ORIGINAL RESEARCH

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Investigation of Viral Serology in Patients Admitted to the Emergency Department with Symptoms of Upper Respiratory Tract Infection Following the COVID-19 Pandemic

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Abstract

Objective: Respiratory tract infections (RTIs) are a significant public health problem, especially during winter, causing increased emergency department (ED) visits and antibiotic prescriptions. Rapid and accurate identification of causative pathogens is crucial for appropriate management and infection control.

Materials and Methods: This prospective, observational, single-center study included 322 adult patients presenting with symptoms of upper respiratory tract infection to a university hospital ED between October 2023 and March 2024. Nasal and oropharyngeal swab samples were collected from all participants and analyzed using multiplex RT-qPCR for 21 respiratory pathogens, including SARS-CoV-2. Demographic data, clinical features, and physicians' initial intentions regarding antibiotic or antiviral prescriptions were recorded.

Results: At least one respiratory pathogen was detected in 68.6% of patients, with Influenza A (17.1%), COVID-19 (11.2%), and Influenza B (6.8%) being the most common. Coinfection with two pathogens was found in 6.2% of cases, most frequently involving Influenza A and RSV. Before receiving PCR results, physicians reported that they would prescribe antibiotics to 32.9% of patients.

Conclusion: These findings highlight the importance of rapid diagnostic testing in reducing unnecessary antibiotic use and provide updated epidemiological data on adult RTIs in the post-COVID-19 era.

Keywords: Antibiotic stewardship, emergency department, multiplex PCR, upper respiratory tract infection, viral pathogens

Introduction

Respiratory tract infections (RTIs) are a major health concern worldwide, especially during winter due to seasonal epidemics [1]. They contribute significantly to morbidity and mortality, as well as increased emergency department (ED) visits and antibiotic prescriptions [1,2]. Respiratory viruses play an important role in the etiology, followed by bacteria [3].

It is important to differentiate COVID-19 and influenza from other viral upper respiratory tract infections or bacterial pneumonia because there are specific treatments available for some respiratory viruses [4,5]. PCR tests for the rapid detection of respiratory pathogens have high sensitivity and specificity and are easy to apply, providing rapid results—particularly important in ED settings [1]. These diagnostic tests for respiratory viral infections targeting influenza virus, COVID-19, and respiratory syncytial virus (RSV) may change treatment modalities and isolation procedures [2,6]. Most hospitals face challenges due to the restricted number of isolation rooms designated for specific patient groups, such as oncologic patients. Hospital bed management may be improved with the use of rapid diagnostic tests applied in the ED to assist in decisions regarding hospital admission and appropriate bed selection [3,4,7]. Gaining insight into the epidemiology and causes of acute respiratory infections is vital for developing effective strategies for rapid treatment, prevention, and control [8].

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There are few studies evaluating viral agents in respiratory tract infections in the adult population, especially from Türkiye, and most focus on children or on lower respiratory tract infections [9,10]. The aim of this study was to investigate respiratory pathogens detected in adult patients presenting to the emergency department with symptoms of upper respiratory tract infection following the COVID-19 pandemic.

Materials and Methods

Design and Setting

This study was designed as a prospective, observational, single-center study conducted in an academic emergency department. Ethical approval was obtained from the institutional review board and relevant local committees before data collection (date: 08.02.2024, approval no.09.2023.1752, Marmara University Faculty of Medicine Clinical Research Ethics Committee).

Study Population and Sample

Between October 2023 and March 2024, consecutive patients admitted to the emergency department of a tertiary care center with a preliminary diagnosis of acute upper respiratory tract infection (URTI) were included in the study. The patients' electronic medical data at the time of admission and during treatment were collected and analyzed.

Inclusion and Exclusion Criteria

This study was conducted on adult patients (>18 years old) who presented to a tertiary care hospital emergency department. The inclusion criteria were as follows: (i) presence of symptoms consistent with acute URTI, such as fever, cough, sore throat, runny nose, nasal congestion, fatigue, weakness, nausea, vomiting, or diarrhea, along with a preliminary diagnosis of upper respiratory tract infection; (ii) having undergone a viral respiratory panel and COVID-19 PCR test requested by the emergency department physician; (iii) informed consent from the patient, a relative, or a legal guardian.

Patients were excluded if they had a fever persisting for more than seven days, had received antibiotics within the past week, or had not provided consent. Patients who withdrew their consent during the study or had incomplete data in the collected forms were also excluded.

Study Process and Data Collection

Patients with a preliminary diagnosis of upper respiratory tract infection who met the inclusion criteria were followed up and treated according to the recommendations of the emergency department physician. No additional tests or alternative treatments were administered by the study physicians. The patients' vital signs and demographic data at the time of admission were recorded. In addition, the results of nasal and oropharyngeal swab samples obtained from the patients were recorded.

The researcher asked the patient's primary physician whether they had considered prescribing antibiotics or antiviral drugs for the patient with suspected respiratory tract infection and recorded the response. At the time of answering this question, the physician was not aware of the nasal swab results.

Patients were divided into two groups: <50 years and >50 years. This classification was based on the significant increase in the frequency of chronic diseases (heart disease, diabetes, hypertension, cancer, etc.) after the age of 50 and associated lifestyle differences. The identified pathogens were further analyzed within these groups.

Oro-nasopharyngeal samples were obtained twice from each patient: one for the detection of respiratory pathogens and the other for SARS-CoV-2. Nasal and oropharyngeal swabs were first taken from the posterior oropharyngeal region and then from both nostrils, rotating 360 degrees within the nasopharynx.

Analysis of Respiratory Tract Viruses

The swabs were placed in capped tubes containing transport medium (NAT Transfer Tube, Bioeksen AR GE Technologies, Türkiye). The Bio-Speedy® Respiratory RT-qPCR MX-24 Panel (Bioeksen AR GE Technologies, Türkiye) was used to identify respiratory tract pathogens, which is a one-step reverse transcription and real-time PCR (RT-qPCR) test. This kit can differentiate 21 respiratory tract pathogens simultaneously (Influenza A, Influenza B, Human Coronavirus 229E, Human Coronavirus OC43, Human Coronavirus NL63, Human Coronavirus HKU1, Human Parainfluenza 1, Human Parainfluenza 2, Human Parainfluenza 3, Human Parainfluenza 4, Human Metapneumovirus, Enterovirus, Human Rhinovirus, Adenovirus, Human Bocavirus, Human Parechovirus, Respiratory Syncytial Virus A/B, Legionella pneumophila, Mycoplasma pneumoniae, Haemophilus influenzae, Bordetella pertussis, Streptococcus pneumoniae) in a single run.

Analysis of SARS-CoV-2

The swabs were placed in capped tubes containing transport medium (DiaVnat; TUSEB DiaVnat Extraction and Transfer Tube, Türkiye). SARS-CoV-2 analysis was performed using the DiaKit SARS-CoV-2 RT-qPCR Kit (TUSEB, Türkiye).

Both samples were analyzed using the Bio-Rad CFX96 device (Bio-Rad, USA).

Statistical Analysis

Statistical analyses were performed using Jamovi version 2.3.26 (The Jamovi Project, Australia). Continuous variables were reported as median and interquartile range (IQR, 25th–75th percentiles), depending on the distribution pattern. Categorical variables were presented as counts and percentages. Categorical variables were analyzed using the chi-square test. A p-value<0.05 was considered statistically significant within a 95% confidence interval.

Results

A total of 322 adult patients who presented to the emergency department with symptoms of upper respiratory tract infection were included in this study. The median age of the patients was 36 years (IQR:26–49), and 53.4% were male. Comorbidities and vital signs of the patients on admission are shown in Table 1. While the rate of those who had received the influenza vaccine was 8.1%, none had received a COVID-19 vaccine.

Among the collected samples, 221 (68.6%) tested positive for at least one respiratory pathogen, whereas no pathogen was detected in 101 (31.4%) patients. The most frequently identified pathogens were Influenza A (17.1%), COVID-19 (11.2%), and Influenza B (6.8%). Other detected viruses included Rhinovirus (5.6%), Human Bocavirus (5%), and Respiratory Syncytial Virus (6.2%) (Fig.1). Notably, coinfection with two pathogens was identified in 6.2% of cases. The most common coinfections involved Influenza A and RSV (Fig.2). Human metapneumovirus was more prevalent in patients >50 years of age (6.4% vs. 0.8%), while Influenza A and Rhinovirus were more prevalent in the younger group (18% vs.14.1% and 6.6% vs.2.6%, respectively) (Table 2).

Table 1. General characteristics of patients

Gender	Female	150 (46.6)
	Male	172 (53.4)
Age (year)		36 (26-49)
Duration of symptoms (day)		2 (2-3)
Fever (celsius)		36.7 (36.4-37.2)
SBP (mmHg)		128 (119-136)
DBP (mmHg)		75 (70-81)
Chronic medical conditions	Hypertension	53 (16.5)
	Diabetes mellitus	36 (11.2)
	Chronic lung disease	36 (11.2)
	Congestive Heart Failure	19 (5.3)
	Chronic Renal Failure	12 (3.7)
	Cancer	9 (2.8)
Have you received the influenza vaccine? (yes)		26 (8.1)
Have you had an UTRI in the past month? (yes)		54 (16.8)
Does anyone in your home have similar symptoms? (yes)		81 (25.2)

Data are median (IQR, 25th-75th percentile) or n (%); SBP: systolic blood pressure, DBP: Diastolic blood pressure; URTI: Upper respiratory tract infection.

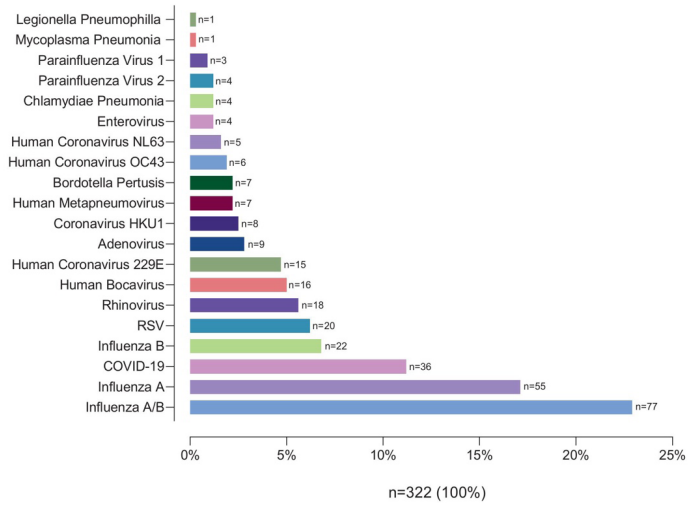

Figure 1. Distribution of respiratory pathogens in patients.

Table 2. Prevalence of respiratory pathogens in the age group

Results	18-49 years n=244	≥50 years n=78
Not detected	69 (28.3)	32 (41)
Adeno virus	7 (2.5)	2 (2.6)
Coronavirus HKU1	6 (2.5)	2 (2.6)
Human coronavirus NL63	3 (1.2)	2 (2.6)
Human coronavirus 229E	12 (4.9)	3 (3.8)
Human coronavirus OC43	6 (2.5)	0 (0)
Human metapneumovirus	2 (0.8)	5 (6.4)
Influenza A	44 (18)	11 (14.1)
Influenza B	18 (7.4)	4 (5.1)
Parainfluenza Virus 1	3 (1.2)	0 (0)
Parainfluenza Virus 2	4 (1.6)	0 (0)
Respiratory Synscytial Virus	17 (7)	3 (3.8)
Bordotella pertusis	6 (2.5)	1 (1.3)
Mycoplasma pneumoniae	0 (0)	1 (1.3)
Chlamydiae pneumoniae	2 (0.8)	2 (2.6)
Rhinovirus	16 (6.6)	2 (2.6)
Legionella pneumophila	0 (0)	1 (1.3)
Enterovirus	3 (1.2)	1 (1.3)
Human Bocavirus	12 (4.9)	4 (5.1)
Covid-19	30 (12.3)	6 (7.7)

Data are median n (%)

Table 3. The rates of antibiotic and antiviral prescriptions given to patients before swab results were available

Physicians were asked before the swab results were available	Detected influenza A/B n=77	Non-influenza A/B pathogen or not detected n=245	*p*
Have you considered prescribing antibiotics? (yes)	39 (51%)	67 (27%)	***<0.001***
Have you considered prescribing antivirals? (yes)	12 (16%)	14 (6%)	***0.006***
Chi-square test, p<0.05			

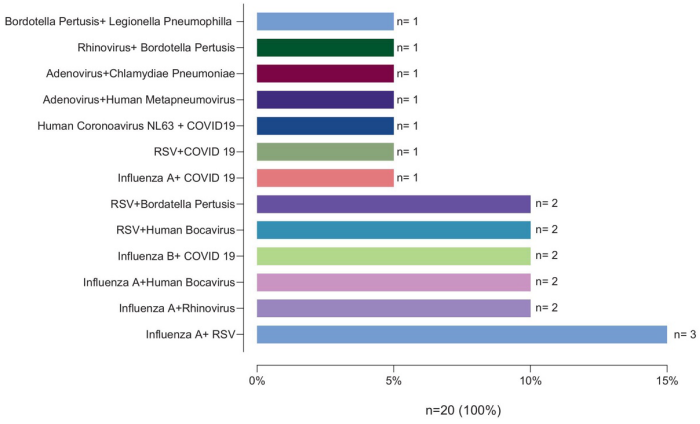

Figure 2. Co-pathogens detected groups.

Physicians stated that they would prescribe antibiotics to 32.9% of patients and antiviral treatment to 8.1% of patients before receiving swab results. The likelihood of prescribing antibiotics was significantly higher in patients with Influenza A/B compared to patients with non-influenza or undetectable pathogens (51% vs.27%) (Table 3).

Discussion

This study highlights the distribution of respiratory pathogens in patients presenting to the emergency department with upper respiratory tract infection after COVID-19.

With the rapid screening kit used, pathogens were detected in approximately 70% of patients, and the most common respiratory pathogen detected was Influenza virus in this study. This rate has been reported to range from 41.8% to 67.8% in a limited number of studies conducted in our country [9–11]. The positivity rate for the respiratory tract panel was 75.8% according to Uğur et al. [12] in 2022–2023. Remarkably high viral detection rates were reported in other countries, such as 85.3% in Japan and 88.7% in France; these were observed in studies from 2010–2011 that utilized the multiplex PCR technique [6,13,14]. Our study shows the increased vulnerability of older adults to Human Metapneumovirus. In a recent review, three distinct life stages are described regarding the risk of Human Metapneumovirus: Early Life (5–20% prevalence, attributed to immature immunity), Middle Life (5–10%, with increased prevalence in individuals with chronic illnesses), and Late Life (10–15%, influenced by immunosenescence and comorbidities). The increased occurrence of Human Metapneumovirus in older individuals observed in this study corroborates existing findings about their heightened vulnerability [15].

In our study, respiratory infections were often complex, as highlighted by the 6.2% coinfection rate, which can make diagnosis and treatment more challenging. The most frequent coinfections involved Influenza A with RSV, Rhinovirus, and Human Bocavirus. We found that multiple infections occurred at a lower rate compared to other studies conducted mostly in the pediatric age group [9,10]. In another study, the most frequently observed coinfections were rhinovirus/enterovirus-RSV (19.1%) across all age groups [12]. Some prior research suggests that viral co-infections can worsen illness, whereas other studies suggest the opposite due to lower viral loads [14,16,17].

The significant proportion of patients with undetected pathogens (31.4%) suggests that some infections may be due to bacterial etiologies or viruses not included in the testing panel. This result is similar to previous studies [1,18]. Some studies using multiplex respiratory pathogen PCR have reported lower detection rates in adults [1]. The positivity rate of PCR decreased as patient age increased, a finding consistent with other multiplex respiratory PCR studies reporting lower positivity in adults. This may be due to older adults shedding lower viral titers, necessitating more sensitive detection methods. Current multiplex PCR assays might lack the sensitivity needed to detect these lower viral loads in older patients [19,20].

Influenza A emerged as the most prevalent virus, followed by COVID-19 and Influenza B, consistent with prior epidemiological studies. A study by Çiçek et al. [21] found influenza viruses to be the most prevalent in adult patients, a finding supported by pre-COVID influenza surveillance data in Türkiye. According to a comprehensive review of multiplex respiratory panels [1], a study conducted by Yang et al. [22] also identified Influenza A as the most frequently detected pathogen in their cohort. Studies show that Influenza virus transmission is higher in winter than in summer. It has been emphasized that high humidity and warmer temperatures reduce the stability of the virus in the air and on surfaces, thereby decreasing transmission rates [23].

In our study, COVID-19 positivity was 11.2% overall. In another study from Türkiye, COVID-19 PCR positivity was detected in 142 patients (18.6%)[18]. Therefore, COVID-19 was found to be a significant contributor to upper respiratory tract infections [23].

An important finding of this study was the high rate of antibiotic prescription tendency (32.9%), despite the primarily viral etiology of these infections. This suggests potential overuse, which could contribute to antimicrobial resistance. These findings emphasize the importance of rapid viral diagnostic tests. Additionally, there was a low rate of antiviral treatment (8.1%), which may reflect hesitancy in prescribing antivirals.

Study Limitations

There are several limitations to this study. First, due to the single-center nature of the study, the results cannot be generalized. Second, the study included only patients who underwent viral panel testing, potentially introducing selection bias. Third, bacterial co-infections were not investigated.

Conclusion

In conclusion, this study provides important epidemiological data on viral respiratory infections after COVID-19. It also emphasizes the importance of rapid viral diagnostic tests in reducing unnecessary antibiotic use.

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Ethics Committee Approval: This study was approved by the Marmara University Ethics Committee (Date: 08.02.2024, Decision no: 09.2023.1752).

Informed Consent: Written informed consent was obtained.

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