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Burden of respiratory tract infections among paediatric in and out-patient units during 2010-11

J. MAZUMDAR[1], M. CHAWLA-SARKAR[1], K. RAJENDRAN[2], A. GANGULY[1], U.K. SARKAR[3], S. GHOSH[1], M.D. SARKAR[1], S. MAULIK[4]

[1]Division of Virology and [2]Division of Data Management; National Institute of Cholera and Enteric Diseases (NICED), Beliaghata, Kolkata, West Bengal, India
[3]B.C.Roy Memorial Children Hospital, Kolkata, India
[4]NRS Medical College and Hospital, Kolkata, India

Abstract. – INTRODUCTION: Respiratory tract infections due to viral etiology were studied with an objective to identify and compare the pathogens between Hospital Indoor and Outdoor Units.

MATERIALS AND METHODS: A hospital-based cross-sectional study was conducted among children below 12 years over a period of one year. The throat and nasal swabs were collected from both the Units and screened for viral infections by real time RT-PCR technique.

RESULTS: Out of 880 samples collected, 87% and 13% were from outdoor and indoor Department with total viral positivity rate of 30% and 25% respectively. Influenza B virus (IBV) (n=126, 16%) was more prevalent in Outdoor Unit, whereas respiratory syncytial virus (RSV) (n=18, 16%) among indoor admitted cases. The multinomial logistic regression analysis revealed that both RSV and Influenza viruses were predominant in children of pre-school age groups < 5 years. In the year 2010-11, the prevalence of human metapneumovirus (HMPV) was low. The pandemic influenza A virus (pH1N1/2009) accounted for 4% (n=29) and 0.8% (n=1) cases among Outdoor and Indoor Units respectively.

CONCLUSIONS: The Outdoor Department outnumbered the Indoor Unit in terms of patient attendees and the rate of viral infections. An effective vaccination and continuous surveillance program is the need of the hour.

Key Words:
Human metapneumovirus, India, Influenza, Kolkata, Pediatrics.

Introduction

The viral respiratory tract infections especially in children have a major impact in India and around the world. Of all the respiratory viruses, influenza and respiratory syncytial virus account for a substantial morbidity, with more than 40% pre-school aged children having influenza illness and almost 100% children with RSV infection by the age of three[1-4]. It is estimated that influenza virus infects 5-15% of global population resulting in approximately 250,000 to 500,000 deaths per year[5-6].

In developing countries, about 1.9 million children die per year due to acute respiratory tract infections and among these 20% deaths are in India[7]. According to an analysis in Tripura, India, the prevalence of respiratory tract infections was about 23 and 17.65 percent in the urban and rural areas respectively[8]. Moreover, children admitted in hospitals in India with acute respiratory distress, about one half was due to viral infections[9-11].

Most of the studies on respiratory tract infection in India are based either on outdoor patients or hospitalized cases. Thus, the present study was conducted in a Tertiary Care Teaching Hospital in Kolkata, India as a part of surveillance program to identify and compare the pathogens between hospital indoor and outdoor departments. Among all the viruses, emphasis was given to RSV, HMPV and influenza virus infections.

Methods

Study Area

The study area was in Kolkata, capital city of west Bengal state, located in the eastern region of the India at a longitude of 88° 20' E and latitude of 22º 82' N with an altitude of 17 feet from sea level. The relative humidity is between 70-80% and rainy season is considered to be from mid June to end of September.

Corresponding Author: Jaydeep Mazumdar, MD; e-mail: jaymaz28@gmail.com;

As a part of the multi-site influenza surveillance network; a hospital based study was conducted in two teaching institutes in Kolkata, India. The institutes were NRS Medical College & Hospital and B.C. Roy Memorial Children Hospital. These institutes were selected as they cater to large number of patients, part of them are referred cases from the primary and secondary health care centers. Moreover, B.C. Roy Memorial hospital is the largest children's hospital in Eastern India[12].

Target Population

Children below 12 years of age visiting the outdoor Department and those getting admitted in paediatric wards within 1-5 days of onset of symptoms were enrolled for the study. The sample collection started from 1st of April 2010 till 31st March 2011. The clinical findings along with history of illness were recorded in a standard data sheet.

Case Definitions

The cases were identified according to World Health Organization (WHO) guidelines as patients presenting to an outdoor Clinic with more than one of the following features such as, a measured temperature of more or equal to 38°C with either cough, sore throat, running nose, earache, as influenza-like-illness (ILI). On the other hand, cases hospitalized indoor patients with shortness of breath (respiratory rate of > 40/minute), chest indrawing/sub-costal retraction, crepitation and wheezing were enrolled as severe acute respiratory infection (SARI)[13].

A physician was recruited for both the sites and two field assistants were deployed to help the physician to collect biological samples. The sample collection was done thrice in a week from both the outdoor and indoor Departments of the respective hospitals. On an average depending upon the seasonality, the physician collected about forty to fifty samples from outdoor Unit and less than ten samples from indoor Unit each month. Among the two hospitals, highest number of cases was enrolled from B. C. Roy Memorial Hospital.

The samples were collected in a tube containing viral transport media and then sent immediately to the virology laboratory of National Institute of Cholera and Enteric Diseases (NICED), Kolkata, India maintaining the cold chain. The RNA was extracted from clinical sample by using QIAamp viral RNA Mini Kit (Qiagen GmbH, Hilden, Germany) and Real time RT-PCR was used for clinical confirmation of the presence of viruses in the collected samples using specific probes and primers described previously[14].

Ethical Issues

The ethical clearance was taken from the institutional Ethical Committee of the Institute prior to the commencement of the study. A written informed consent form was obtained from the parents/guardians prior to commencement of the study after the children met the inclusion criteria.

Statistical Analysis

In this study, the inferential age was explored for the Outdoor Unit by Multinomial Logistic Regression[15]. The infections caused by IBV, IAV pH1N1/(2009), RSV and HMPV were classified in number as '0' for organism present and '1' for its absence. The data were entered into pre-designed format of the excel sheet with inbuilt entry validation by trained data entry professionals in the computers. Data were randomly checked and matched to derive consistency and validity. The edited data was exported and the final analysis was done using the SPSS version 19.0 (SPSS Inc., Chicago, IL, USA). $p < 0.05$ was considered statistically significant.

Results

Demography Patterns

Out of the total samples (n=880) collected, 764 (85%) were from outdoor department and the rest of the samples 116 (13%) were from the indoor admitted cases. The proportion of male and female patients in outdoor cases was 407 (53%) and 357 (47%) whereas among indoor admitted cases it was 73 (63%) and 43 (37%) respectively (Table I).

It was found that more than fifty percent of patients 420 (55%) from the outdoor department were in the pre-school age group (1 year – < 5 years) followed by 229 (30%) patients in the infant age group.

Among the indoor case-patients, the infant age group registered higher percentage of cases 81 (70%) followed by 27 (23%) in the pre-school age group (Table I).

Positive Cases for Viral Infections

A total of 232 (30%) and 29 (25%) case-patients were positive for viral infections among outdoor and indoor departments respectively.

Table I. Comparison of characteristics between outdoor and indoor departments.

Characteristics	Outdoor no. (%) n = 764	Indoor no. (%) n = 116	Total (%) n = 880
Gender			
Male	407 (53)	73 (63)	480 (55)
Female	357 (47)	43 (37)	400 (45)
Age groups			
< 1 YR	229 (30)	81 (70)	239 (27)
1 - < 5 YRS	420 (55)	27 (23)	479 (54)
≥ 5 YRS	115 (15)	8 (7)	162 (19)
Single infection			
IAV (pH1N1/2009)	29 (4)	1 (0.8)	30 (3)
IBV	126 (16)	9 (1.1)	135 (15)
RSV	70 (9)	18 (16)	88 (10)
HMPV	7 (0.9)	1 (0.8)	8 (0.9)
Co-infections			
RSV + IBV	35 (5)	5 (4)	40 (5)
RSV + HMPV	9 (8)	1 (0.8)	10 (1.1)
IBV + HMPV	1 (0.8)	0	1 (0.1)
IBV + RSV + HMPV	2 (0.26)	0	2 (0.22)

IBV: Influenza B virus; RSV: Respiratory syncytial virus; HMPV: Human metapneumo virus; IAV (pH1N1/2009): Influenza A virus pandemic H1N1 (2009).

Among the outdoor patients, 16% (n=126) were positive for IBV, 4% (n=29) were IAV (pH1N1/2009), 9% (n=70) were RSV and 0.9% (n=7) were HMPV positive cases.

Among indoor admitted cases, RSV infection registered higher proportion of infection (n=18, 16%), followed by IBV (n=9, 1.1%). HMPV and IAV (pH1N1/2009) infections were detected at very low percentage of less than one (n= 1, 0.8%) each (Table I).

Co-infections

A subset of patients was suffering from more than one type of viral infections, as shown in Table I. IBV and RSV were found to be most common co-infections and almost in equal proportion of 5% (n=35) and 4% (n=5) between outdoor and indoor cases respectively.

Distribution Between Age-Group and Infection

The outdoor patients age was categorized into 3 categories, in which 229 (30%), 420 (55%) and 115 (15%) cases were in the age groups of < 1, 1-5 and ≥5 years, respectively (Table I). The MLR analysis showed that, RSV (p = 0.009) and HMPV (p = 0.783) were associated in children of less than one year group, although HMPV was not significant and were significantly less affected by IAV (p = 0.001) and IBV (p < 0.001). Similarly, 1-5 years children were vulnerable for RSV and HMPV infection though statistically not significant, whereas IBV (p = 0.004) and IAV (p = 0.001) viruses were vulnerable to children less than five years age group, when compared to more than 5 years (Table II). The MLR was performed for Indoor Unit as well, but the table has not been populated as it showed abnormality owing to small number of infection rate.

Month-Wise Distribution of Viral Infections

On comparing both the indoor and outdoor cases, it was quite evident from this investigation that the prevalence of viral infections was during the month from May to September. In the outdoor cases, IBV infection peaked in the month of June (n=37; 4.8%) and declined thereafter with lowest in the month of October (n=7; 0.9%).

IAV (pH1N1/2009) infection was found to be highest (n= 43; 4%) in the month of July, followed by sharp decline in the succeeding months. Respiratory syncytial virus infection also peaked in the month of June (n=22; 2.8%). Both IBV and RSV had a secondary peak in the month of August (2.2%) and September (2%) respectively (Figure 1).

The proportion of viral infections among indoor cases was quite low as compared to outdoor cases. In June' 2010, Influenza B positivity

Table II. Multinomial Logistic Regression models exploring inferential age group of predominant influenza-like-illness of outdoor patients at two Hospitals, Kolkata, India.

Age	Organism	B	OR (95% CI)	*p*-values
< 1 yr	IBV	-1.333	0.26 (0.15-0.46)	0.000
	IAV (pH1N1/2009)	-1.586	0.21 (0.08-0.52)	0.001
	RSV	1.210	3.36 (1.35-8.33)	0.009
	HMPV	0.306	1.36 (0.15-12.08)	0.783
1 - < 5 yrs	IBV	-0.728	0.48 (0.30-0.79)	0.004
	IAV (pH1N1/2009)	-1.474	0.23 (0.10-0.53)	0.001
	RSV	0.862	2.37 (0.97-5.78)	0.058
	HMPV	0.756	2.13 (0.26-17.05)	0.477
≥ 5 yrs	Reference category			

IBV: Influenza B virus; IAV(pH1N1/2009) - Influenza A Virus pandemic H1N1 (2009), RSV: Respiratory syncytial virus; HMPV: Human metapneumo virus.

was found to be 6% (n=7) and RSV of 8% (n=9). The HMPV and IAV pH1N1/2009 infections were found to be in equal proportion of 1 (0.8%) each in the month of June and July respectively (Figure 2).

Discussion

It was quite evident from our report that male patients were comparatively in higher proportions than the females among outdoor and indoor Units similar to finding in Delhi City, India[16]**.** This trend can be explained by the fact that females are neglected population in India and are usually taken to healthcare institutes until their condition deteriorates[9,17].

Our findings detected that influenza and respiratory syncytial virus, were predominant respiratory tract viruses affecting significantly children below five years in Kolkata and causing considerable morbidity. More than 80% of the indoor and outdoor cases were below five years of age (Table I), similar to the study in Bangladesh[18]. There could be several factors like socio-economic, environmental, education, overcrowding and others which may affect the seasonality and distribution of viral infections.

The proportion was almost equal in terms of coinfected cases between indoor and outdoor units. It was also evident from the study that the burden of positive cases was relatively higher in outdoor Departments than the indoor Unit similar to the findings in Taiwan[19]. It could be due to the

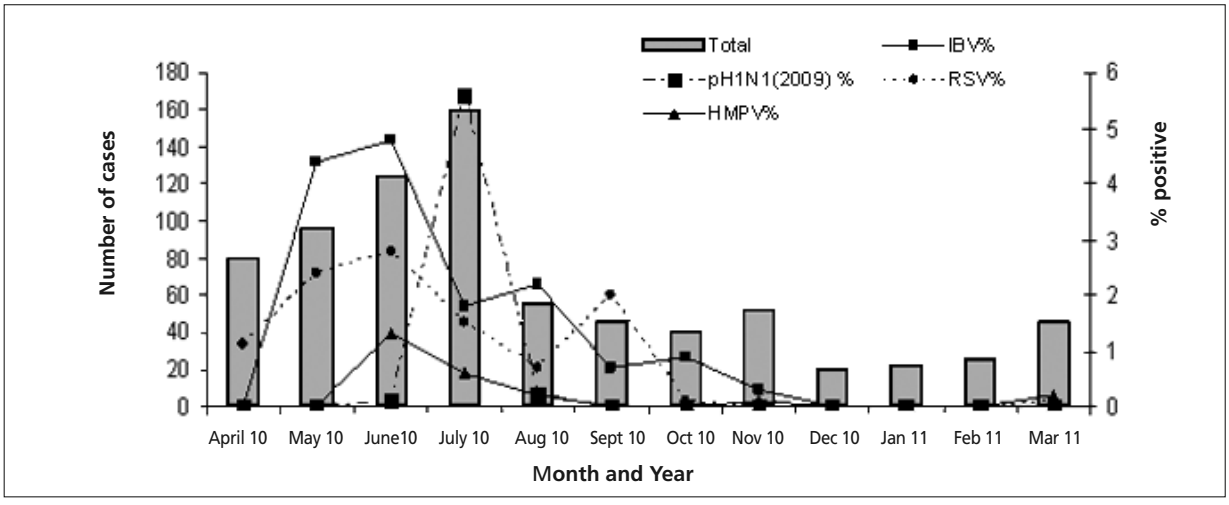

Figure 1. The distribution of cases attending the outdoor Department of both the hospitals and the viral positivity rates during April 2010 to March 2011.

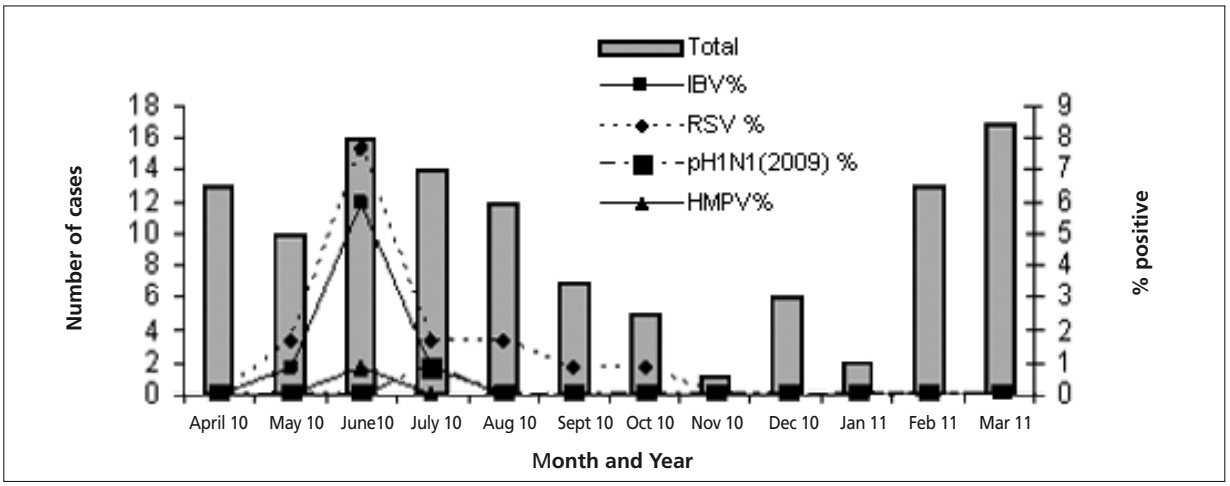

Figure 2. The distribution of samples collected from the hospitalized indoor cases of both the teaching institutes and the viral positivity rates during April 2010 to March 2011.

fact of early presentation of cases in outdoor Department. Moreover, due to poor ratio between hospitals and population in India only very critical cases which fail to respond to the treatment in outdoor Department get hospitalized[20]. Thus by the time the patients get admitted after more than a week of initial disease symptom the chances of detecting positive cases gets meager.

IBV infection was found to be more prevalent among outdoor cases followed by RSV. In the indoor cases, the prevalence of RSV was similar to IBV infection (Table I). Such predominant viral infections were consistent with studies from Vietnam[21] and other Asian countries[22]. However, in earlier studies from Kolkata, India[12] IAV was detected in higher proportions than IBV during 2005-2009. It could be due to the post pandemic effect (2009) following which seasonal IAV (H1N1 and H3N2) disappeared completely resulting in unusually low prevalence of IAV in 2010.

The multinomial logistic regression analysis detected RSV infection to be statistically significant in lower age group similar to the study in countries of Central America[23]. This could explain the higher proportions of indoor patients were affected with RSV infection in comparison to other viral infections.

The seasonality of RSV infection was similar to the studies in China and Vietnam[24,21] but contradictory to the studies done earlier in Kolkata, India[12,25] and Bangladesh[26] when RSV infection was observed more in the winter months or dry seasons. Such variations of infection with seasonality are hard to describe although an association of some other factors or infections could be a possibility[27]. A long term study (≈ 10 years) in the region will probably clarify the seasonality of this virus.

In spite of very low prevalence rate, the HMPV infection among the outdoor cases was directly proportional to the age group distribution (Table not shown). Such upward trend was similar to the study in China[28] although the number of positive cases was much higher than our study. As only one HMPV positive case was detected among indoor wards, which was found in coinfection with RSV no correlation could be drawn as it was statistically insignificant.

This work had some limitations. The research was conducted thrice in a week from each of the two hospitals; thus, we may have missed more number of positive cases. The number of cases collected from indoor were low than expected. The reason could be that most of the cases were admitted after several days post symptom and didn't meet the inclusion criteria. Most of those cases received initial treatment in local nursing homes or district hospitals and then shifted to our study site. Among others, few refused to consent for the research. None of the samples were collected from the patients admitted in the intensive care unit (ICU) or respiratory care unit. The associated clinical symptoms apart from our inclusion criteria were not considered during sample collection.

Conclusions

As the objective of our investigation was to detect and compare the viral pathogens in both

Table III. Distribution of age-groups and viral infections among indoor unit during 2010-2011.

	Infections (%) n = 29				
Age groups*	IBV	IAV (pH1N1/2009)	RSV	HMPV	Total (%)
< 1 yr	7 (24.1)	1 (3.4)	17 (58.6)	1 (3.4)	26 (89.6)
1- < 5 yrs	2 (6.8)	0	1 (3.4)	0	3 (10.3)
Total (%)	9 (31)	1 (3.4)	18 (62)	1 (3.4)	

*There were no viral positive cases in more than 5 years age groups. IBV: Influenza B virus; RSV: Respiratory syncytial virus; HMPV: Human metapneumo virus, IAV (pH1N1/2009) – Influenza A virus pandemic H1N1 (2009).

the Hospital Departments, it was quite evident that the number of patient attendees and the positivity rate of viral respiratory tract infection were higher in the outdoor Unit. Thus to conclude, it may be beneficial to continue the present surveillance program along with interventional studies like vaccination program to curb the burden to a certain extent.

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