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Sapporo Medical Journal

Scopus coverage years: from 1961 to 1971, from 1973 to 2013, from 2016 to 2019, from 2021 to Present

Publisher: Sapporo Ika Daigaku

ISSN: 0036-472X

Subject area: Medicine: General Medicine

Source type: Journal

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Medicine
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PUBLISHER

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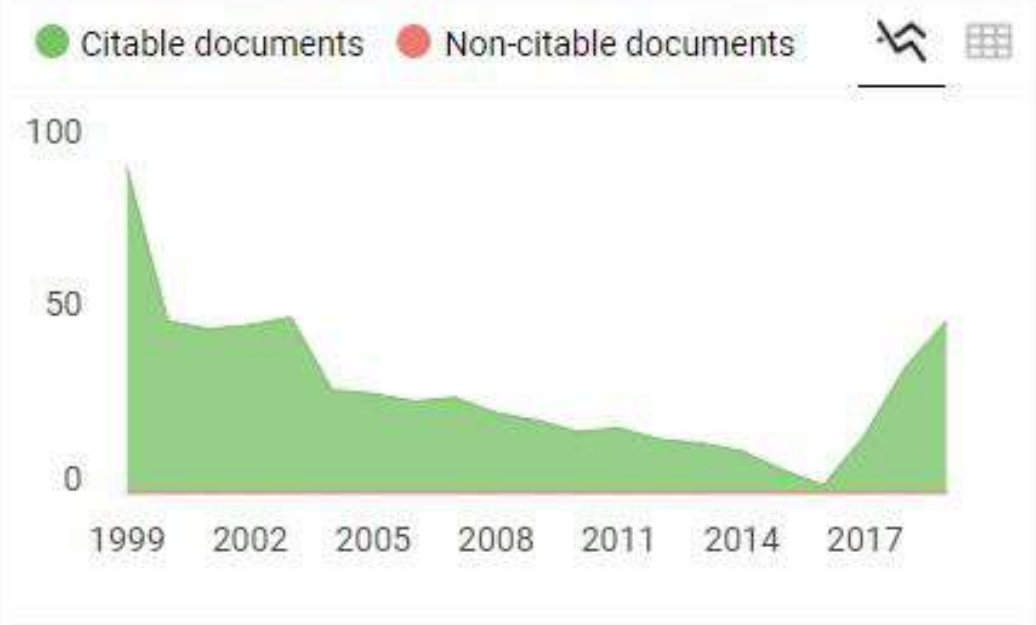
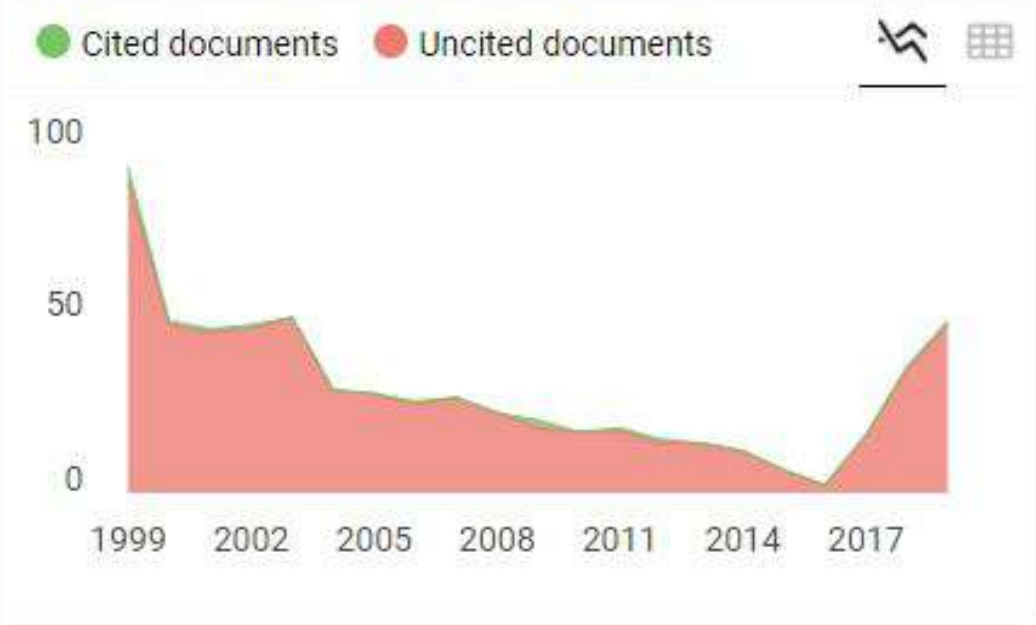
H-INDEX	PUBLICATION TYPE	ISSN
3	Journals	0036472X





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札幌医学雑誌

THE SAPPORO MEDICAL JOURNAL

第 42 巻

第 [illegible] 号

[illegible]

VOL. 42

[illegible]

1973

札 幌 医 科 大 学

SAPPORO MEDICAL COLLEGE

SAPPORO, JAPAN

PAPER ID : SMJ2109205408117

Title : CLINICAL FEATURES AND VIRUS IDENTIFICATION OF PEDIATRIC VIRAL PNEUMONIA IN DR SOETOMO HOSPITAL SURABAYA, INDONESIA

Author : Retno Asih Setyoningrum, Wigit Kristianto, Andi Cahyadi, Irwina Rahma Andriani, Prapti Dewi Suhirman, Gatot Soegiarto, Laksmi Wulandari, Aldise M. Nastri, Resti Yudhawati, Yohko K. Shimizu, Yasuko Mori, Kazufumi Shimizu,

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SAPPORO MEDICAL JOURNAL EDITORS-PANEL

Sapporo Medical Journal
Volume 54, Issue 08, August, 2020

CLINICAL FEATURES AND VIRUS IDENTIFICATION OF PEDIATRIC VIRAL PNEUMONIA IN DR SOETOMO HOSPITAL SURABAYA, INDONESIA

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Abstract— Pneumonia remains a leading infectious cause of morbidity and mortality in children. Pneumonia is mainly caused by viruses, but current therapeutic regimen often consists of antibioticdue to the lack of etiologic diagnosis. Irrational antibiotic often leads to antimicrobial resistance and high expenditure of healthcare resources.The aim of this study was to characterize the clinical features and etiology of viral pneumonia in children.A cross-sectional study was conducted in children aged 1-60 monthswith pneumonia according to WHO 2013 criteria, at the Dr. Soetomo Hospital from January to April 2014. Identification of virus was carried out by multiplex PCR, using Luminex primer xTag ®RVP-FASTv2. Seventy-five children met the criteria of enrolment to this study. The most common observed symptoms were fever (86.7%), coryza (60.0%) and vomiting (46.7%). The most common clinical signs were rales (95.6%), fast breathing (88.9%) and flaring nostril (80.0%). In terms of the detected viruses, EnV-HRV had the highest detection rate (46.7%), followed by HBoV (17.8%), InfV (8.9%), RSV (8.9%), HMpV (6.7%), HPIV (6.7%), CoV (4.4%) and none for AdV.The disease was typically a single infection (57.8%), with no observed specific seasonal trend.Fever, coryza, vomiting, rales and fast breathing were the most common symptoms and signs of pneumonia observed in this study. The most common viruses identified in children with viral pneumonia were EnV-HRV and HBoV.

Keywords— Clinical features, virus identification, viral pneumonia

1. Introduction

Pneumonia remains the leading infectious cause of morbidity and mortality in children. In low and middle-income countries, it is the most common reason for hospital admission in children[1]. The global burden of pneumonia is the highest in Southeast Asia and Africa in terms of incidence and occurrence of severe disease. The incidence of pneumonia in Southeast Asia was estimated to be around 0.13 - 0.61 episodes per children-year, with total deaths of 336.700–534.200 per year [1]. Globally, Indonesia is among 15 countries, which contribute to 65% of total episodes, 64% of severe episodes and 74% of mortality caused by pneumonia worldwide[1]. In Indonesia, 6 million children are estimated to be affected by pneumonia each year[2].

Etiologic diagnosis of pneumonia is difficult to be confirmed by clinical features due to many etiologic agents are presenting with similar manifestations. Although pneumonia is mainly caused by virus, the therapeutic regimen often consists of antibiotic[3]. This problem occurs due to current absence or limited measures of etiologic diagnosis for pneumonia in children, especially in Indonesia. Irrational antibiotic use often leads to antimicrobial resistance and high expenditure of healthcare resources [4]. Therefore, virus identification is essential to be carried out, not only to avoid irrational use of antibiotic, but also to ensure

proper implementation of antiviral therapy in children with viral pneumonia.

To better understand the clinical features and etiology of viral pneumonia in children, we conducted a cross sectional study among hospitalized children admitted to Dr. Soetomo Hospital in Surabaya, Indonesia from January to April 2014. This study is expected to provide information and improve current practice on the management of pneumonia in children, especially in developing countries.

2. Method

2.1 Participants

Participants of this study were children with pneumonia and severe pneumonia diagnosed based on the World Health Organization (WHO) criteria [5]. In brief, children were diagnosed with pneumonia if they presented with cough or difficult breathing and fast breathing (2-11 months: ≥50/minute, 12-60 months: ≥40/minute), and severe pneumonia if they suffered from pneumonia with any general danger sign. Participants were excluded if they presented with several conditions which rendered nasopharyngeal swab sampling difficult, including choanal atresia, nasal polyp, meningoencephalocele at naso-orbital region, cleft lip palate and epistaxis associated with leukemia, or if the patients had pneumonia caused by aspiration, fungi or Pneumocystis jirovecii (PCP). In this study, forty-seven participants were choosen using convenience non-random sampling technique among children with pneumonia and severe pneumonia who were aged 1-60 months and admitted as inpatient in the ward from January to April 2014.

2.2 Data Collection

Data from history taking, physical and laboratory examinations, X-ray chest imaging and PCR result were recorded in a case report form.

2.3 Laboratory Methods

Nasopharyngeal swab was performed within 24 hours after diagnosis using cotton swab (Nylon® Swabs in Tube), which was then placed in a universal transport medium(UTM) to be analyzed in Institute of Tropical Disease (ITD), Airlangga University. Polymerase Chain Reaction (PCR) assay was performed by extraction and purification of DNA/RNA, reverse transcription to form complementary DNA (c-DNA) and amplification of c-DNA using xTAG® Respiratory Virus Panel FASTv2 primer (xTAG® RVP FASTv2) (Luminex Molecular Diagnostic Inc., Ontario, Toronto, Canada). Results of the PCR assay were read using Luminex MAGPIX®xPONENT software (Luminex Corporation, Ontario, Toronto, Canada) to identify 7 type of viruses: Respiratory Syncytial Virus (RSV), Coronavirus (CoV), Human Parainfluenza Virus (HPIV), Enterovirus-Human Rhinovirus (EnV-HRV), Human Metapneumovirus (HMpV), Adenovirus (Adv) and Human Bocavirus (HBoV. Influenza virus (InfV) identification was performed using reverse transcription (RT)-PCRwith QIAGEN®OneStep RT-PCR kit (QIAGEN, Valencia, CA). Assay was performed according to the manufacturer's instruction.

2.4 Data Analysis

Data analysis was performed using SPSS 17.0.The data were presented as descriptive statistics in the form of tables and graphics of distribution, mean, frequency and other descriptive measures.

2.5 Ethical Statement

Informed consent of participants were obtained from their parents or legal guardians. Ethical approval was provided by Health Research Ethic Committee of Dr. Soetomo Hospital, Surabaya, East Java Province, Indonesia (301/Panke.KKE/XII/2013).

3. Result

Forty-seven children aged 1-60 months with pneumonia who were admitted to Dr. Soetomo Hospital were enrolled as participants to this study, however 2 of them were excluded from subsequent data analysis due to no-call results on PCR (Figure 1). Co-morbid diseases were found in 28/45 (62.2%) participants and viruses were identified in 35/45 (77.8%) participants. Co-morbid diseases in this study were congenital heart

disease, malnutrition, neurological disorder, HIV infection, and hypothyroid.

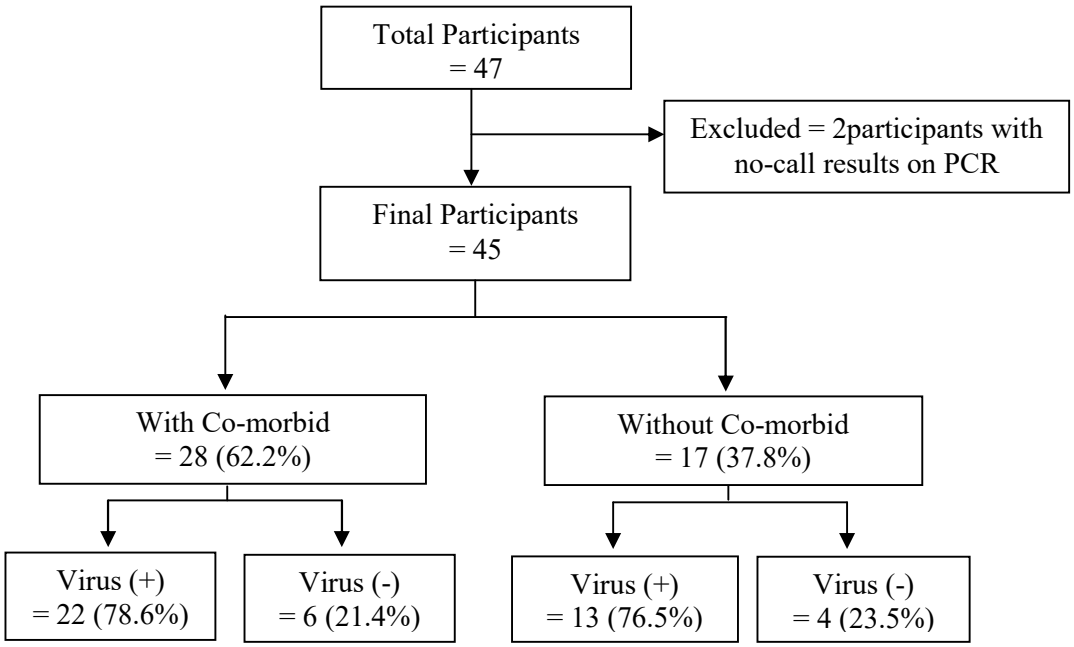

Figure 1. Outline of enrolled participants

Using Luminex xTAG assay, all viruses, except InfV, were identified in 32/45participants (71.1%). OneStep RT-PCRpositively identified InfV in 4/45 participants (8.9%).

3.1 Characteristics of Participants

Forty-five hospitalized children with pneumonia were enrolled as participants. All parents or legal guardians of participants had signed the informed consent form and agreed for participation to this study. Characteristics of those 45 participants were shown in Table 1. The average age of participants were 9.9 months, with most of them (77.8%) were under 12 months, and 48.9% of them were male. A majority of the participants were from Surabaya (80.0), and mostly lived in densely populated urban area 77.8%). We found that 57.8% participants had history of contact with person suffering from upper respiratory tract infection (URTI), while 77.8% had a history of contact with smokers. Among participants, only 33.3% of them were exclusive breastfeeding, while 22.2% of them were born with low birth weight and 15.6% were delivered preterm.

Table 1. Characteristics of participants

Characteristics	Comorbid		Total N (%)
	Yes N (%)	No N (%)	
Total	28 (62.2)	17 (37.8)	45 (100)
Age			
Mean (SD), in month	10.1 (8.69)	9.6 (11.59)	9.9 (9.76)
Age group			
<12 month	22 (78.6)	13 (76.5)	35 (77.8)
13-36 month	6 (21.4)	3 (17.6)	9 (20.0)
37-60 month	0	1 (5.9)	1 (2.2)
Male gender	11 (39.3)	11 (67.7)	22 (48.9)
Live in Surabaya	20 (71.4)	16 (94.1)	36 (80.0)
Area			
Densely populated urban	18 (64.3)	17 (100.0)	35 (77.8)
Elite area	6 (21.4)	0	6 (13.3)

Rural or suburban	4 (14.3)	0	4 (8.9)
URTI contact	15 (53.6)	11 (64.7)	26 (57.8)
Smokers in family	18 (64.3)	17 (100.0)	35 (77.8)
Breastfeeding baby	8 (28.6)	7 (41.2)	15 (33.3)
Low birth weight baby	7 (25.0)	3 (17.6)	10 (22.2)
Preterm baby	5 (17.9)	2 (11.8)	7 (15.6)

3.2 Clinical Manifestations of Pneumonia

The participants presented at the hospital with various symptoms such as fever, poor feeding intake, grunting, coryza, diarrhea, vomiting, seizure, rash and red eye (Table 2). The three most commonly identified symptoms were fever (80.3%), coryza (56.6%) and vomiting (44.7%). The presence of symptoms between participants with and without comorbid diseases tended to be similar in percentage.

The typical clinical signs of pneumonia also presented in most participants (table 2). The observed signs were fast breathing, cyanosis, chest indrawing, flaring nostril, head nodding, rales, wheezing and decreased auscultatory respiration soundd. The three most commonly identified signs were rales (97.6%), fast breathing (86.8%) and flaring nostril (78.9%). The presence of signs between participants with and without comorbid also tended to be similar in percentage, except for cyanosis and wheezing. Percentages of participants with cyanosis and wheezing were two-fold in the group with comorbid compared to the group without comorbid.

Table 2. Symptoms and signs of pneumoniain children with and without comorbiddiseases

Symptoms and Signs	Comorbid		Total
	Yes (28) N (%)	No (17) N (%)	N (%)
Total	28 (62.2)	17 (37.8)	45 (100)
Symptoms			
Fever	26 (92.9)	13 (76.5)	39 (86.7)
Poor feeding ntake	7 (25.0)	9 (52.9)	16 (35.6)
Grunting	8 (28.6)	7 (41.2)	15 (33.3)
Coryza	17 (60.7)	10 (58.8)	27 (60.0)
Diarrhea	14 (50.0)	4 (23.5)	18 (40.0)
Vomiting	14 (50.0)	7 (41.2)	21 (46.7)
Seizure	6 (21.4)	2 (11.8)	8 (17.8)
Rash	9 (32.1)	0	9 (20.0)
Red eye	6 (21.4)	0	6 (13.3)
Signs			
Fast breathing	26 (92.9)	14 (82.4)	40 (88.9)
Cyanosis	5 (17.9)	1 (5.9)	6 (13.3)
Chest indrawing	14 (50.0)	11 (64.7)	25 (55.6)
Flaring nostril	23 (82.1)	13 (76.5)	36 (80.0)
Head nodding	5 (17.9)	6 (35.3)	11 (24.4)
Rales	27 (96.4)	16 (94.1)	43 (95.6)
Wheezing	4 (14.3)	5 (29.4)	9 (20.0)
Low respiratory sound	6 (21.4)	2 (11.8)	8 (17.8)

3.3 Virus Identification

Virus were identified in more than half of participants (77.8%%). PCR results were shown in Table 3. EnV-HRV had the highest detection rate (46.7%) followed by HBoV (17.8%). The others virus wereInfV (8.9%), RSV (8.9%), HMpV (6.7%), HPIV (6.7%) and CoV (4.4%). AdV was not found in this study.

Table 3. Specific virus detection rate in participants

Virus	Total

	(N=45) (%)
Virus (+)	35 (77.8)
Single Virus Infection	26 (74.3)
Dual Infection	8 (22.9)
Triple Virus Infection	1 (2.8)
Virus detection	
InfV	4 (8.9)
RSV	4 (8.9)
CoV	2 (4.4)
HMpV	3 (6.7)
HBoV	8 (17.8)
HPIV	3 (6.7)
EnV-HRV	21 (46.7)
AdV	0

Virus identification also revealed that some participants had more than one type of virus in their nasopharyng (Table 3). Single virus infection was identified in 26/45 (57.8%) children, double virus infection in 8/45 (17.8%) children and one with triple virus infection (2.2%). Multiple infections were caused by EnV-HRV (7 cases in dual infection and one in triple infection). Viruses were commonly identified in participants aged less than 12 month (27/35 cases), and this tended to decline by older age (Figure 2).

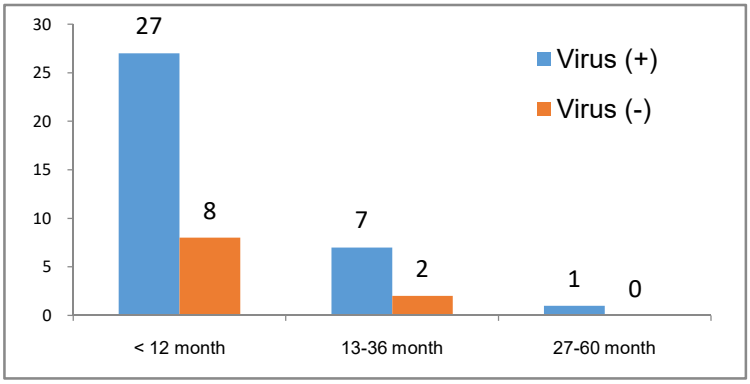

Figure 2. Proportion of virusesin specificagegroup

The month in a year in which viruses commonly appeared was March 2014 (16 cases) (Figure 3). Monthly trend of virus detection was fluctuated from January to April 2014 (Figure 4). EnV-HRV was the most common virus identified in January until April. HBoV was more prevalent in March while InfV in February to March.

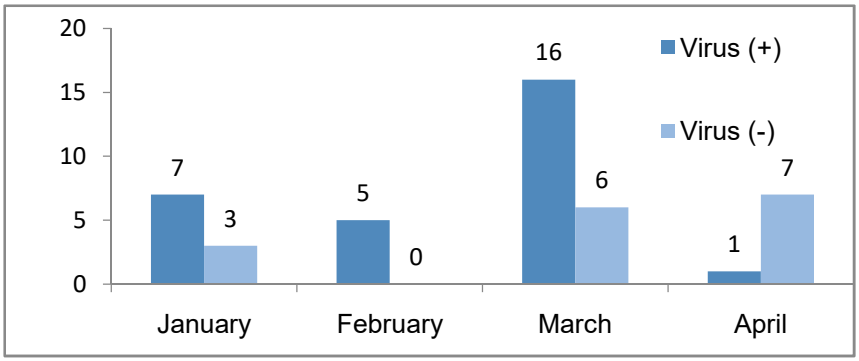

Figure 3. Monthly viral detection rate

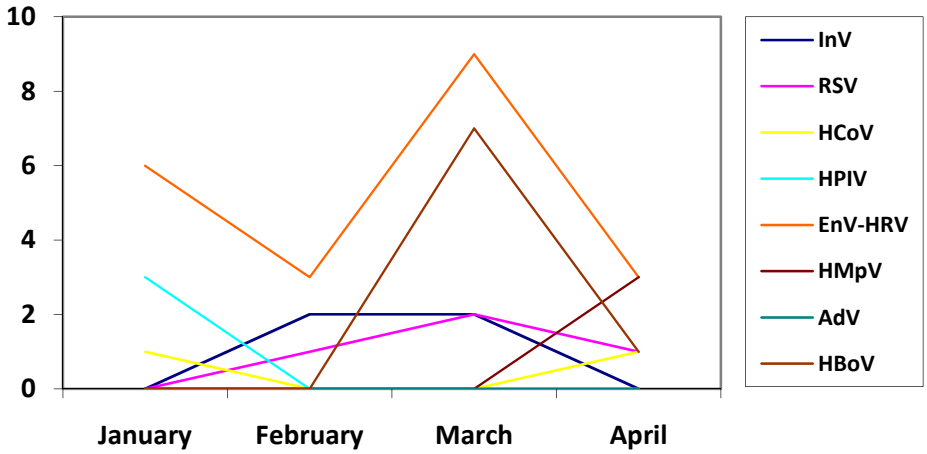

Figure 4. Seasonality of specific viruses

Multiple virus infections were found in malnutrition (2) but 5/9 were found in pneumonia without comorbid (Table 4).

Table 4.Combination of virus infection in various comorbid diseases

Virus	Number of Cases	Comorbid
CoV+HPIV+ EnV-HRV	1	Malnutrition
EnV-HRV + HBoV	2	Malnutrition and without comorbid
EnV-HRV+HMpV	1	Without comorbid
HPIV+EnV-HRV	1	HIV
InfV+EnV-HRV	1	Without comorbid
RSV+EnV-HRV	2	Cardiology and without comorbid
RSV+HBoV	1	Without comorbid

4. Discussion

Most children with pneumonia enrolled in this study were aged less than 12 months. Such trend has been observed in previous studies by [6]and[7]. Their study concluded that specific groups of < 12 months old and male children were more exposed to pneumonia. In our study, most pneumonia cases happened in children who lived in densely-populated urban area of Surabaya. Previous studies also shown that most cases of pneumonia occuring in developing countries with low income were in densely-populated and polluted area[8-11]. Most cases of pneumonia in our study were associated with family members who are smoking. Passive smoking of a primary care giver has been shown to be a likely risk factor for pneumonia, although the association was inconsistent [12]. Another study has concluded that children who had ≥ 2 smokers in their family had longer length of stay in hospital and were more likely to require intensive care compared to children from households without smokers[13]. Therefore, it is likely that children living with smokers will experience greater pneumonia severity.

In our study, lack of breastfeeding, low birth weight and preterm babies were only found in less than 50% participants. Exclusive breastfeeding has been shown to be protective againts pneumonia and suboptimal breastfeeding elevated the risk of pneumonia morbidity and mortality outcomes across age groups (OR 2.7 95% CI 1.7 to 4.4)[12,14]. Low birth weight was not commonly identified in our study participants, althought it is one of significant risk factors for pneumonia (OR 3.2 95% CI 1.0 to 10.0) [12].History of preterm delivery was also not observed. It is consistent with another study which concluded that the association between preterm baby and pneumonia was not significant (OR 1.3 95% CI 0.8 to 2.1) [12].

4.1 Clinical Features of Pediatric Viral Pneumonia

Clinical features are used as an initial orientation for most clinicians in developing countries for identifying probable etiology of pediatric cases, despite insufficient specificity of such features for this purpose. Fever, coryza, vomiting, flaring nostril, fast breathing and rales were most common symptoms and signs of pneumonia identified in this study. Younger children more often presented with grunting and poor feeding intake. These signs and symptops were also identified in other published studies and were consistent with our findings[6,10,15-17].

Many studies have been conducted in the effort of distinguishing the etiology of pneumonia by clinical features, but there had been overlapping results and no consistent findings were observed. A study conducted in 4277 children with laboratory-confirmed viral respiratory infections had compared clinical features of eight different respiratory viruses (HRV-EnV, RSV, AdV, HPIV-1, HPIV-2, HPIV-3, influenza virus A and influenza virus B). The study showed that the symptoms and signs were overlapping with bacterial pneumonia [18,19].

Some studies have observed that wheezing was a significant sign for viral pneumonia, and the sign was identified in 17-64% of children[20], whereas in our study wheezing occured in 20% of cases. RSV-related acute lower respiratory infection has more severe clinical courses and often occurs with rales, wheezing, nasal flaring, lower chest indrawing, rhinorrhea and nasal obstruction compared to other viruses, although such clinical signs were not specific to RSV[21,22].

Clinical features of pediatric viral pneumonia varies between participants. Moreover it is influenced by the presence of comorbid diseases. Some clinical features of pneumonia are also occuring in comorbid diseases, so it is difficult to distinguish clinical features of pneumonia in the presence of comorbid. Clinical features are also influenced by the type of viruses, viral load and immunity profile of children[23-25]. Some viruses are also more likely to occur in certain diseases, for example RSV in heart diseases and InfVin malignancy [26].

Comorbid diseases were found in 62.2% participants of our study, i.e. CHD, malnutrition and neurological disorder. The other comorbid diseases were HIV infection and central hypothyroidism. Comorbid diseases such as malnutrition and HIV infection increased the risk of pneumonia in children aged 2-59 months in Kenya, but in that study the disease prevalence was much lower compared to our study. Risk of pneumonia was also increased fourfold in children with heart diseases[27]. Another study conducted in Egypt showed that comorbid diseases were found in 40.1% of pneumonia cases, consisting of heart diseases (34%), neurological disorder (15.9%), respiratory tract disease (10.6%) and malnutrition (1.9%)[17].

4.2 Virus Identification in Pediatric Viral Pneumonia Cases

In our study, viruses were identified in two-third of participants. The virusespattern varied and we did not observed any specific pattern of infection. A study conducted in Kenyan children aged 1-59 months similarly identified etiologic agent in 76% of the samples, in which mostly viruses were detected[11].

The virus prevalence in our study is similar to other studies conducted in developing countries. Virus prevalence varied, depending on study design, location, assay technique and type of collected samples. A hospital-based study in children with pneumonia aged <5 years in Brazil identified virus in 8.4% children [28], while it was 40.0% in Nepal (Mathisen *et al.*, 2009) and 77% in Ghana [6]. Findings in our study were also consistent with studies conducted in Bangladesh (Homaira *et al.*, 2012), Philippine(Suzuki *et al.*, 2012), Nepal [10], and several other countries[11,16,29-35]. These studies were mostly conducted in developing countries which have the same geographic and demographic characteristics as Indonesia.

Our study was unable to show any seasonal trend of virus infection because it was only conducted in a transition season for 4 months. In countries with 4 seasonal climate, most of the viruses have seasonal trends, such as InfV andCoVin winter and spring, and RSV in autumn, winter and spring[34]. In our study, virus was mostly found in March. For each specific viruses, InfV was mostly found in February-March, CoVin January and April, HBoVin March and EnV-HRV in every month. A study conducted in Istanbul,

Turkey found that InfV was mostly found in Januari, March and May,HBoVandAdVin July, August and September, with HPIV and HRV had no specific trend[34].

In our study, cumulative viruses were found in 60% of children aged <12 months and 97.1% in children aged <3 years. Meanwhile, the studies conducted in Bangladesh and Nepal showed that there were 77.5% children aged <24 months[6]and 40% children aged <3 years who had virus in their respiratory tract[10]. Three most common viruses found in this study were EnV-HRV (60.0%), InfV (11.4%) and RSV (11.4%). It is different from the study conducted in Nepal, which found that the three most common viruses were RSV (12.6%), InfV (5.3%) and HPIV (19.1%)[30].

4.3 Respiratory Syncytial Virus (RSV)

RSV is the most common virus found in a study in children with viral pneumonia, but not in our study. It commonly causes a single infection in children with heart diseases. RSV was related to severe pneumonia and lower respiratory tract infection in Thailand, Gambia, Indonesia and Ghana[36]and Nepal[10]. RSV was found in 37.3% children aged <5 years in Brazil(Bezerra *et al.*, 2011), 22% in children aged <2 yearsin Bangladesh[6], 24% in children aged <13 years in Philippine [16] and 52.2% children aged <5 years in Egypt[17].

RSV infection is mostly associated with the presence of wheezing in children in developed country, but in this study RSV infection was only found in a quarter of children with pneumonia who showed wheezing sign.

4.4 Entero-Rhinovirus (EnV-HRV)

The most common virus found in this study was EnV-HRV (60%). EnV and HRV was joined because the Luminex xTAGreagent could not distinguish EnVand HRV. In a previous study in which 92 samples were positive with EnV-HRV, it was shown that a single HRV infection was observed in 81 samples, EnValone in 5 samples, and the combination of both in 8 samples[37]. HRV infection was found in 30.5% children aged <13 years with pneumonia in Philippines[16]. Proportion of HRV infection in children aged <2 years in our study was comparable with study in Bangladesh, in which HRV infection was found in 12% children aged <2 years[6].

4.5 Human Metapneumovirus (HMpV)

HMpVinfection was found in 3/45 children with pneumonia in our study, and all were in >1 years old group. In the study in Egypt, HMpVinfection was found in 10.9% children with pneumonia and 82.3% of them were in <1 year old group. HMpVinfection was associated with hospitalisation and severe disease, especially in children aged <3 years[17].Another study had shown that thecvf 6f reason for this tendency was HMpVseroprevalence in children 6-12 months was 25% and increased up to 100% in children aged 5 years old[38].

4.6 Human Bocavirus (HboV)

Our study observed that HBoVinfection was found in 17.8% children with pneumonia, 5 among them were <12 months old and 3 were 13-36 months old. Another study also highlighted the finding that HBoVinfection was mainly found in young children. HBoV seroprevalenceincreases with age, and become 100% in children aged 6 years[38].

4.7 Coronavirus (CoV)

CoV was one of the virus that have caused an epidemic in Middle East Region. Our study evaluated CoVsubtype 229E, HKU1,NL63 and OC43. Those subtype was different with MERS-CoVwhich caused epidemic in Middle East[39]. CoV detection rate in this study was only in two children. Our result showed similar detection rate than the study in Kenya, in which CoVdetection rate was 5.3%, consisted of 229E (2.1%), NL63 (0.5%) and OC43 (2.7%)[11].

4.8 Human Parainfluenzavirus (HPIV)

HPIV infection was found in two children aged <12 months old and in 1 child aged 1-3 years old.Age was a significant risk factor in the pathogenesis of HPIV infection. Children aged 2-5 months old were more susceptible to infection than 6-35 months old[30].

4.9 Adenovirus (AdV)

AdV in this study was not found in our study. AdV commonly caused upper respiratory tract infection (81.5%), rather than lower respiratory tract infection (8.5%). AdV was found in 8.4% cases of severe pneumonia in Egypt, and contributed to 17.7% of multiple infection[17].

4.10 Influenza Virus (InfV)

InfV was found in 8,9% children, consisted of 2 with InfV A and 2% with InfV B. A study in Finland found that InfV detection rate was 7% in children with viral pneumonia[40], and a study in Nepal observed that InfV A and InfV B detection rate were 7.4% and 3.8% respectively[10].

4.11 Multiple Virus Infection

Multiple virus infection was found in 14.6% children aged <5 years old in Egypt, 24.3 % in Istanbul, Turkey [34], 16.7% in Bangladesh [6] and 3.3% in Nepal[10]. These results were similar with our study, in which the rate of combined infection was in 20%.

Multiple infection was mainly found in children who lived in urban area. It is associated with contact to another person with upper respiratory tract infection. Children who lived in densely populated urban area in this study were 77.8%, in which 80.0% of them had viruses in their nasopharynx. Among 88.9% children with multiple infection also lived in urban area. Children in this study came from various areas in East Java provinces, hence they have a greater risk to be infected by various viruses during referral process until they were admitted to our hospital. Nevertheless, most of the children in this study only had a single virus infection.

5. Conclussion

This study has shown that viruses were commonly found in children with pneumonia in Surabaya, Indonesia. Our study concluded that fever, coryza, vomiting, rales and fast breathing were most common symptoms and signs of pneumonia, with younger chlidren more often showed grunting and poor feeding intake. These symptoms and signs were consistent with findings from other studies in developing countries. In our study, the pattern of virusesvaried and there was no specific seasonal pattern observed. The three most common viruses found in children with pneumonia were EnV-HRV andHBoV.

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KOMITE ETIK PENELITIAN KESEHATAN
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KETERANGAN KELAIKAN ETIK
(" ETHICAL CLEARANCE ")

301 / Panke.KKE / XII / 2013

KOMITE ETIK RSUD Dr. SOETOMO SURABAYA TELAH MEMPELAJARI SECARA SEKSAMA RANCANGAN PENELITIAN YANG DIUSULKAN, MAKA DENGAN INI MENYATAKAN BAHWA PENELITIAN DENGAN JUDUL :

"Studi Diagnostik dan Faktor Resiko Terjadinya *Community Acquired Pneumonia* Anak Usia 1-60 Bulan yang Dirawat di RSUD Dr. Soetomo Surabaya"

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