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Investigation of 2019-2020 Seasonal Influenza Activity at a University Hospital in Northern Cyprus

Sahem Mowafaq A. Abujamous[1], Ayse Arikan[1,2], Emrah Guler[1,2], Kaya Suer[3], Tamer Sanlidag[2,4]

[1]Department of Medical Microbiology and Clinical Microbiology, Near East University, Faculty of Medicine, Near East University Nicosia, Northern Cyprus
[2]Near East University, DESAM Institute, Near East University Nicosia, Northern Cyprus
[3]Department of Infectious Diseases and Clinical Microbiology, Near East University Hospital, Nicosia, Northern Cyprus Turkish Republic of Northern Cyprus
[4]Department of Medical Microbiology, Manisa Celal Bayar University Faculty of Medicine, Manisa, Turkey

ABSTRACT

BACKGROUND/AIM: Influenza (flu) is a contagious respiratory disease caused by influenza viruses, which is more common in the late autumn, winter and early spring of the year. We aimed to estimate the rate of seasonal influenza A and B at Near East University Hospital in Northern Cyprus and to correlate the rate of the infection with the gender and age of the patients, and by month in which the infection occurred.

MATERIALS AND METHODS: Nasopharyngeal swabs collected from 844 individuals with flu like symptoms who were admitted to our hospital between December 2019 and March 2020 were involved. ABON™ Influenza A&B chromatographic immunoassay was used for the qualitative detection of Influenza A and B antigens. The rate of the infections was assessed among different ages, gender and by month.

RESULTS: Among 844 individuals, 234 (27.7%) were positive for either Influenza A virus or Influenza B virus. Among these infected cases, 97 (11.5%) and 137 (16.2%) were positive for influenza A and B, respectively. Influenza B was more dominant especially in children between 5–14 years of age. The major group of cases infected with Influenza A were aged 0–4 years. The difference between either Influenza A (p=0.679) or B (p=0.255) positivity and gender was not statistically significant. However, the rate of Influenza B differed by the month in which it occurred (p=0.034), peaking in February.

CONCLUSION: Our findings show that the rate of Influenza B was more dominant compared to the rate of Influenza A and age is an important factor in the rate of seasonal influenza. Therefore, early identification and investigation of influenza cases is critical to control human-human transmission.

Keywords: Influenza virus, immunochromotographic test, prevalence, Northern Cyprus

INTRODUCTION

Influenza (commonly referred as flu) is a contagious respiratory disease which is caused by Influenza viruses.[1] Influenza viruses, as members of the family *Orthomyxoviridae,* are enveloped, negative sense-single stranded segmented RNA viruses approximately 100 nm in diameter.[2] According to the antigenic differences in nucleoprotein (NP) and matrix (M) proteins present on the surface, which are associated with infecting a host cell, three different types (A, B and C) of Influenza viruses have been defined.[3] Influenza A [commonly

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ORCID iDs of the authors: S.M.A.A. 0000-0003-0017-1005; A.A. 0000-0003-1942-1203; E.G. 0000-0002-1635-0051; K.S. 0000-0002-2565-3425; T.S. 0000-0001-5084-7902.

Address for Correspondence: Ayşe Arıkan
E-mail: aysearikancy@yahoo.com; ayse.arikansarioglu@neu.edu.tr
ORCID ID: orcid.org/0000-0003-1942-1203

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referred as avian influenza (AI)] viruses can be further divided into subtypes based on the glycoproteins present on the surface of the viral envelope; hemagglutinin (HA) glycoproteins which allow the virus to bind to sialic acid receptors on a surface of epithelial cells in the upper respiratory tract and neuraminidase (NA) glycoproteins which let the new viruses leave the cell by simply budding out from it by cleaving sialic acid in the membrane.[4] To date, 18 distinct HA and 11 NA varying from H1 to H18 and N1 to N11 subtypes respectively, have been identified.[5,6] Influenza A and B viruses have a similar structure with eight gene segments that encode 17 proteins, however, Influenza B viruses do not have subtypes and are not associated with pandemics.[5,6] Influenza C viruses cause mild infections whereas, the Influenza D virus, which affects only cattle, does not cause infections in human. Thus, these two viruses do not pose a risk for public health.[7-9]

Influenza viruses can progress from mild to severe illnesses. Their transmission occurs from person to person with direct contact of respiratory droplets produced during coughing and/or sneezing at distances of less than 1 meter.[10] A total of 3 to 5 million cases and approximately 290,000 to 650,000 deaths associated with influenza are reported annually.[11] While the flu is generally common at the highest rates among young people, high mortality rates have been reported among the elderly, pregnant women, children below 59 months and individuals with severe and chronic illness such as chronic cardiac, pneumonia, sepsis and immunosuppressive conditions including acquired immunodeficiency syndrome (AIDS), those receiving chemotherapy, or with malignancy.[12-14] Laboratory diagnosis of Influenza by swabs or samples of secretions taken from the patient's nose or throat involve rapid antigen testing, immunofluorescence assays, rapid molecular assays such as reverse transcription polymerase chain reaction (RT-PCR) and virus culture.[15] Most of these assays provide an excellent analytical performance with high sensitivity and specificity. However, they require a longer time, and equipment and reagents which can only be used by experienced laboratory staff. As early identification and investigation of Influenza cases is critical to control human-human transmission, rapid antigen testing assays are commonly used for screening.

According to a modeling analysis of population-based surveillance data for the 2010–2013 Influenza seasons, approximately 114,018–633,001 hospitalizations, 18,476–96,667 intensive care unit (ICU) admissions, and 4,866–27,810 deaths per year were reported.[16] Moreover, it is estimated that 9.2–35.6 million illnesses, 4.3–16.7 million outpatient medical visits, and 139,000–708,000 hospitalizations can be attributed to all-season Influenza during the 2010–2016 seasons.[16] Therefore, the early identification and investigation of Influenza cases is critical to control human-human transmission and manage influenza outbreaks.

Due to the lack of scientific data on the rate of seasonal Influenza infections in Northern Cyprus, this study aimed to investigate the annual seasonal Influenza A and B virus activities in circulation during the 2019 winter and 2020 spring seasons at a university hospital in Northern Cyprus. Furthermore, the Influenza infections were evaluated with respect to multiple factors including gender, age, and the month in which they occurred to correlate these factors with the rate of the infection.

MATERIALS AND METHODS

Ethical Approval

The study was approved by Near East University Institutional Review Board (decision no: NEU/2020/79-1069, date: 28.05.2020). Since our study was retrospective, an informed consent form was not used.

Study Group and Analysis

Nasopharyngeal/oropharyngeal swab specimens collected from a total of 844 individuals with flu-like symptoms who were admitted to the Near East University Hospital clinics including the pediatric, cardiology, chest disease, emergency service, intensive care, and infectious disease clinics between December 2019 and March 2020 were investigated in the current study. Different parameters including age, gender, clinics and laboratory findings were documented and assessed all together for each case. The rate of Influenza activity was assessed among different age groups in the ranges of 0–4, 5–14, 15–44 and over 45 years. The ABON™ Influenza A&B Rapid Test Strip (Swab) chromatographic immunoassay (ABON Biopharm Co., Ltd, Hangzhou, China) was used for the qualitative detection of Influenza A and B antigens according to manufacturer's recommendations. Each chromatographic immunoassay is intended to aid in the diagnosis of Influenza A and B viruses. The manufacturer claims both the analytical sensitivity and specificity for Influenza A to be >99%. The analytical sensitivity and specificity for Influenza B is given as >99% and 98.6%, respectively.

Statistical Analysis

Categorical variables were summarized as frequencies and percentages, and continuous variables were described using their mean. The frequencies of categorical variables were compared using the Pearson chi-square and Fisher's exact tests. Tests with a $p<0.05$ were considered statistically significant.

RESULTS

A total of 844 swab samples collected from individuals who were admitted to the clinics of Near East University Hospital including the pediatric (356, 42.2%), emergency service (344, 40.8%), infectious disease (104, 12.3%), internal disease (19, 2.3%), chest disease and allergy (8, 0.9%), ear-nose-throat (8, 0.9%), cardiology (3, 0.4%) and dialysis (2, 0.2%) clinics were screened for Influenza A and B viruses in this study. The demographic characteristics of the study patients are shown in Table 1. A total of 1,688 analyses involving either Influenza A or B infection were obtained from the 844 patients. Among these individuals, 443 (52.5%) were females and 401 (47.5%) were male. Overall, from the individuals screened for Influenza viruses, 234 (27.7%) were determined as positive either for the influenza A or B virus. With regards to the overall Influenza positivity, the highest rate was obtained from those individuals coming from Nicosia (28.9%). Among the cases who tested positive for Influenza A and B, the highest rate was obtained from Nicosia and Morphou with 12% and 17.3%, respectively. No significant correlation was obtained between Influenza A and B positivity and the cities with $p=0.763$ and $p=0.838$, respectively. The seasonal pattern of Influenza activity in the cities of Northern Cyprus is given in Table 2.

Of the infected cases, 97 (11.5%) were positive for Influenza A virus and 137 (16.2%) were positive for Influenza B virus. Among the Influenza A positive cases, 48 (49.5%) were male and 49 (50.5%) were female. Moreover, 59 (43.1%) males and 78 (56.9%) females were reported as

Table 1. Clinical characteristics of the study patients

Characteristics	Patient group
Patient, n	844
Gender, M/F, n (%)	401(47.5)/443 (52.5)
Age, years (mean)	0–92 (15.74)
Clinics, n (%)	
Pediatrics	356 (42.2)
Emergency service	344 (40.8)
Infectious disease	104 (12.3)
Internal diseases	19 (2.3)
Chest disease and allergy	8 (0.9)
Ear nose and throat	8 (0.9)
Cardiology	3 (0.4)
Dialysis	2 (0.2)

M: male; F: female, n: number.

being Influenza B virus positive (Table 1). The difference between either Influenza A or Influenza B positivity and gender was not statistically significant (p=0.679, p=0.255 respectively) (Table 3).

During December 2019, a total of 70 Influenza A and B tests were performed of which 6 (17.1%) and 3 (8.6%) tested positive for Influenza A and B viruses, respectively. The number of performed Influenza tests peaked in January with a total of 980 tests, of which, 65 (13.3%) were positive for Influenza A virus and 83 (16.9%) were positive for Influenza B virus. In February 2020, a total of 490 tests were carried out in which 9% and 19.2% were positive for Influenza A and B viruses, respectively. In March 2020, 148 tests were performed, of which, 5.4% were positive for both the Influenza A and the Influenza B viruses. After February 2020, the number of tests carried out decreased by 70% in March. There was no statistically significant relationship between the rate of Influenza A virus and the month (p=0.088). However, the relationship between the rate of Influenza B virus and the month was statistically significant (p=0.034) and Influenza B was found to be the most common in February, 2020. The distribution rate of Influenza A and B virus positivity versus the month is given in Figure 1.

In this study, it was shown that age is an important factor in being infected with different types of seasonal Influenza viruses. During the Influenza season in Northern Cyprus (December 2019–March 2020), the major group of cases infected with Influenza A virus were aged 0-4 years. In addition, a steady decrease in Influenza A virus positivity (p=0.047) with increasing age in the same period showed a statistically significant relationship between the Influenza A infection rate and age. Moreover, the rate of Influenza B infection was the highest in the ages 5–14 years (p=0.000), which also confirms a statistically significant relationship between Influenza B infection and age. In Table 4, the rate of Influenza A and Influenza B virus positivity among different age groups in the ranges of 0–4, 5–14, 15–44 and over 45 years is given.

DISCUSSION

The rate of Influenza virus infection varies by 5%–20% each year.[17] This current study presents the estimation rate of seasonal influenza type A and/or B of a population who were admitted to a university hospital in Northern Cyprus in the 2019–2020 Influenza seasons. During this period, overall, for individuals screened for Influenza viruses, approximately 28% were determined to be positive for either Influenza A or B viruses. The positivity rate for Influenza B infections was higher (16.2%) compared to Influenza A infections (11.5%). Similar to a study in France, the number of Influenza B cases (29.7%) was higher than the number of Influenza A cases and the Influenza B outbreak peaked after the Influenza A outbreak.[18] In contrast, another study by Tamerius et al.[19] from the United States of America showed that the number of Influenza A infections (136,793 cases) was higher than that of Influenza B infections (86,498 cases).

Risk factors including the month of the year, age and gender play significant roles in the distribution of the Influenza illness and its treatment, which may have important public health implications.[20-22] We correlated the rate of Influenza-positivity by month between December 2019 and March 2020. Our findings show that Influenza A or B infection positivity was detected at the highest rate in December 2019. However, the highest number of tests was performed in January with a total of 980. Unusually, most of the positive cases were infected with Influenza B virus in our study. Influenza type A viruses are generally more common than Influenza type B virus due to the antigenic shift of proteins present on the virus surface or a combination with those viruses circulating in animals.[23] In similar studies, Influenza type A was reported at higher rates. Yang et al.[24] reported the positivity rate for Influenza type A (77.1%) to be higher than that of type B (22.9%) in China and other neighboring Asian countries such as Korea and Japan. Moreover, the incidence rate of Influenza type A and B were reported as 16.7 and 4.7 per 100,000 people-years, respectively in Iraq by Aufi et al.[25] After the 2009 pandemic in the World Health Organization European Region, Mook et al.[26], focused on alternating patterns of seasonal Influenza activity from 2010 to 2018 and their team showed that Influenza virus type A was the predominant circulating Influenza during five seasons (2010–2011, 2011–2012, 2013–2014, 2014–2015, and 2016–2017). Similarly, Panayiotou et al.[27] reported only Influenza A virus circulating in Cyprus in four consecutive seasons (2009–2013).

Furthermore, in February 2020, only half of the tests compared to January were performed due to a decrease in the number of patients and the positivity rate was determined to be higher for Influenza B (19.2%). During March 2020, 148 test kits were used, of which, 5.4% were positive for both Influenza A and Influenza B. After February 2020, the number of tests started to drop, reaching a 70% decrease in March, but there was no statistically significant relationship between Influenza A prevalence and the month (p=0.088). In contrast, the relationship

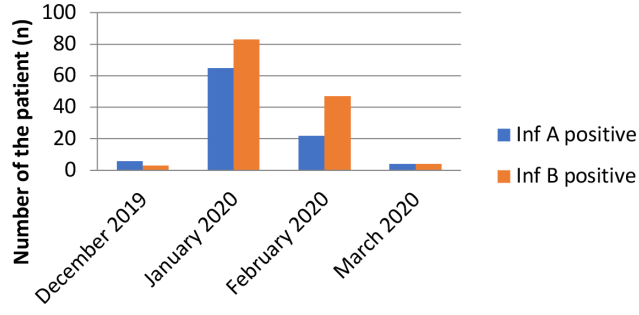

Figure 1. The distribution rate of Influenza A and B positivity by month.

*p<0.05 significant, Inf: influenza, n: number

Table 2. Seasonal pattern of Influenza activity in cities of Northern Cyprus

	Kyrenia (n, %)	Nicosia (n, %)	Morphou (n, %)	Famagusta (n, %)	p-value
Influenza A positive	17, 11.8%	69, 12%	4, 7.7%	7, 9.6%	0.763
Influenza B positive	21, 14.6%	97, 16.9%	9, 17.3%	10, 13.7%	0.838
Total positive	38, 26.4%	166, 28.9%	13, 25.0%	17, 23.3%	0.702

*p<0.05 significant, n: number.

Table 3. Influenza A and Influenza B positivity among genders

	Influenza A			Influenza B		
	Negative n (%)	Positive n (%)	p-value	Negative n (%)	Positive n (%)	p-value
Male	353 (88%)	48 (12%)	0.679	342 (85.3%)	59 (14.7%)	0.255
Female	394 (88.9%)	49 (11.1%)		365 (82.4%)	78 (17.6%)	
Total	747 (88.5%)	97 (11.5%)		707 (83.8%)	137 (16.2%)	

n: number.

Table 4. The rate of Influenza A and Influenza B positivity among different age groups

Influenza types	0–4 years, n (%)	5–14 years, n (%)	15–44 years, n (%)	>45 years, n (%)	p-value
Influenza A					
Negative	307 (86%)	187 (87.4%)	172 (91.5%)	81 (95.3%)	0.047*
Positive	50 (14%)	27 (12.6%)	16 (8.5%)	4 (4.7%)	
Influenza B					
Negative	313 (87.7%)	162 (75.7%)	153 (81.4%)	79 (92.9%)	0.000*
Positive	44 (12.3%)	52 (24.3%)	35 (18.6%)	6 (7.1%)	

*p<0.05 significant, n: number.

between the prevalence of Influenza B and the month was statistically significant (p=0.034). During the period between December 2019 to March 2020, the Influenza B positivity was more common (59%) than Influenza A (41%). In a study conducted by Basile et al.[28] in 2017–2018, it was shown that Influenza type B positivity was higher (63%) in comparison to that of Influenza type A (32.3%). In addition, according to the results of another study conducted by Karolyi et al.[29], 75.8% of Influenza positive cases were reported as Influenza type B positive in hospitalized patients via routine polymerase chain reaction (PCR). A study conducted by Yang et al.[24] showed that Influenza type B was predominant in Mongolia and Russia during the 2019 and 2020 seasons (80.7% and 77.2%, respectively).

The distribution of Influenza virus types also varies by age and by sex and this has important public health implications.[30] Children especially under the age of two years are at higher risk of serious illness compared to older children.[31] Therefore, we investigated the rate of the infections among different ages and genders in the current study. Our findings suggest that gender was not associated with the rate of Influenza infections for our study period. However, seasonal Influenza positivity was associated with age and this may be an important factor in becoming infected with the virus. The overall age distribution of Influenza type A cases was the highest among young children aged 0–4 (14.0%, p=0.047) and the lowest was detected among the elderly (4.7%). Koliou et al.[31] reported the first cases of Influenza in children aged 15 years and under in Cyprus in 2009. According to our findings, Influenza type B was most frequently determined in the 5–14 years age group (p=0.000). In a similar study by Mosnier et al.[18], Influenza type B was very common, especially in school-age children. For the Influenza species, it showed that the number of cases decreases with age and indicates a statistically significant inverse relationship.

Limitations of the Study

Our study has some limitations. The sample size and the technique we used lead to the limitations of our study. We could only test samples of individuals who attended Near East University Hospital and were tested using rapid antigen detection test kits. Although these tests provide rapid test results, they have limited analytical sensitivity to detect Influenza viruses in respiratory specimens and they do not provide information on the subtypes of specific virus strains. Therefore, a larger sample set is needed to estimate the accurate rate of seasonal Influenza viruses of the whole population in Northern Cyprus by means of molecular tests.

CONCLUSION

This study presents data on the rate of seasonal Influenza type A and B infections during the winter months between January and February and the beginning of spring. Despite the presence of Influenza, A cases, Influenza B cases remained predominant, especially in children between 0–14 years of age throughout the years 2019 and 2020. Our study shows

that the distribution of seasonal Influenza types was not associated with gender, however, age and the month of the year may have a significant role in infection rates and types. Therefore, people at risk age groups are recommended to have seasonal Influenza vaccinations as protection against pandemic Influenza strains.

MAIN POINTS

- In Northern Cyprus, there is not much data available on the prevalence of Influenza infections and this study presents scientific data on the rate of seasonal Influenza type A and B infections during the winter season.
- According to our results, the rate of Influenza B was more dominant compared to the rate of Influenza A in the period 2019-2020.
- Our findings also suggest that the seasonal Influenza positivity was associated with age, which is an important factor in becoming infected with the virus. Influenza A and Influenza B were found to be more dominant in individuals aged 0-4 years and in those between 5-14 years of age, respectively.
- Our results show that gender was not a significant factor in the rate and type of the infections. However, the rate of Influenza B infection differed by the month in which it occurred and the Influenza B activity was shown to peak in February, 2020.

ETHICS

Ethics Committee Approval: The study was approved by Near East University Institutional Review Board (decision no: NEU/2020/79-1069, date: 28.05.2020).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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