



PREVALENCE OF RESPIRATORY VIRUSES AMONG PATIENTS WITH SEVERE ACUTE RESPIRATORY TRACT INFECTIONS AND INFLUENZA-LIKE ILLNESS IN ANDAMAN ISLANDS

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ABSTRACT Acute respiratory infections (ARI) are a major public health concern worldwide that affects a large number of the world's population. Amongst the respiratory viruses, Influenza viruses are becoming a major public health challenge with even greater concern. Out of 1174 samples collected, 43 were positive with a total positivity rate of 3.66% for at least one virus. 41.86% subjects were under 10 years old. Among the virus-positive cases, the influenza A rate was highest 35(81.39%), followed by influenza B 4(9.3%), Para influenza 2(4.65%), Rhino virus 1(2.3%), and RSV 1(2.3%).

KEYWORDS : Respiratory Viruses, prevalence Influenza like illness, Severe acute respiratory infection

Introduction:

Acute respiratory infections (ARI) are a major public health concern worldwide that affects a large number of the world's population. Despite advances achieved in the twentieth century with the advent of antibiotics, antivirals, and vaccines, there are no specific interventions for the majority of viral respiratory infections. Respiratory viruses are a diverse group of viruses that infect the pulmonary system, cause respiratory and other symptoms, and are primarily spread through infected secretions. Respiratory viral infections are often difficult to distinguish medically. Respiratory viruses belong to several virus families that differ each in viral and genomic structures, mode of transmission, vulnerable population, transmissibility, seasonality of circulation, and disease severity. Although significant progress in the management of respiratory viruses such as influenza and other respiratory viral infections in recent years, the world still suffers from these illnesses every year, resulting in increased morbidity (James, S. L. et al., 2017), mortality (Roth, G. A. et al., 2018), and economic losses (Fendrick, A. M. et al., 2003).

According to the National Health Portal of India in 2018, respiratory infections caused 41,996,260 illnesses and 3,740 fatalities occurred in India. ARI was responsible for 69 percent of all communicable disease cases. (Worldometer. 2021)

Viruses are the most common cause of ARI (Choi E et al., 2018), with human influenza virus, RSV, parainfluenza virus, rhinovirus, metapneumovirus, adenovirus, human coronavirus, and Boca virus accounting for over seventy percent of respiratory viral infections. (Ramaekers K et al. 2017). Most of the SARI cases were viral infections that cause generalized clinical symptoms that cannot be easily differentiated from other respiratory infections. (Akshay R. Yadav et al., 2020)

Amongst the respiratory viruses, Influenza viruses are becoming a major public health challenge with even greater concern. Influenza virus infection is prevalent over the world, causing around 39 million episodes each year. Influenza A (INF-A) and influenza B (INF-B) are the most common viruses found. Multiple influenza strains have emerged over time, with the H3N2 and H1N1 subtypes related to INF-A being the most prominent. INF-B, which differs from INF-A virus, consists of two antigenically different lineages ("B/Yamagata/16/88-like" and "B/Victoria/2/87-like," referred as Yamagata and Victoria respectively) (Narayan et al., 2020). A new strain of influenza is exposed to the human population during flu epidemics, which happen every 6–10 years owing to antigenic drift and have a negative or positive impact on morbidity and mortality. The first human influenza epidemic of the twenty-first century is caused by the influenza

A(H1N1) pdm09 subtype virus, which evolved from the reassortment of swine Eurasian Avian (EA)-like viruses and North American Triple reassortment (TRIG) viruses. (Trevenec K., et al., 2012)

In 2009, the first influenza A (H1N1) pdm09 outbreak was recorded in the Andaman and Nicobar Islands, with a 33.5 percent attack rate among settlers and 26.3 percent among the aboriginal Nicobarese tribe. (Singh SS et al., 2011) However, no death occurred during this period and all the patients recovered without complications.

The Andaman and Nicobar Islands is located on the Indian subcontinent. Despite having a diversified population and the information available is scanty on the prevalence of respiratory viruses among patients with influenza-like illnesses and severe acute respiratory infections in this region.

The main aim of this study is to estimate the prevalence of Respiratory viruses among patients with Severe Acute Respiratory Infections and Influenza-like Illnesses in the south Andaman district in Andaman & Nicobar Islands.

Materials and Methods:

1. Study Setting:

The Andaman and Nicobar Islands (92-94°E; 6-14°N), a Union Territory of India, is an archipelago of 572 islands or islets stretching over 700 km from north to south in the Bay of Bengal. The territory is situated about 150 km (93 mi.) north of Aceh in Indonesia and is separated from Thailand and Burma by the Andaman Sea. Thirty-eight islands are inhabited, with a population of approximately 4.34 lakhs. Andaman and Nicobar Islands are divided into 3 districts namely North and Middle Andaman district (Headquarters: Mayabunder), South Andaman district (Headquarters: Port Blair), and Nicobar District (Headquarters: Car Nicobar). The Directorate of Health Services operates three district hospitals, various Community Health Centers, and Primary Health Centers in remote areas. (Directorate of Economics and Statistics, 2011)

Present observations are noted in a surveillance project on the Establishment of a Grade I Virology laboratory to investigate the various respiratory viruses among patients with ILI and SARI in the A&N Islands.

The format of ILI and SARI for data collection about each case, according to the case definition as per WHO. ILI is an acute respiratory infection with measured fever of $\geq 38^{\circ}\text{C}$ and cough with onset within the last 10 days. SARI cases additionally require hospitalization.

The study samples are being collected from tertiary Hospital, district

hospital, and PHCs of south Andaman district such as G.B. Pant hospital, Garacharma district hospital, PHC Chouldari, PHC Manglutan, CHC Bambooflat, PHC Wimberlygunj, and PHC Ferragunj.

2. Study Population:

In the period from January 2018 to October 2019, the patients who met case definitions of ILI and SARI were enrolled in this study (n=1174). Nasopharyngeal, oropharyngeal, and both swabs were tested for the presence of Influenza A, Respiratory Syncytial Virus (RSV), Influenza B, adenovirus, Parainfluenza 1/2/3/4, Human metapneumovirus (HMPV), and Rhinoviruses.

3. Laboratory methods and analysis:

All samples (Nasopharyngeal, oropharyngeal, and both) were collected from various parts of South Andaman and transported to Regional Medical Research Centre's laboratory in viral transport media. Viral RNA was extracted and the presence of respiratory viruses was detected using the Invitrogen Superscript™ III Platinum® one-step Quantitative kit according to the manufacturer's protocol. Primer and probe information for the detection of respiratory viruses were used from the ICMR-NIV kit protocol. This assay is based on Taq man Fluorogenic probe-based chemistry real-time RT-PCR assay. The RT-PCR testing was conducted for the qualitative detection and characterization of Influenza A (H1N1) pdm09, Influenza A (H3N2), and Influenza B Yamagata and Victoria lineage.

4. Data Analysis:

Data were analyzed with Minitab statistical software 21. The gender distribution of respiratory viruses was compared using the chi-square test. Statistical significance was defined as a p-value of <0.05.

5. Ethical considerations:

Clinical samples and data were collected after getting informed consent or assent from the patient or guardian. This study was approved by the Institutional Ethics Committee of ICMR-Regional Medical Research Centre, Port Blair. The study was conducted based on the tenets of Helsinki.

Results:

1. Overall viral detection

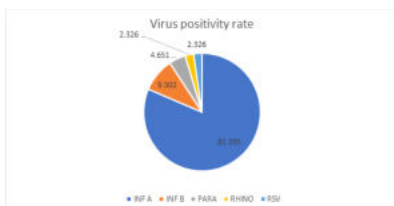
From January 2018 to October 2019, among 1174 samples collected, 43 were positive with a total positivity rate of 3.66% for at least one virus. There were 62.8 % were males and 37.2 % were females, (p=0.00) with a mean age of 18.3 years. 18 (41.86%) were under 10 years old, 8 (18.6%) were 11-20, 10 (23.25%) were 21-30, 4 (9.3%) were 31-40, 1 (2.32%) were 41-50, and 2 (4.65%) were 51-60. (Table 1)

Table 1: Demographic Characteristics

| Characteristic | N | PDR (%) |
|----------------|----|---------|
| Gender | | |
| Males | 27 | 62.8 |
| Females | 16 | 37.2 |
| Age group | | |
| 0-10 | 18 | 41.9 |
| 11-20 | 8 | 18.6 |
| 21-30 | 10 | 23.3 |
| 31-40 | 4 | 9.3 |
| 41-50 | 1 | 2.3 |
| 51-60 | 2 | 4.6 |

Among the virus-positive cases, the influenza A rate was highest 35(81.39%), followed by influenza B 4(9.3%), Para influenza 2(4.65%), Rhino virus 1(2.3%), and RSV 1(2.3%). (Figure 1)

Figure 1: Prevalence of virus positivity rate of respiratory viruses



The viral infection positivity rate was more in males (62.8%) compared to females (37.2%).

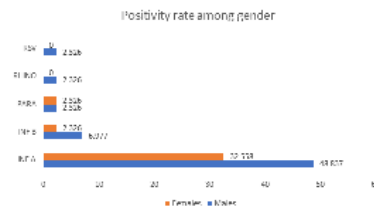
2. Detection of each virus

In this study, we screened for the detection of Influenza A, Respiratory Syncytial Virus (RSV), Influenza B, adenovirus, Parainfluenza 1/2/3/4, Human metapneumovirus (HMPV), and Rhinoviruses. Among these viruses, Influenza A, Influenza B, Parainfluenza, Respiratory Syncytial Virus, and Rhinoviruses are detected. (Figure 2)

Influenza A virus (81.4%) was the most prevalent etiological agent for respiratory viruses among the ILI and SARI in A&N Islands. It is more in males (48.84%) under 10 years old. The monthly number of positive cases of influenza A was more in the winter season (December).

Influenza B was also seen more in males (7%) compared to females (2.3%) but parainfluenza was equivalent in both males and females and Rhino and RSV were seen in only males. (Figure 2) Influenza B was also seen as more common in those under 10 years old. But other viruses do not have distinct age differences in positivity rate. The monthly number of positive cases of influenza B was more in march month. The other respiratory viruses do not show a clear seasonal pattern.

Figure 2: Comparison of positivity rate of respiratory viruses among gender



Discussion:

All respiratory viral infections have overlapping symptoms, making it challenging to diagnose a specific respiratory viral infection from the symptoms alone. Testing for the presence of respiratory viruses using molecular detection is the only way to validate a diagnosis. The PCR and its variants, which can be carried out with a singleplex or multiplex formats and probes after being developed and optimized in the lab, are the most popular diagnostic modalities. (Malhotra B. et al., 2016)

Numerous studies have concentrated on particular demographics (children or elderly), or only included SARI or ILI data, but we examined the frequency of influenza and other respiratory viruses in ILI and SARI patients in the Andaman Islands without regard to age. The heterogeneity of international data demonstrates that the observed prevalence data is influenced by the study period, respiratory viruses tested, ILI or SARI cases, a number of variables, the target population, the geographic location, the severity of the epidemic, the climate, and the historical disease burden of the area. As a result, it was difficult to compare the data from different studies. In this study, the five respiratory viruses (influenza A, influenza B, Para influenza, Rhinovirus, and RSV) were detected in 1174 patients. Among them, 43 are positive with a total positivity rate of 3.66% for at least one virus, which is not aligned with the positivity of respiratory viruses in the prior studies as 32.5 to 35.8 percent (Panda S et al., 2017; Fernandes-Matano L et al., 2017). Various studies have published higher rates are 69.1 to 85.8 percent and lower are 14.6 to 24.5 percent [Choi E et al., 2018; Richter J et al., 2016; Dong W et al., 2016; Wang H et al., 2016].

Rushabh Waghmode et al. concluded that RSV was the most prevalent virus in India except East, which included varying percentages of other viruses. When compared to other geographical regions, influenza was most prevalent in Eastern India, followed by Northern India. In Eastern India, records suggest a higher prevalence of INF-B, preceded by INF-A, with a few data reporting influenza as one group without specifying the types. In addition, compared to other regions, this area has a greater positivity rate of the parainfluenza virus. Due to its very cold winters and harsh temperature variations throughout the year, Northern and Eastern India may have higher rates of influenza and parainfluenza virus. (Rushabh Waghmode et al., 2021)

The positivity rates of influenza A, influenza B, Para influenza, Rhinovirus, and RSV were 81.39%, 9.3%, 4.65%, 2.3%, and 2.3% respectively. In this study, the overall positivity rate of influenza A was

the more in winter and there is no distinct seasonal variation for other respiratory viruses. A study conducted by Wang et al. also reported the greatest rate of Influenza During the period April 2018 to March 2019, the overall positive rate and positivity in Zhejiang Province were highest in winter, whereas the peak of viral detection occurred in spring. (Wang H et al., 2016); Kurskaya revealed that there was no significant seasonal variation. [Kurskaya O et al., 2018].

It was consistent with earlier studies that there were no significant variations in influenza detection between males and females. (Caini S et al., 2019; Horton KC et al., 2017) but in our study, there is a significant difference between the sexes.

The positivity rates of various studies are related to different kinds of patients, geographical areas, and detection methods. Among the 38,355 patients, 38 percent were male and 36.2 percent female. (Zhu et al., 2021) which was consistent with our results. In our study, there were no distinct differences were seen in age groups.

Limitations of the study:

In this study, We focused only on viral positivity rate, gender & age variation, and seasonal variation. However, we did not address the comorbidities/co-infections, clinical profile, hospitalization, etc. It is a single-center study, Inclusion of additional sentinel sites in the A & N Islands is strongly advised to add more sentinel sites to improve the generalizability of the results.

Conclusion:

This study showed that among ILI and SARI cases, the Influenza A viral positivity rate was highest in Andaman & Nicobar Islands. Influenza A positivity was more in males under 10 years old and it was highest in winter season.

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