ORIGINAL RESEARCH

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The Rate of Influenza and Respiratory Syncytial Virus in Patients with Upper Respiratory Infection Symptoms During the COVID-19 Pandemic Period

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Abstract

Objective: This study investigates the rates of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) influenza and respiratory syncytial virus (RSV) in patients who presented to the emergency department with symptoms of upper and lower respiratory tract infections during the coronavirus disease-2019 (COVID-19) pandemic.

Materials and Methods: This study was conducted on patients admitted to the University of Health Sciences Turkey, Kartal Dr. Lutfi Kirdar City Hospital, Clinic of Emergency with symptoms of upper respiratory tract infection between 15.03.2021 and 15.05.2021. SARS-CoV-2 and RSV were studied using multiplex polymerase chain reaction (PCR) test on nasopharyngeal swab samples taken from these patients. The research was conducted as a prospective, descriptive case study. Patient selection was determined by physicians working in green area polyclinics. The samples are taken in the "COVID-19 PCR sample collection area of our hospital". Two nasopharyngeal swabs were taken from all patients.

Results: A total of 359 patients participated in this study. Of these patients, 51% were men and 49% were women. The age range of these patients ranged from 17 to 70, with a mean age of 36.2. Three hundred forty nine of these patients followed up as outpatients. Of the patients,71.3% included in our study had no history of comorbid disease. SARS-CoV-2 was positive in 94 of the patients participating in our study. Cough, shortness of breath, wheezing and fever were found to be significantly higher in SARS-CoV-2 patients, however nasal discharge was significantly higher in the group with patients had not SARS-CoV-2.

Conclusion: Measures taken against the transmission of SARS-CoV-2 during the pandemic period also reduced the incidence of other respiratory viruses. Historical declines have been found in the influenza and RSV ranks. When the restrictions are lifted, epidemics from other respiratory viruses are also expected. Surveillance studies of these viruses should be closely followed and should be prepared for new outbreaks.

Keywords: SARS-CoV-2, influenza, RSV, multiplex, RT-PCR

Introduction

Coronavirus disease-2019 (COVID-19) illness is a highly infectious respiratory disease that initially surfaced in Wuhan, China, in December of this year and has spread around the world. On February 11, 2020, the World Health Organization (WHO) issued a definition for it [1]. The most common symptoms are fever, coughing, shortness of breath, muscular and body pains, and fatigue.

The virus that causes COVID-19 illnesses is severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), which is a member of the Coronaviridae family. İt was discovered on January 7, 2020, and the virus's name has been provisionally designated as 2019-new cooperative virus [2]. On February 11, 2020, the WHO issued a definition for it [1]. Acute respiratory distress syndrome (ARDS) is the most serious consequence in patients with severe illness, and it may develop as soon as the beginning of dyspnea has been seen in the patient. Studies

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have indicated that on average, it takes 8 days from the onset of symptoms to develop ARDS [3].

Influenza viruses are members of the orthomyxoviridae family of viruses [4]. Viruses of this size (80-120 nm in diameter) are enclosed RNA viruses with helical nucleocapsids and RNA genomes [5]. There are four separate influenza strains (types A, B, and C), each with its own set of antigenic characteristics, as well as a fourth kind (D) that has just recently been discovered [6]. Influenza A and B are the types of influenza that are most often associated with sickness in humans. Influenza is a disease that affects people of all ages. Pregnant women, children under 5 years old, the elderly, those with chronic conditions, and those using immunosuppressive medications are among the most at risk, since they are at greater risk of developing more severe disease and complications. Influenza A viruses in particular can cause pandemics due to the exchange of components between two distinct viruses that infect the same cell (a process known as antigenic shift). When it comes to pediatric populations, respiratory syncytial virus (RSV) is a major source of respiratory illness worldwide. After an RSV infection, there is no development of permanent immunity, and the virus may be transmitted throughout one's life [7]. When it comes to persons over 50 years of age with underlying illness, it is a significant and difficult to identify the cause of lower respiratory tract infection (LRTI). Among adults over the age of 50, prospective research found that the yearly hospitalization rate for RSV was 15 per 10,000 people [8]. Over the age of 50, a 6%-8% death rate was seen among people admitted to the hospital with respiratory RSV [9]. Pediatric lower respiratory tract illness (bronchospasm, bronchiolitis, pneumonia, acute respiratory failure) and apnea are common in newborns who have contracted the virus via their mother's breast milk. In newborns with RSV infection, wheezing is evident in 20% of cases, and 2%-3% need inpatient treatment [10].

While the COVID-19 pandemic was underway, this research aimed to determine the prevalence of SARS-CoV-2, influenza, and RSV in patients who presented to the emergency room with symptoms of upper and lower respiratory tract illnesses.

Materials and Methods

Design and Settings

An exploratory, descriptive case study design was used in our research. The study was conducted in polyclinics of University of Health Sciences Turkey, Kartal Dr. Lutfi Kirdar City Hospital, Emergency Service between March 15, 2021 and May 15, 2021. University of Health Sciences Turkey, Kartal Dr. Lutfi Kirdar City Hospital Local Ethics Committee was appropriated the study (rulling number: 514/196/21). When patients with upper respiratory tract infection presented with symptoms, nasal swab samples were obtained and tested for the presence of SARS-CoV-2, influenza, and RSV agents using a multiplex polymerase chain reaction (PCR) assay. They were collected at our hospital's "COVID-19 PCR sample collection area," which was designated for this purpose. On average, every patient had two nasopharyngeal swabs collected. Using the first, we could create an RV2 panel, while using the second, we could create our hospital's standard COVID-PCR test.

Participants

The inclusion criteria for this study included at least oa symptomof upper and LRTIs, such as rhinorrhoea, cough, shortness of breath, sore throat, coughing, fever, muscle and joint discomfort, loss of taste and smell, weakness, and being above the age of 18. Patients under the age of 18 who did not match the inclusion criteria, as well as those who had been to the emergency department with the same complaint within the previous seven days, were omitted from the research.

Data Collection and Processing

Following the entry of the patients' demographic information, the data form was also used to record their blood pressure, temperature, pulse, respiration rate, and the results of their physical examination. Patients with suspected COVID-19 infection who present to the emergency room are typically given a nasopharyngeal swab sample. The patients also had a second sample taken from their nose and placed into virus transport medium (VTM) tubes, which were then transported to the emergency microbiology laboratory during the day without the need to wait and stored at -80 °C in a Nuve 590 deep freezer, which was specifically purchased for our study. After the samples were thawed from the deep freeze on the day of the analysis, 50 mL of sample was extracted from the sample and 50 mL viral RNA extraction solution buffer for nucleic acid extraction was transferred to a PCR tube for further analysis. Incubation took place at room temperature for 5 min after being pipetted and mixed up and down five times. One hundred microliters of the mixture were made. By vortexing and mixing the PCR tubes, it was possible to swiftly centrifuge them. According to the Biorad CFX96 parameters, measurements were initiated after one cycle of 10 min at 50 °C, one cycle of 2 min at 95 °C, and one second at 95 °C and 60 °C, respectively. Bio-RAD company's CFX96 *in vitro* diagnostics real time-PCR instrument was utilized in this investigation. The causal culprit was identified using the GeneMAP respiratory viral PCR panel 2 test from the Genmark firm. A nasopharyngeal swab was used to collect samples, which were then transferred to the VTMs.

Outcome Measures

As the main endpoint of this research, we will look at the incidence of SARS-CoV-2, influenza, and the number of patients who presented to the emergency department with symptoms of upper and LRTIs during the COVID-19 pandemic period.

Statistical Analysis

SPSS 19.0 for Windows was used to conduct the statistical analyses. In the percentage distribution of descriptive criteria, the mean and standard deviation, the median and the minimum-maximum values are displayed as percentages. Kolmogorov-Smirnov test was used to determine if the data conformed to the normal distribution. When comparing distributions across groups, the chi-square test was employed, and when comparing continuous variables, the Student's t-test was used. It was decided that $p<0.05$ would be the threshold of significance.

Results

Three hundred and fifty nine patients were included in the study. Males accounted for 183 (51% of the total) of the patients, with female accounting for 176 (49%). A positive SARS-CoV-2 test resulted in 44 (12.25%) of the male patients, whereas the test resulted in 139 (38.7%) of male patients. In our hospital's COVID-19 PCR findings, SARS-CoV-2 was positive in 88 patients (24.5%) and SARS-CoV-2 was negative in 271 patients, according to the results of the COVID-19 tests. According to our findings, 94 (26.2%) patients had positive SARS-CoV-2 tests, whereas 265 (73.8%) had negative test results. Although 13 patients were found to be positive on respiratory viral PCR panel 2, they were found to be negative according to the COVID-19 PCR results, and on the other hand, 7 patients were found to be positive according to the COVID-19 PCR results but negative on respiratory viral PCR panel 2, indicating that the COVID-19 PCR results were unreliable. Table 1 presents a graphical representation of the distribution of additional illnesses based on PCR data obtained from individuals who took part in the study. Following this pattern, cardiovascular illness was shown to be the comorbidity that was most often related to PCR positive. Patients' clinical results are presented in Table 2 as well as the characteristics of the patients. Table 3 summarizes the findings of the respiratory viral PCR panel 2 and the COVID-19 PCR tests that were conducted at our institution. No patients were detected infected with RSV or influenza.

Discussion

A total of more than 200 viruses and viral subtypes have been identified as causing upper respiratory tract infections. Infections of the upper respiratory tract are caused by several different pathogens including coronaviruses (coronaviruses), influenza (flu), parainfluenza (parainfluenza) (rsv), rhinoviruses (rhinoviruses), metopnomovirus (metopnomoviruses), bocavirus (bocavirus) and adenovirus. Although they generate non-life threatening symptoms such as rhinorrhoea and sore throat, most these infections are self-limiting and clear within a week or less. Since LRTIs are associated with significant morbidity and death, early and prompt diagnosis and treatment are essential. Lung infections are mainly caused by viruses such as influenza, rhinoviruses (shingles), human metapneumoviruses, and parainfluenza viruses. Other reasons

Table 1. Examination of the distribution of chronic disease characteristics in the positive and negative groups according to the PCR results

Variabels	Absent/present	Negative (n=265)		SARS-CoV-2 (n=94)		Total	Sig.
		n	%	n	%	n	p
Cardiovascular disease	Absent	256	96.6	84	89.4	340	**0.007**
	Present	9	3.4	10	10.6	19	
Hypertension	Absent	243	91.7	79	84.0	322	**0.04**
	Present	22	8.3	15	16.0	37	
Diabetes mellitus	Absent	253	95.5	81	86.2	334	**0.002**
	Present	12	4.5	13	13.8	25	
Chronic renal failure	Absent	262	99.2	94	100.0	356	0.39
	Present	2	0.8	0	0.0	2	
Malignancy	Absent	260	98.5	93	98.9	353	0.75
	Present	4	1.5	1	1.1	5	
Chronic lung disease	Absent	255	96.2	89	94.7	344	0.52
	Present	10	3.8	5	5.3	15	
Cerebrovascular disease	Absent	264	99.6	94	100	358	0.55
	Present	1	0.4	0	0.0	1	
Other	Absent	227	85.7	67	71.3	294	**0.002**
	Present	38	14.3	27	28.7	65	

PCR: Polymerase chain reaction, SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2

may also cause lung involvement, although they are far less common. Because RSV and influenza (flu) create seasonal epidemics, they are associated with significant increases in hospitalizations, as well as significant morbidity and death, particularly during the winter. RSV and influenza were found to be the most frequent respiratory viruses, according to research conducted at Ege University in 2015. The study measured the incidence of respiratory viruses between 2002 and 2014 [11].

According to a review of the literature, research conducted on 250 patients to identify co-infected individuals between 19 January and February 26, 2020 at the beginning of the pandemic period revealed that 30 (15.6%) of 250 patients tested positive for at least one respiratory tract infection [12]. It was discovered that the frequencies of influenza and parainfluenza had reduced dramatically in research conducted in Texas between 11 and 23 and 2020 in the latter

Table 2. Examination of the distribution of clinical signs and features in SARS-CoV-2 positive and negative groups

Variables	Absent/present	Negative (n=265)		SARS-CoV-2 (n=94)		Total	Sig.
		n	%	n	%	n	p
Cough	Absent	139	52.5	30	31.9	169	**0.001**
	Present	126	47.5	64	68.1	190	
Shortness of breath	Absent	240	90.6	77	81.9	317	**0.03**
	Present	25	9.4	17	18.1	42	
Throatache	Absent	95	35.8	44	46.8	139	0.06
	Present	170	64.2	50	53.2	220	
Grunt	Absent	258	97.4	86	91.5	344	**0.02**
	Present	7	2.6	8	8.5	15	
Fever/chills	Absent	202	76.2	50	53.2	252	**0.001**
	Present	63	23.8	44	46.8	107	
Tiredness	Absent	148	55.8	51	54.3	199	0.79
	Present	117	44.2	43	45.7	160	
Headache	Absent	189	71.3	62	66.0	251	0.33
	Present	76	28.7	32	34.0	108	
Muscle and body pain	Absent	141	53.2	46	48.9	187	0.48
	Present	124	46.8	48	51.1	172	
Loss of taste and odor	Absent	250	94.3	83	88.3	333	0.05
	Present	15	5.7	11	11.7	26	
Diarrhea	Absent	253	96.2	90	95.7	343	0.85
	Present	10	3.8	4	4.3	14	
Nausea	Absent	247	93.6	88	93.6	335	0.99
	Present	17	6.4	6	6.4	23	
Sneeze	Absent	224	84.8	83	89.2	307	0.29
	Present	40	15.2	10	10.8	50	

SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2

Table 3. Comparison of respiratory viral PCR panel 2 and COVID-19 PCR results performed in our hospital

			COVID-19 PCR		Total
			Negative	Positive	
Respiratory viral PCR panel 2	Negative	Count	258	7	265
		% of total	71.9	1.9	73.8
	SARS-CoV-2	Count	13	81	94
		% of total	3.6	22.6	26.2
Total		Count	271	88	359
		% of total	75.5	24.5	100.0

PCR: Polymerase chain reaction, SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2, COVID-19: Coronavirus disease-2019

phases of the pandemic, and that coinfection had not been detected in 262 SARS-CoV-2-positive individuals throughout the study period [13]. According to surveillance tests done in Australia between March and September 2020, influenza and RSV agents were found to have fallen considerably compared to the previous year's figures [14]. Nine hundred two of 6,079 individuals who applied for COVID-19 were tested for influenza at the same time in a trial conducted in New York; just three patients were found to have co-infection [15]. Approximately 269,303 samples were analyzed between May 10 and May 23 by global influenza surveillance and response system labs in 89 countries associated with the WHO. Influenza was discovered in 484 (0.17%) of the samples tested [16]. According to WHO statistics broken down by year, the number of cases in January in prior years was 60,000 per week. This season's total number of cases was assessed to be 484 [17]. Figure 1 depicts the graphs examining the effects of viruses by year in the report of changes in influenza and other respiratory tract

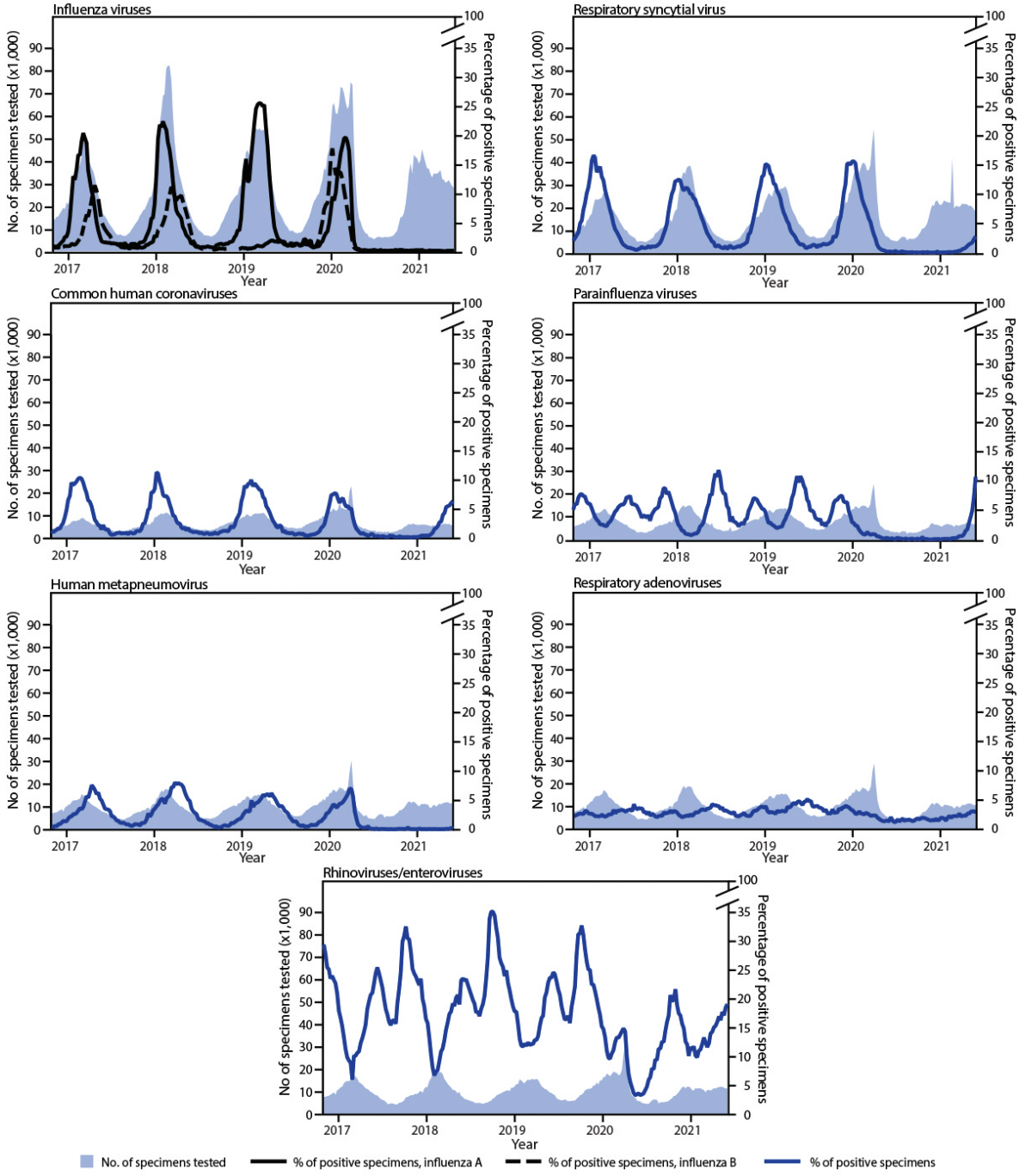

Figure 1. Changes in MMWR influenza and other respiratory viruses by year

MMWR: Mortality and morbidity weekly report

virus activity in the COVID-19 pandemic published in the CDC mortality and morbidity weekly report published on July 23, 2021 and examining the effects of viruses in the report of changes in influenza and other respiratory tract virus activities in the COVID-19 pandemic.

In our investigation, there were certain limitations. The fact that this is a single-center study with a limited sample size, as well as the small number of patients who tested positive for influenza and RSV, are all significant limitations of the study.

Conclusion

It was discovered that no patients had been infected with influenza or RSV throughout our research. Although it can make a methodological contribution to the new studies, it also can push the notion of pandemia-on-pandemia to the forefront of the discussion in the literature.

Ethics

Ethics Committee Approval: University of Health Sciences Turkey, Kartal Dr. Lutfi Kirdar City Hospital Local Ethics Committee was appropriated the study (rulling number: 514/196/21).

Informed Consent: Prospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.A., Ö.T., İ.T., A.U.S., E.Y., R.A., N.M.H., Concept: M.A., Ö.T., A.U.S., R.A., Design: M.A., Ö.T., İ.T., N.M.H., Data Collection or Processing: M.A., Ö.T., E.Y., E.K., Analysis or Interpretation: Ö.T., R.A., N.H., Literature Search: M.A., İ.T., R.A., Writing: N.H., Ö.T., A.U.S., E.Y.

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