Original article

Clinical profile of respiratory viral infections: A study from tertiary care centre of South India

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A B S T R A C T

Background: The recent influenza pandemic caused by the 2009 California H1N1strain increased awareness of the importance of influenza among hospitalized patients but there are few reports on other influenza strains and other non influenza respiratory viral infections in hospitalised patients.
Aim: To study epidemiological, clinical profile and outcome in patients hospitalised with respiratory viral infections.
Materials and methods: A prospective, observational study was conducted in a tertiary care hospital in Chennai, Tamil Nadu from September 2015 to July 2016. Respiratory samples from patients hospitalised with suspected acute viral respiratory infections were sent for molecular PCR based technique.
Results: Total 40 patients were studied. The most common respiratory virus was rhino virus in 9(22.5%) patients followed by influenza H3/H3N2 in 7(17.5%), H1N1 in 6(15%) and RSV in 4 (10%). After the diagnosis of the viral infection, antibiotics were completely stopped in 10(30.3%) patients and de-escalated to a narrower spectrum agent in another 10 (30.3%) patients. No patient whose antibiotics were de-escalated died, whereas there were 5 deaths in patients in whom de-escalation was not done.
Conclusion: Diagnosis with PCR facilitates early use of antiviral agents, droplet isolation, prevention of cross-transmission of viruses and antibiotic stewardship practice.

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1. Introduction

Lower respiratory tract infections cause 3.5 million deaths annually and are the leading cause of global disability associated life years [DALY] at an estimated 113 million DALY. The highest disease burdens are in sub-Saharan Africa (21.4% of global total) and India (20.9%) [1]. The most common cause of community acquired respiratory infections are respiratory viruses [2] and up to one-third of cases of community-acquired pneumonia (CAP) among hospitalized adults are viral in aetiology [3]. Several outbreaks of respiratory viral infections in hospitalised patients have also been reported [4]. The recent influenza pandemic caused by the 2009 California H1N1strain increased awareness of the importance of influenza among hospitalized patients but there are few reports on other influenza strains and other non influenza

respiratory viral infections in hospitalised patients[6]. There is also unnecessary antibiotic use in the management of respiratory viral infections on account of poor diagnostics for viruses and concern about bacterial etiologies, leading to antibiotic resistance in bacteria [6].

We therefore attempted to look into the epidemiological, clinical profile, antibiotic exposure and outcome in patients hospitalised with respiratory viral infections.

2. Materials and methods

A prospective, non-interventional observational study was conducted in a tertiary care hospital in Chennai, Tamilnadu from Sep 2015 to July 2016. Respiratory samples from patients hospitalised with suspected acute viral respiratory infections were sent for molecular PCR based techniques [Luminex/Filmarray]. Sample sites included were nasopharyngeal swab and broncho-alveolar lavage [BAL] in intubated patients. The Biofire FilmArray Respiratory Panel is a nested PCR-melt curve analysis

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platform that detects 20 different viral and bacterial targets within an hour including Adenovirus, Coronavirus (229E, HKU1, OC43, NL63), Human Metapneumovirus, Human Rhinovirus-HRV/Enterovirus, influenza virus A (H1/2009, H1, H3); influenza virus B; Parainfluenza 1, 2, 3, 4; Respiratory Syncytial Virus-RSV, *Bordetella pertussis*, *Chlamydophila pneumoniae*, and *Mycoplasma pneumoniae*. The procedure was performed according to manufacturer instructions. The FilmArray RP contains its own internal controls within each pouch—an RNA process control and a second-stage PCR control. The xTAG Respiratory Viral Panel (xTagRVP) is a fluorescence-labeled bead array based on a multiplex RT-PCR reaction in which the target-specific primers are chimeric, including a terminal universal tag sequence. The targets are similar to the viral targets of BioFire (no bacterial targets included) and RSV is typeable into RSV A and B. Nucleic acids were extracted using the EZ1 Virus Mini Kit v2 on the EZ1 advanced XL Biorobot workstation (Qiagen). Elution was performed in a 90 μL volume. The reverse transcription and PCR reactions were performed immediately after extraction according to manufacturer instructions. Bacteriophage lambda was used as a run control for the xTAG assays, as well as external positive and no-template controls. The study was approved by the hospital ethics clearance committee and the data was analyzed using Microsoft excel software and statistical analysis was done using SPSS software.

3. Results

A total of 40 patients were analysed (Table 1). Mean age of the study population was 50.6 years, 18(45%) of the subjects were more than 55 years of age and 28 (70%) were male. The commonest co-morbidity was diabetes mellitus in 17 patients (42.5%) followed by chronic kidney disease (CKD) in 9 (22.5%) and drug induced (prednisone, tacrolimus and mycophenolate mofetil in various combinations) T cell immunosuppression in 8 (20%) patients. In 13 (32.5%) patients there were no co-morbidities. The most common respiratory virus was rhino virus in 9 (22.5%) patients followed by influenza H3/H3N2 in 7 (17.5%), H1N1 in 6 (15%) and RSV in 4 (10%). All strains of influenza taken together constituted 19 (47.5%) patients. Mixed infections were found in 5 (12.5%) patients. Most

cases of influenza were seen during November (Fig. 1) which coincides with the Northeast monsoon in Chennai and surrounding areas. Two peaks of HRV were seen in March and June. Fever was the most common clinical feature seen in 29 (72.5%) patients followed by cough in 24 (60%), rhinorrhea in 23 (57.5%) and dyspnea in 23 (57.5%). A history of contact with another person with a respiratory virus like illness was present in 22 (55%) patients. Chest X Ray was normal in 12 (30%) of the subjects and other subjects had varied findings as summarised in Table 2. Patients infected with HRV had dyspnea at presentation in 88.9%, higher than with other viruses. H3N2, Influenza A and HMPV tended to infect patients older than 60 years. Patients infected with H3N2 and H1N1 required mechanical ventilation in more than 50% of cases. Four out of 5 deaths in the study group had infection with the influenza (H3N2, H1N1, influenza B) viruses. Twenty percent of patients infected with the influenza group of viruses required mechanical ventilation compared with only 5% of patients with other viruses, a statistically significant difference (p = 0.02). Of 40 patients studied, 33 were started on antibiotics before the receipt of respiratory viral diagnostics. After the diagnosis of the viral infection, antibiotics were completely stopped in 10 (30.3%) patients and de-escalated to a narrower spectrum agent in another 10 (30.3%) patients. The remaining 13 patients (39.4%), all >55 years of age, were continued on original or escalated to broad spectrum antibiotics due to suspected or confirmed concomitant bacterial infections, 5 of these developed ventilator associated pneumonia (VAP) and 1 had bacteremia due to unknown source. Seven out of these 13 patients were either organ transplant recipients or were getting immunosuppression. No patient whose antibiotics were de-escalated died, whereas there were 5 deaths in patients in whom de-escalation was not done (Table 3). Total 5 patients had VAP. Four out of 5 deaths were due to VAP and cause of death of the 5th patient could not be identified. All the 5 patients had some co-morbidity (4 had DM and 1 was COPD).

4. Discussion

Our study is the largest on patients hospitalized with viral pneumonia involving both adults and children from India, while

Table 1
Summary of various parameters among study population with sub group analysis.

	HRV (n = 9)	H3/H3N2 (n = 7)	H1N1 (n = 6)	Influenza A (n = 3)	Influenza B (n = 3)	RSV (n = 4)	HMPV (n = 2)	PIV-3 (n = 1)	Co-infections (n = 5)	Total (n = 40)
Age(mean) in years	40.1	64.4	43.1	67.6	52.1	41.5	65	31	51.2	50.6
DM	4(44%)	6(85.7%)	2(33.3%)	1(33.3%)	2(66.6%)	0	2(100%)	0	0	17(42.5%)
CKD	3(33.3%)	0	1(16.6%)	0	1(33.3%)	1(25%)	1(50%)	1(100%)	1 (20%)	9(22.5%)
COPD	0	1(14.2%)	1(16.6%)	1(33.3%)	0	0	0	0	0	3(7.5%)
Organ transplant recipient	1(11.1%)	0	1(16.6%)	0	0	1(25%)	0	1(100%)	0	4 (10%)
Immunosuppression	1(11.1%)	0	1(16.6%)	0(0%)	0(0%)	2(50%)	1(50%)	1(100%)	2	8 (20%)
Heart failure	1(11.1%)	3(42.8%)	0	0	1(33.3%)	1(25%)	0	0	0	6(15%)
Sick contact	5(55.5%)	3(42.8%)	6(100%)	1(33.3%)	3(100%)	0(0%)	1(50%)	0	3 (60%)	22(55%)
Fever	6(66.6%)	5(71.4%)	5(83.3%)	3(100%)	2(66.6%)	3(75%)	1(50%)	0	4 (80%)	29(72.5%)
Rhinorrhea	6(66.6%)	3(42.8%)	2(33.3%)	1(33.3%)	2(66.6%)	3(75%)	2(100%)	0	5 (100%)	23(57.5%)
Sore throat	1(11.1%)	2(28.5%)	4(66.6%)	0	0	0	0	0	2 (40%)	9(22.5%)
Cough	4(44.4%)	3(42.8%)	4(66.6%)	1(33.3%)	2(66.6%)	3(75%)	2(100%)	1(100%)	4 (40%)	24(60%)
Dyspnea	8(88.9%)	5(71.4%)	4(66.6%)	2(66.6%)	1(33.3)	1(25%)	1(50%)	1(100%)	0	23(57.5%)
WBC(Mean)	9.25	10.34	12.86	10.53	9.83	7.6	7.5	11	4.4	9.25
Average duration of symptoms(in Days)	2.88	3.28	4.33	2	3.33	2.25	3.5	4	4	3.28
Ventilator requirement	1(11.1%)	4(57.1%)	3(50%)	0	1(33.3%)	1(25%)	0	0	0	10 (25%)
Ventilator Associated Pneumonia (VAP)	1	2	1	1	0	0	0	0	0	5 (12.5%)
Bacteremia	0	1	0	0	0	0	0	0	0	1 (2.5%)
Mortality	0	2(28.5%)	1(16.6%)	0	1(33.3%)	1(25%)	0	0	0	5 (12.5%)

DM: Diabetes mellitus, CKD: chronic kidney disease, COPD: chronic obstructive pulmonary disease, CHF: Heart failure.
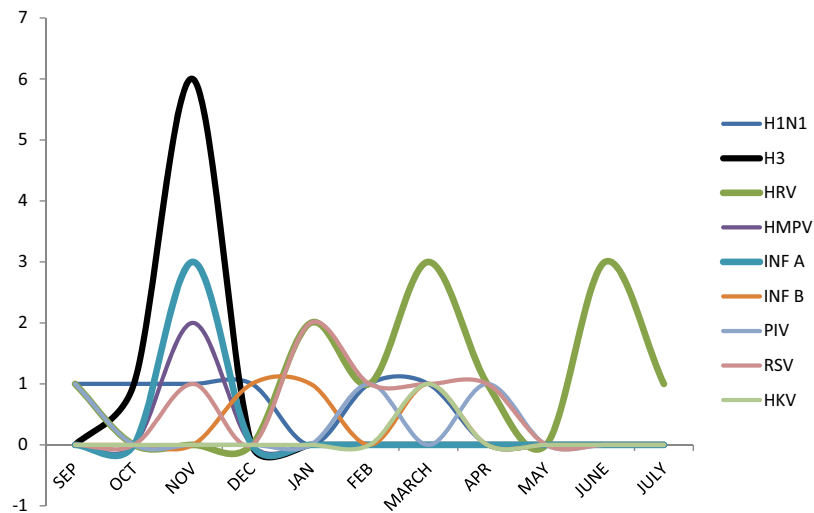
Fig. 1. Seasonal distribution of viruses.

Table 2
Chest X Ray findings of the study population.

Chest x ray findings	Study population(%)
Bilateral interstitial infiltrates	12(30%)
Lobar infiltrates	9(22.5%)
Increased broncho-vascular markings	5(12.5%)
Multilobar infiltrates	2(5%)
Normal	12(30%)

Table 3
De-escalation of antibiotics and mortality.

Antibiotics	Alive	Death
De-escalated	20(71.4%)	0(0%)
Not de-escalated	8(28.6%)	5(100%)
Total	28	5

there are many published studies from India on hospitalised patients with 2009 H1N1 influenza, there are relatively few studies on non H1N1 influenza and other respiratory viruses [5,7–9].

In our study most patients were above the age of 55, with males being more commonly affected than females (70% and 30% respectively). In a third of our patients there were no co-morbidities noted; the commonest co-morbidities in the remainder were diabetes and CKD, and up to 20% were immunocompromised by medications. Respiratory viral infections in immunocompromised patients tend to be severe requiring mechanical ventilation and vasopressors support in significant proportions of patients [10,11]. In our study 8 (20%) patients were immunosuppressed, of which only one patient required mechanical ventilation and all survived.

Consistent with the other studies, influenza and rhinovirus were more common compared with other viruses [12,13]. Non influenza viruses (52.5%) were more common than influenza viruses (47.5%): this highlights the large volume of disease which may be missed if testing for H1N1 alone is done, as is the widespread practice in India. This is consistent with the data published by Walker et al and Seo et al. [10,11]. Influenza strains other than H1N1 were in fact more common than H1N1 influenza, highlighting that there are many patients who may potentially benefit from oseltamivir or other antivirals. Our study highlights

the importance of testing for non H1N1 influenza and other respiratory viruses, especially outside the peak influenza season.

Rhinovirus (22.5%) was the most common non influenza virus followed by RSV (10%) and metapneumovirus (5%). This is consistent with findings of Jain et al where rhinovirus was the most common viral cause of community acquired pneumonia [15]. Mixed infections were seen in 12.5% of the patients. Influenza H3N2, influenza A and HMPV tended to affect older patients.

Influenza infections tend to be clustered in November. This is consistent with other published data from India [9] and is related to the annual Northeast monsoon every year during this period in this part of India. This supports administering influenza vaccine annually in the months of September-October in Chennai and surrounding areas, especially as the updated Northern Hemisphere vaccine will be available at that time. HRV tended to cluster in the months of March and June.

Fever and cough were the commonest symptoms at presentations followed by rhinorrhea and dyspnea, consistent with the study by Walker et. al. and Seo et al where most common symptoms were running nose, cough and dyspnea [10,11]. The presence of a sick household contact was noted in 55% percent of cases, an important diagnostic clue. The most common finding on chest X-ray was bilateral interstitial infiltrates typical of viral pneumonia [14]. The chest X Ray was normal in 30% of the cases.

In our stud,y influenza infections tend to be severe at presentation requiring mechanical ventilation more often in comparison with the non influenza viruses (p = 0.02), in contrast with the study of Seo et al. [11] and Walker et al where influenza and non-influenza viruses were equally severe at presentation.

There is lot of inappropriate antibiotic use in India as antibiotics are used to treat respiratory viral infection on suspicion of concomitant bacterial infection. In our study a total of 33 out of 40 patients were started on antibiotics at presentation: after diagnosis of the respiratory virus, antibiotics were de-escalated or stopped in a total of 20 (71.4%) patients. Outcome was good in all 20 patients. Our study signifies the importance of diagnosing respiratory virus and safety of de-escalation of antibiotics without adverse outcomes. There were a significantly increased number of deaths in patients in whom antibiotics were not de-escalated, this may reflect confounding factors like age of the patient, co-morbidities, severity of disease at presentation and hospital acquired infections. Nevertheless our data support the practice of stopping or de-escalating antibiotics when viral pneumonia is confirmed.

There is increasing data to suggest that hospital acquired pneumonia due to respiratory viruses are common, usually due to cross transmission between patients, and mandate early diagnosis and droplet isolation to prevent outbreaks [16]. Prior to the introduction of multiplex PCR for diagnosis of respiratory viruses, droplet isolation used to be done only in those patients in whom H1N1 PCR was positive: as only 6(15%) patients had H1N1 infection, there would have been a potential risk for spread of infection in the remaining 85%. With the introduction of multiplex PCR now droplet isolation could be extended for patients infected with all of the respiratory viruses.

We conclude that respiratory viruses are an important cause of community acquired pneumonia leading to hospitalization, and mandate the use of multiplex PCR for diagnosis, especially when outside the peak influenza season. Patients usually present with fever, cough, a household contact with respiratory symptoms and have bilateral pulmonary infiltrates. Diagnosis facilitates early use of antivirals and droplet isolation, resulting in better patient outcome and prevention of cross-transmission of viruses in the hospital. Antibiotic de-escalation for patients with viral pneumonia would reduce costs and may slow development of antibiotic. A policy of looking for influenza H1N1 only may result in missing as many as 85% of respiratory viruses, including other influenza viruses which may respond to antivirals, and policy makers and clinicians should switch to a policy of routinely ordering multiplex PCR in the appropriate clinical setting for a viral pneumonia, especially when outside the peak influenza season.

Conflict of interest

None.

Competing interests

All the authors have seen the final manuscript and approve it for submission.

The authors have no competing interests in the publication of this manuscript to declare.

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