the type of lesion being interstitial tissue lesions (87.3%) at the time of diagnosis. According to the literature, alveolar consolidation or lobar pneumonia is more common in typical bacterial pneumonia, whereas interstitial and bilateral tissue damage occurs more frequently in viral pneumonia or atypical agent pneumonia such as Mycoplasma or Chlamydia, X-ray of the lungs with bilateral symmetrical lesions: interstitial lesions, opaque glasses [1,2,4,5,11].

The bacteria that make up a large proportion of community-acquired pneumonia in children (*S. pneumoniae*, H. influenzae, *Moraxella catarrhalis*, *S. aureus*) are usually commensals in the upper respiratory tract of children. While residing there, they do not cause illness. However, for some reason, they can descend into the lower respiratory tract and cause pneumonia. Many authors agree that pneumonia often starts with an upper respiratory tract infection. Due to the high rate of coinfection between viruses and bacteria, we suspect that the primary mechanism (accounting for the majority of cases) causing community-acquired pneumonia by microbial agents (bacteria, viruses) begins as a viral infection in the upper respiratory tract. After a viral infection, the body's immunity is reduced (temporarily), and the local defense mechanisms against respiratory infections are disrupted, providing an opportunity for resident (or newly introduced) upper respiratory tract bacteria to cause infection. Viruses newly introduced into the system might also penetrate the lower respiratory tract and cause pneumonia. Additionally, there are mechanisms where bacteria or viruses can directly invade the lower respiratory tract through droplet inhalation or via the bloodstream, leading to pneumonia [12,13].

The treatment outcomes noted in the study observed that the viral group was primarily treated for less than 7 days and did not require antibiotic change, although they needed more NCPAP respiratory support. The bacteria-virus coinfection group showed less initial response to antibiotics and required longer treatment. Viruses can act as facilitators for the invasion of resident or newly introduced bacterial agents from the upper respiratory tract into the lungs, causing pneumonia. When both bacteria and virus are isolated from the same sputum sample, it cannot be conclusively determined whether VK, VR, or both are the primary causative agents of pneumonia [1,2,14].

About 5% - 10% of *S. pneumoniae* in the United States are erythromycin-resistant. In Asia, this resistance rate generally reaches 55%, in Vietnam it's 92%, and in Japan, it's around

70%12,13. Penicillin is used to treat infections caused by non-central nervous system-related pneumococci, with 96% being susceptible, 2% intermediate, and 2% resistant. In 11 Asian countries, resistance rates are recorded at 52%, with high rates up to 74% in Vietnam. The broad vaccination of children with pneumococcal conjugate vaccines has led to the emergence of new strains (termed "replacement strains"), which exhibit resistance to penicillin and other antibiotics8,12,13. After a viral infection, a child's temporary immune suppression might occur due to decreased food and liquid intake, compromised ciliary function, lung parenchymal damage, or interstitial lung tissue injury. All these factors can complicate antibiotic treatment and contribute to initial treatment failure.

V. CONCLUSIONS

Bacteria-virus coinfections account for a high proportion in pneumonia of young children under 2 years old, with *S. pneumoniae* and RSV being the most common, where RSV-associated pneumonia tends to manifest with more coughing and respiratory distress compared to bacterial pneumonia. Bacteria-virus coinfections result in a poorer response to initial antibiotic treatment and requires a longer duration of therapy. Rapid tests detecting RSV and AdV in this study have shown quick results within 15 minutes and exhibit a similar detection rate for these viruses compared to PCR.

LIST OF ACRONYMS

Vietnamese

BC: White blood cell

LRI: Lower respiratory infections

Hospitalization

Bacteria

Pneumonia

Virus

English

BPS: Bacterial Pneumonia Score

CRP: C-reactive protein

N: Neutrophil

NTA: Nasal trachio aspiration

PCR: Polymerase Chain Reaction

SpO2: Pulse Oximetry

CONFLICT OF INTEREST

The author group affirms that there is no conflict of interest in conducting this study.

ETHICS IN RESEARCH

This study is entirely aimed at protecting human health. Personal information about the research subjects is kept confidential. Data management and analysis are conducted in a scientific and precise manner. The use of NTA and other clinical assessments follows the current protocols of Children's Hospital 1. The outline was approved for research by the Scientific Council, Medical Ethics Council of the Faculty of Medicine of Vietnam National University of Ho Chi Minh City and Children's Hospital No. 1.

AUTHOR'S CONTRIBUTIONS

MSc. MD. Nguyen Thi Thu Suong designed the study; collected data; process and analyze data; write manuscripts, edit and finalize manuscripts.

MSc. MD. Tran Anh Tuan guided the design and supervised data collection; guided discussing research findings.

Assoc.Prof.Dr.MD Phan Huu Nguyet Diem guided the design and supervision of data collection; guided discussing research findings.

ACKNOWLEDGMENTS

We are grateful to School of Medicine, Vietnam National University Ho Chi Minh City for the support of time for this study.

REFERENCES

1. **Phan HND, Le MQ**. Clinical and microbiological characteristics of first-time hospitalized community-acquired pneumonia in infants aged 2 months to 59 months at Children's Hospital 1, Thesis of Specialist Level II, Ho Chi Minh City Medicine and Pharmacy University 2019.
2. **CaoPHG,PhamTMH**.Clinical,microbiological and therapeutic characteristics of children

with severe pneumonia requiring oxygen at Children's Hospital 2, Graduation thesis of resident doctors, Ho Chi Minh City Medicine and Pharmacy University 2014.

3. **Nguyen NTK, Tran TH, Roberts CL** *et al.* Risk factors for pneumonia. Paediatr Respir Rev 2017;21:95-101. https://doi.org/10.1016/j.prrv.2016.07.002
4. **Tran AT**. Hospital-acquired respiratory syncytial virus infections in children, Doctoral Thesis in Medicine, University of Medicine and Pharmacy Ho Chi Minh City 2016.
5. **Tran AT**. Molecular characteristics of respiratory syncytial virus in children with severe lower respiratory infections in communities and hospitals in Ho Chi Minh City. Ho Chi Minh City Medicine 2014;18(4):109-115.
6. **Bruning AHL, Leeflanmg MMG, Vos JM** *et al.* Rapid Tests for Influenza, Respiratory Syncytial Virus, and Other Respiratory Viruses: A Systematic Review and Meta-analysis. Clinical Infectious Diseases 2017;65(6):1026-1032. https://doi.org/10.1093/cid/cix461
7. **Castro-Rodriguez JA, Daszenies C, Garcia M** *et al.* Adenovirus pneumonia in infants and factors for developing bronchiolitis obliterans: a 5-year follow-up. Pediatr Pulmonol 2014;41(10);947-953. https://doi.org/10.1002/ppul.20472
8. Ensinck G, Lazarte G, Ernst A *et al.* Community-acquired methicillin-resistant Staphylococcus aureus pneumonia in a children's hospital. Our ten-year experience. Arch Argent Pediatr 2021;119(1):11-17. https://doi.org/10.5546/aap.2021.eng.11
9. **Harris M, Clark J, Coote N** *et al.* British Thoracic Society guidelines for the management of community acquired pneumonia in children: update 2011. Thorax 2011;66 Suppl 2:ii1-23. https://doi.org/10.1136/thoraxjnl-2011-200598
10. **Le Roux DM, Nicol MP, Vanker A** *et al.* Factors associated with serious outcomes of pneumonia among children in a birth cohort in South Africa. PLoS One 2021;16(8):e0255790. https://doi.org/10.1371/journal.pone.0255790
11. **Gonapaladeniya M, Dissanayake T, Liyanage G**. Burden of Respiratory Syncytial Virus Associated Severe Pneumonia in Hospitalized Children. International Journal of Pediatrics 2021. https://doi.org/10.1155/2021/8269400
12. **Musher DM**. Resistance of Streptococcus pneumoniae to beta-lactam antibiotics. www.uptodate.com © 2022 UpToDate, This topic last updated: May 31, 2022.
13. **Musher DM**. Resistance of Streptococcus pneumoniae to the fluoroquinolones, doxycycline, and trimethoprimsulfamethoxazole. www.uptodate.com © 2022 UpToDate, This topic last updated: Jul 11, 2022.
14. **Musher DM**. Resistance of Streptococcus pneumoniae to the macrolides, azalides, lincosamides, and ketolides. www.uptodate.com © 2022 UpToDate, This topic last updated: Jun 02, 2022.
15. **Pacheco GA, Gálvez NMS, Soto JA** *et al.* Bacterial and Viral Coinfections with the Human Respiratory Syncytial Virus. Microorganisms 2021;9(6):1293. https://doi.org/10.3390/microorganisms9061293
16. **Sonego M, Pellegrin MC, Becker G** *et al.* Risk factors for mortality from acute lower respiratory infections (ALRI) in children under five years of age in low and middle-income countries: a systematic review and meta-analysis of observational studies. PloS one 2015;10(1):116-380. https://doi.org/10.1371/journal.pone.0116380
17. **UNICEF**. Save the Children, and Every Breath Counts. Every child's right to survive: a 2020 agenda to end pneumonia deaths", UNICEF. Available at https://www.unicef.org/reports/every-childs-right-survive-pneumonia.