CERASUS JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Distribution of pathogens of respiratory tract infections by months and age groups

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Received: 22 December 2023
Accepted: 11 January 2024
Published: 31 January 2024

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Abstract

Objective: Respiratory tract infections are a significant public health problem worldwide. The aim of this study is rapidly identify respiratory tract infection pathogens, classify them according to months and age groups, development of appropriate treatment recommendations according to pathogen and age.

Methods: Patients with a pathogen in their respiratory tract panels between September 2022 –March 2023 have been included in the study. Samples for respiratory tract panel were studied on QIAstat-Dx Analyzer 1.0 (Qiagen®, Hilden, Germany) device with QIAstat-Dx® Respiratory SARS-CoV-2 Panel kit. Results of six months were evaluated retrospectively.

Results: A total of 557 pathogens were found in 437 patients among 576 inpatients whose respiratory tract panel has been requested. The most frequently seen agent was determined as rhinovirus/enterovirus (25.13%) and the most frequent co-occurrence was determined to be rhinovirus/enterovirus - respiratory syncytial virus (RSV). The most frequently seen pathogen in September, October, January and February was rhinovirus/enterovirus while RSV was the most frequent agent in November and December.

Conclusion: Respiratory tract infection pathogens were analyzed a six-month period, and the highest positivity rate was detected in December. The 1-18 age range was the group in which the highest number of pathogens were detected. And the fact that RSV positivity in <1 age group was at high rates (51.58%) is important. Very short detection time for viral pathogens thanks to molecular methods in 75.86% of patients, who have been hospitalized due to respiratory tract infection with panel testing done, is considered to contribute in reducing improper use of antibiotics.

Keywords: Respiratory Tract Infection, Viral Infections, RSV

You may cite this article as: Uğur M, Şahin AM. Distribution of pathogens of respiratory tract infections by months and age groups. *Cerasus J Med.* 2024;1(1):35-41.

Introduction

Acute respiratory infections account for a large proportion of all acute morbidity and mortality worldwide [1]. As viral pathogens cause disease at a rate of 80%, they also rank high among the list of reasons of improper use of antibiotics. The main viral pathogens are influenza virus, respiratory syncytial virus (RSV), coronavirus, adenovirus and rhinovirus [1]. Viral respiratory tract infections increase especially common in autumn-winter months. The disease is self-limiting in individuals while they cause morbidity and mortality in vulnerable individuals. These infections are among significant causes of hospitalization especially in pediatric and geriatric patients [2,3].

Distinguishing between viral and bacterial causes in respiratory tract infections is only possible through laboratory diagnosis since clinic symptoms specific to viral pathogens are very few [4].

Real-time polymerase chain reaction (RT-PCR) tests with high sensitivity which give results in shorter periods and which can identify coinfections are preferred rather than classical virology diagnosis tests such as routine laboratory virus culture, hemagglutination inhibition test, enzyme-linked immuno sorbent assay test and immunofluorescence test. Respiratory tract viruses may be identified with high sensitivity and specificity through RT-PCR and thus enabling prevention of unnecessary antibiotics usage [3,5].

Accurate and rapid identification of viral pathogens is quite important for estimating the course of illness, implementing the proper treatment, reducing mortality and morbidity rates, stopping epidemics and reducing unnecessary use of antibiotics [1]. Knowing which virus is an agent other than bacterial and viral distinction would provide information about the progress of illness and the risk of pneumonia. The progress of illness, and thus the treatment approach vary depending on age groups and the pathogens [6]. Fast and correct identification of the agent through molecular methods plays a key role in the correct treatment.

Our study analyzes the six-month period in autumn-winter seasons in which viral respiratory tract infection outbreaks increased. The aim was to implement the right antiviral treatment through early detection of agents by determining the distributions of pathogens by months and age groups and to prevent unnecessary antibiotic usage by ending empirically initiated antibiotic treatment.

Methods

The study has obtained the approval of the ethical board with the ethical board decision number 22.05.2023/07 from Giresun Training and Research Hospital Clinical Research Ethics Committee. The study included patients with identified respiratory tract infections in the 6-month period between September 2022-March 2023. Samples obtained from patients who were hospitalized for respiratory tract infectionswere sent to laboratory to be studied on with QIAstat-Dx Analyzer 1.0 (Qiagen®, Hilden, Germany) device and QIAstat-Dx® Respiratory SARS-CoV-2 Panel kit. Panel kit identifies SARS-CoV-2 and 21 additional pathogens (Influenza A, Influenza A subtype H1N1/2009, Influenza A subtype H1, Influenza A subtype H3, Influenza B, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Parainfluenza virus 1, Parainfluenza virus 2, Parainfluenza virus 3, Parainfluenza virus 4, Respiratory syncytial virus A/B, human Metapneumovirus A/B, Adenovirus, Bocavirus, Rhinovirus/Enterovirus, *Mycoplasma pneumoniae*, *Legionella pneumophila* and *Bordetella pertussis*). Results of six-month period were assessed retrospectively. Distribution of infection pathogens by months and age ranges was analyzed.

Results

Among 576 inpatients whose respiratory tract panel tests were requested in the six-month period, 557 pathogens were identified in 437 patients. 238 patients were male and 199 patients were female and their mean ages were 14.10± 23.56, 20.57±28.17. There were 90 patients below the age of one, 237 patients between 1-18, 65 patients between 18-65 and 45 patients over 65. 41.11% of the patient group under the age of 1 were intensive care patients together with 23.63% of the patient group of 1-18, 12.31% of the patient group of 19-65 and 48.89% of the patient group over 65. Respiratory tract panel positivity rate was determined as 75.86%. Among 437 patients, one pathogen was identified in 332 patients (75.97%), two pathogens were identified in 92 patients (21.05%), three pathogens were identified in 11 patients (2.52%)

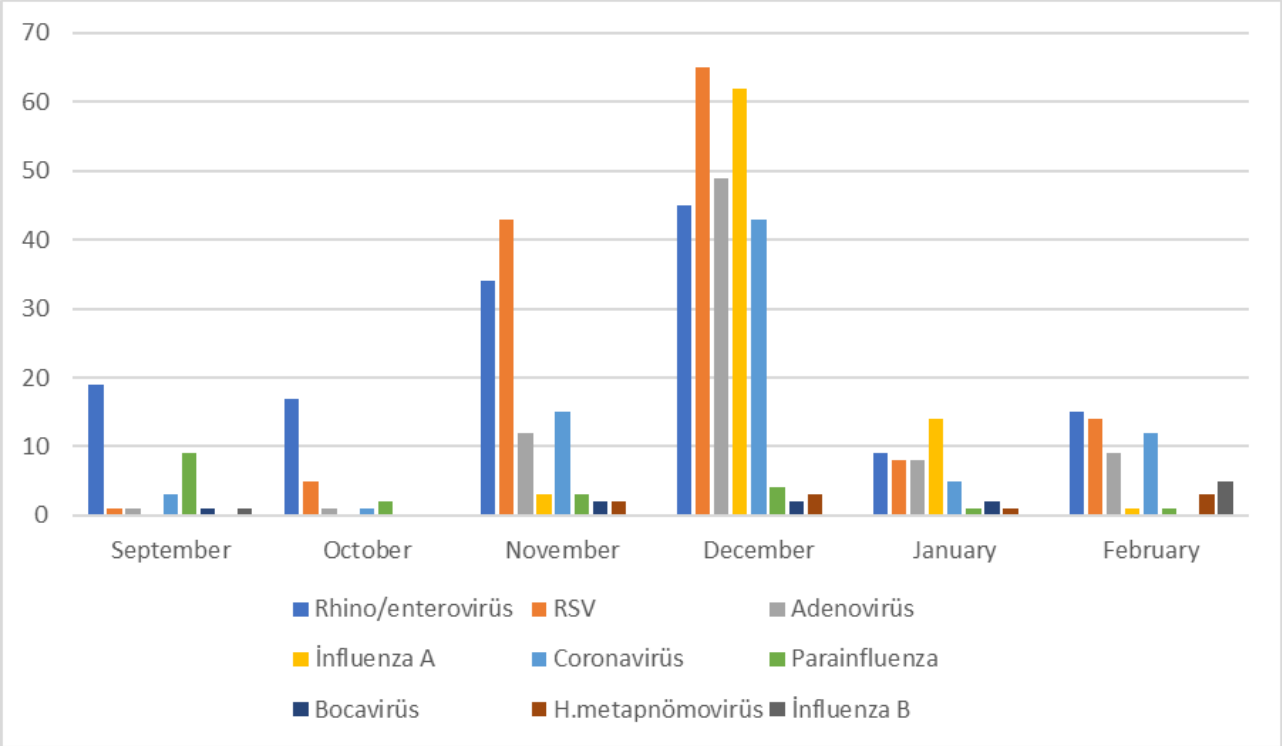

Figure 1: Distribution of pathogens of respiratory tract infection by months

Table 1. Distribution of pathogens of respiratory tract infection by age groups

Pathogens	<1 (%)	1-18 (%)	19-65 (%)	>65 (%)	Total
Rhinovirus/Enterovirus	34 (26.98)	82 (26.28)	15 (21.43)	9 (18.37)	140 (25.13)
RSV*	65 (51.58)	56 (17.95)	5 (7.14)	10 (20.41)	136 (24.42)
Adenovirus	6 (4.76)	69 (22.11)	3 (4.29)	2 (4.08)	80 (14.36)
Influenza A H3	1 (0.79)	41 (13.14)	15 (21.43)	4 (8.16)	61 (10.95)
Coronavirus OC43	10 (7.93)	19 (6.09)	1 (1.43)	5 (10.20)	35 (6.28)
SARS-CoV-2	1 (0.79)	4 (1.28)	20 (28.57)	15 (30.61)	40 (7.18)
Parainfluenza	5 (3.97)	11 (3.52)	3 (4.29)	1 (2.04)	20 (3.59)
Influenza A H1N1	0	13 (4.17)	3 (4.29)	1 (2.04)	17 (3.05)
Bocavirus	0	6 (1.92)	1 (1.43)	0	7 (1.26)
Human metapneumovirus	3 (2.38)	4 (1.28)	1 (1.43)	1 (2.04)	9 (1.62)
Human coronavirus NL63	1 (0.79)	3 (0.96)	0	0	4 (0.72)
Influenza A	0	1 (0.32)	0	1 (2.04)	2 (0.36)
Influenza B	0	3 (0.96)	3 (4.29)	0	6 (1.08)
Total agents	126	312	70	49	557
Number of patients	90 (20.59)	237 (54.23)	65 (14.87)	45 (10.30)	437
INTENSIVE CARE	37 (41.11)	56 (23.63)	8 (12.31)	22 (48.89)	123 (28.15)
SERVICE	53	181	57	23	314

*Respiratory syncytial virus

and four pathogens were identified in 2 patients (0.46%). The most frequent pathogen was identified as rhinovirus/enterovirus (25.13%) and most frequently seen coinfections were rhinovirus/enterovirus-RSV (19.11%). The most frequent pathogen in September, October, January and February was rhinovirus/enterovirus (54.29%, 65.38%, 18.75%, 25%) while the most frequent pathogen in November and December was RSV (37.72%, 23.81%). 273 (49.01%) of the total 557 pathogens were identified in the month of December. Distribution of pathogens by months is presented in Figure 1. The most frequent pathogen among the patient group under the age of one was revealed to be RSV (51.58%) while it was rhinovirus/enterovirus in 1-18 age group (26.28%), SARS-CoV-2 in 18-65 and over 65 age groups (28.57%), (30.61%). Distribution of pathogens by age groups is presented in Table 1. Polymicrobial pathogens were identified in 32 of patients under the age of one (35.55%), 63 of the patients in 1-18 age group (26.58%), 6 of the patients in 18-65 age group (9.23%) and 4 of the patients over 65 (8.88%).

Discussion

Although the clinical findings of bacterial and viral respiratory tract infections are similar, their treatment approaches are different. Timely and correct diagnosis of respiratory tract pathogens is important especially to prevent unnecessary use of antibiotics and antibiotic resistance [7]. Various studies have shown that unnecessary antibiotic usage is at a quite high level in treatment of respiratory tract infections [8-10]. Unnecessary use of antibiotics leads to increased cost as well as contributing in the development of antibiotic resistance [11]. Moreover, it should be noted that antibiotics are not innocent pharmaceuticals, and they may have serious side effects [12]. In this study, panel test was requested from 576 patients who were hospitalized due to respiratory tract infection and 437 of these (75.86%) were revealed to have one or more viral pathogens. This significantly high-rate points at the smart utilization of the test as well as the fact that most of the respiratory tract infections are caused by viral pathogens.

The most frequently identified rhinovirus/enterovirus is the most common reason of upper respiratory tract infections (URTIs) across the world and almost throughout the year and it peaks especially in autumn and spring months [13]. The pathogen which is considered to be the cause of relatively innocent URTIs is associated with chronic obstructive pulmonary diseases exacerbations, development of asthma, sever bronchiolitis in infants and children, and fatal pneumonia in elderly and adults with suppressed immune systems [14,15]. In our study, rhinovirus/enterovirus was identified throughout all months, but it was observed to constitute the majority of agents especially in September (54.28%) and October (65.38%). Although observed in all age groups, rhinovirus is the most common respiratory tract virus among children under the age of five and it is the leading cause of hospitalization for children under the age of two. And it is reportedly the second pathogen, following RSV, for hospitalizations due to bronchiolitis [14,16]. In a study conducted on children hospitalized due to acute respiratory tract infection in Croatia, it was determined that rhinovirus was the most common virus detected in individuals under 18 years of age, 60.4% monoinfection and 39.6% coinfection with other respiratory viruses [16]. In our study, rhinovirus was observed the most among the age group of 1-18 and the pathogen was identified as monoinfection in 59.29% (83) of the patients and as coinfection in 49.01% (57) of the patients.

The study identified RSV as the most frequent pathogen in November and December in line with many other studies [15,16]. When pathogen distribution by age groups is examined, RSV was the most frequently identified pathogenin <1 age group (51.58%). The most important cause of childhood lower respiratory tract infections (LRTIs) is respiratory tract viruses, and the most frequent pathogen is RSV. It is estimated that global mortality rate attributed to RSV-related LRTIs in small children is as high as 150,000 per year [17,18]. It is reported that 2.1 million outpatient treatments and more than 57.500 hospitalizations occur every year in children below the age of five in relation to RSV infections in the U.S. [19]. According to the findings of an extensive study, approximately 33 million RSV-related acute LRTI cases, 3,6 million RSV-related acute LRTI hospitalizations and 26,300 hospital deaths occur every year across the world. 13,300 cases of deaths are reported to be among 0-6-month old infants [20]. Şık et al. identified RSV as the most frequently

seen pathogen in their study conducted on the patients in pediatric intensive care unit [21]. As an pathogen which is frequently identified in the early years of life, RSV is also known as a common and very severe respiratory tract pathogen among 65 year-olds and older individuals [22]. In a multi-centered prospective study, multi pathogen infections with rhinovirus and RSV were identified in 30% of the children hospitalized due to respiratory tract infection [23]. In our study, RSV was identified as monoinfection at the rate of 64.7% and the highest coinfection rate of 19.11% was determined with rhinovirus/enterovirus. The studies show that the most common coinfection is rhinovirus-RSV coinfection [24,25].

Adenovirus may cause infections at all ages, however it is most commonly identified among pediatric population, especially among small children and infants [26]. In our study, adenovirus was identified in 80 patients and most frequently among individuals in the age group of 1-18 (86.25%). In a study conducted by Chen et al. on children below the age of 14, yearly pathogens of respiratory tract infections were analyzed and a significant increase in adenovirus was identified in 2018-2019. Although it has shown a decrease in 2020-2021 in the post-COVID-19 period, 80% of the cases were reported to have been hospitalized [27]. And 59.6% of the cases during an epidemic identified in the U.S. in 2013–2014 were reported to be below the age of 18, and 68.7% of all cases were reportedly hospitalized while 31.6% received treatment in the intensive care unit [28]. 93.75% of adenovirus cases being seen in children under the age of 18 and coinfection having a high rate of 50% are important facts in terms of mortality and morbidity of infection.

Influenza outbreaks which typically start as of the end of October in the Northern hemisphere peak between December-February and continue up until May [29]. Influenza is rarely identified in autumn in the study and a dramatic increase is observed in the month of December. Influenza virus infections generally limit themselves with URTIs while they are also associated with LRTIs especially among elderly people with the possibility of a mortal course of disease. Individuals below the age of one and above the age of 65 are in the most vulnerable age group against the virus and vaccination is recommended for this group [30,31]. In our study, only 7 individuals were diagnosed with this pathogenin the patient group of below the age of one and above the age of 65, and however, the fact that 5 of those received intensive care treatment (71.43%) shows the importance of the pathogen in these age groups. Influenza B viral infections generally lead to localized outbreaks while influenza A virus is a primary pathogen for human infections and thus it is the main reason for epidemics and pandemics [1]. Two subtypes of influenza A which are still in circulation are A (H1N1) and A (H3N2) [31]. According to the data of our country's Weekly Influenza (Flu) Surveillance Report, influenza A H3 virus has the highest rate of 62% of all influenza cases of 2022-2023 [32]. According to the analysis of six-month data in our study, 70.9% of 86 influenza cases in total are observed to be Influenza A H3. According to the data of the Weekly Influenza (Flu) Surveillance Report, the distribution of the cases similar to Influenza virus positive flu by age groups shows that the highest case rate is among the age group of 5-14 [32].

Coronavirus infections generally increase in autumn and winter months across the world [33,34]. Four-season coronavirus strain may cause common cold symptoms in people, and it is responsible of 15-30% of respiratory tract infections each year. The most frequent strain among these was identified as OC43-CoV [16]. In our study, OC43-CoV was identified as the most frequent seasonal coronavirus other than SARS-CoV-2 and NL63-CoV was identified in very few numbers.

Distribution of pathogens of respiratory tract infections identified via molecular method was analyzed in the study for a six-month period covering autumn and winter seasons. Distribution of respiratory tract pathogens by seasons and age groups was similar in our country to the global data. The fact that 78.6% of the pathogens were identified in individuals below the age of 18 shows that children are more at risk in terms of respiratory tract infections compared to other age groups. Especially the high rate of intensive care hospitalizations of infants below the age of 1 due to respiratory tract infections (41.11%) shows the importance of fast and correct diagnosis of respiratory tract viruses in the first year of life and early childhood period and this is possible with molecular methods. Early detection in very short times such as 1 hour is possible with molecular methods for

patients who go to the hospital for respiratory tract infection and are hospitalized due to the severity of their clinical conditions. Identification of positivity in 75.86% of samples and all of it having viral pathogens are important information to be able to prevent empirical antibiotic usage in this patient group.

Conclusion

Knowing that viral agents are so common in respiratory tract infections, which involve the most frequent unnecessary uses of antibiotics, should be instructive for clinicians in terms of initiating empirical antibiotic treatment. Moreover, the use of PCR on the right patients will enable fast identification of the pathogens as well as their proper treatments.

Financial support and sponsorship: There are no financial support and sponsorship.

Conflict of interest: There are no conflicts of interest.

Ethical considerations: The study has obtained the approval of the ethical board with the ethical board decision number 22.05.2023/07 from Giresun Training and Research Hospital Clinical Research Ethics Committee.

Author contribution: Concept: M.U., A.M.Ş., Design: M.U., A.M.Ş., Data Collection or Processing: M.U., A.M.Ş., Analysis or Interpretation: M.U., A.M.Ş., Literature Search: M.U., A.M.Ş., Writing: M.U., A.M.Ş.

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