Original Article

HEALTH SCIENCES
MEDICINE

DOI: 10.32322/jhsm.1216358
J Health Sci Med 2023; 6(1): 178-182

Determination of the frequency of influenza-A and B antigens in swab samples in differentiating the diagnosis of influenza infection from other causes of upper respiratory tract infection

Ali Sağlık

Department of Emergency Medicine, Bahçeşehir Liv Hospital, Faculty of Medicine, İstinye University, İstanbul, Turkey

Cite this article as: Sağlık A. Determination of the frequency of influenza-A and B antigens in swab samples in differentiating the diagnosis of influenza infection from other causes of upper respiratory tract infection. J Health Sci Med 2023; 6(1): 178-182.

ABSTRACT

Aim: The present study aimed to determine the frequency of influenza-A and B antigens in swab samples and to examine their potential changes at the time of initial diagnosis in differentiating the diagnosis of influenza infection from other causes of upper respiratory tract infection by physical examination and vital clinical signs in the emergency room.

Material and Method: This retrospective cross-sectional descriptive research analyzed 113 patients with Influenza-A (n:8) and B (n:15) over the age of 18 who applied to the emergency department in the last three years, were diagnosed with acute upper respiratory tract and underwent nasopharyngeal swab sampling were included in the study. The data of the patients were accessed digitally from the University hospital database.

Results: The headache score was higher, while there was no difference between vital clinical signs and those with positive or negative swab tests ($p>0.05$). White blood cells in blood count parameters were lower in the Influenza test-positive group ($p<0.0001$), platelet distribution width ($p=0.006$), and monocyte counts ($p=0.008$) were significantly higher in Influenza positive patients than negative ones. The influenza swab test was not positive in any patient with tonsillar crypt ($p>0.05$).

Conclusion: Influenza infections should be examined in detail in terms of costs to both public health and social security institutions, considering the burdens of diagnosis and treatment.

Keywords: Influenza-A, influenza-B, swab sample, upper respiratory tract infection

INTRODUCTION

Influenza, a single-stranded RNA virus of the Orthomyxoviridae family that can affect human and animal populations, frequently causes acute respiratory tract infections (1). Although difficult to assess, it is estimated to generate more than 1 billion yearly cases, including severe disease (2). After a short incubation period, sudden onset of weakness, cough, fever, runny nose, sore throat, muscle pain, and frequent symptoms of this disease, whose course is more severe in children, pregnant women, those with chronic conditions, and immunodeficiency (3).

Considering the development of resistance due to antibiotics, rapid and accurate diagnosis of the Influenza virus is essential in starting early treatment, reducing contagiousness, preventing unnecessary antibiotic use, and obtaining epidemiological data (4). Although methods such as antigen testing, polymerase chain reaction, or culture are most commonly preferred in the diagnosis of Influenza virus infections, nasopharyngeal swabs and rapid antigen tests are used in the diagnosis of Influenza virus infections due to immediate results and ease of sampling in emergency medicine practice (5,6). These tests, which are successful in distinguishing between Influenza A and B, are insufficient to distinguish subtypes of Influenza A (7). We observe that Influenza rapid antigen tests are more sensitive than Influenza-B in detecting Influenza A infection, and the preference for nasopharyngeal swab samples increases this sensitivity. Determining the frequency of Influenza A and B antigens in swab samples is of clinical importance in differentiating the diagnosis of Influenza infection from other causes of upper respiratory tract infection by physical examination and vital clinical findings (6).

Corresponding Author: Ali Sağlık, mdalisaglik@gmail.com
Received: 09.12.2022 **Accepted:** 02.01.2023

This study aims to determine the frequency of Influenza-A and B antigens in swab samples and to examine their potential changes at the time of initial diagnosis in differentiating the diagnosis of Influenza infection from other causes of upper respiratory tract infection by physical examination and vital clinical signs in the emergency room. In addition, it is to explain the access to healthcare resources in the most appropriate way in terms of the health status, number, and disability of patients in future Influenza pandemics.

MATERIAL AND METHOD

The study was carried out with the permission of İstinye University Clinical Researches Ethics Committee (Date: 07.11.2022, Decision No: 3/2022.K-85). All procedures were carried out following the ethical rules and the principles of the Declaration of Helsinki.

Study Design

This retrospective cross-sectional descriptive research analyzed 113 patients with Influenza-A (n:8) and B (n:15) over 18 years old who applied to the emergency department in the last three years, were diagnosed with acute upper respiratory tract and underwent nasopharyngeal swab sampling were included in the study. The data of the patients were accessed digitally from the University hospital database. Patients' complaints, vital clinical signs, physical examination findings, antibiotic use in the last week, complete blood count and blood biochemistry values, and Influenza swab test reports were retrospectively analyzed from the database.

Inclusion and Exclusion Criteria

Inclusion criteria covered the cases over 18 years of age diagnosed with acute upper respiratory tract infections and underwent nasopharyngeal swab sampling in the emergency department. Exclusion criteria covered any cases whose files cannot be accessed or are missing, patients with acute upper respiratory tract diagnosis who have used antiviral drugs in the last week, patients whose tests have not been performed, and patients who refused treatment.

Laboratory Assessment

The parameters were analyzed within one hour after being taken on the second day of hospitalization with the standard tubes of routine sampling in the morning after 24-hour fasting. Laboratory measurements included leukocyte, neutrophil, lymphocyte, monocyte, and platelet count (SYSMEX Hemogram Autoanalyzer) as well as serum albumin and CRP (Cobas6000 Biochemistry Autoanalyzer).

Statistical Analysis

We retrospectively collected data, including demographics, laboratory, and clinical findings, and analyzed the windows-based software of IBM-SPSS v26.0. GraphPad Prism v9.4.1 software draws scatter plots or column bar graphs. We collected routine blood count data. The Chi-square test analyzed the categorical data. Categorical data was given as n (%), while all the continuous data were expressed as mean±standard deviation. The Kolmogorov-Smirov test was used to analyze the normality. We used Mann-Whitney U for abnormally distributed data (such as monocyte and lymphocyte count), while the independent Sample T-test was used for normally distributed data. The study accepted $P<0.05$ significance based on a two-way test.

RESULTS

Patients' Characteristics

Influenza swab test was positive in 23 of them (8 Influenza-A / 15 Influenza-B). **Table 1** showed no significant difference between the two groups when comparing kidney function tests, electrolytes, and CRP levels ($p>0.05$). While headache scores were higher and close to significant, there was no difference between vital clinical signs and those with positive or negative swab tests ($p>0.05$). WBC (white blood cell) counts in complete blood count parameters were lower in the Influenza test positive group (10.4±2.8 vs. 6.1±2.1; $p<0.001$), platelet distribution width (10.1±1.6 vs.13.8±2.3; $p=0.006$), and monocyte counts (8.9±3.8 vs. 11.2±4.1; $p=0.008$) were found to be significantly higher in Influenza positive patients than negative ones.

Table 1. Complaints and laboratory values

Features	Influenza (-) (n:90)	Influenza (+) (n:23)	P value
Body Heat, °C	37.6±0.9	37.4±0.8	0.516
Heart Rate, min	96.7±19.7	91.0±16.8	0.521
CRP, mg/dL	5.1±11.4 (5)	3.6±5.6 (4.8)	0.887
WBC, $10^3/mm^3$	10.4±2.8	6.1±2.1	p<0.001
PDW, fL	10.1±1.6	13.8±2.3	0.006
Platelet, $10^3/mm^3$	220.1±50.9	217.6±63.4	0.867
Neutrophile, $10^3/mm^3$	69.4±17.6	67.6±10.9	0.204
Lymphocyte, $10^3/mm^3$	19.5±39.3 (27.3)	19.5±9.8 (26)	0.129
Monocyte, $10^3/mm^3$	8.9±3.8 (8.1)	11.2±4.1(11.7)	0.008

Abbreviations. CRP: C-reactive protein, PDW: Platelet distribution width, WBC: White Blood Cell * Abnormally distributed data, including CRP, Monocyte, and Lymphocyte, were analyzed with Mann Whitney-U test and median values were given in brackets, while other data were analyzed with the Independent Student T-test. All data were presented as mean±standard deviation.

A history of cough was higher in the group with a positive test result. The influenza swab test was not positive in any patient with tonsillar crypt. Submandibular tenderness was significantly less in the group with a positive

Influenza test. The striking part is that antibiotic use in the last week was significantly higher in those with positive test results (**Table 2**).

Table 2. History and physical examination findings

Variables	Influenza (-) (n:90)	Influenza (+) (n:23)	P value
Cough	48.9% (44)	87% (20)	0.004
Nausea	32.3% (29)	39.1% (9)	0.531
Vomiting	11.1% (10)	4.3% (1)	0.091
Feeling of fever	77.8% (70)	82.6% (19)	0.613
Sneezing	18.9% (17)	30 4% (7)	0.454
Hoarseness	34.4% (31)	52.2% (12)	0.118
Eye redness	14.4% (13)	17.4% (4)	0.724
Tonsillar crypt	37.8% (34)	0% (0)	p<0.001
Tonsillar erythema	42.2% (38)	30.4% (7)	0.221
Joint pain	68.9% (62)	78.3% (18)	0.583
Continuous drug use	13.3% (12)	8.7% (2)	0.725
Cervical LAP	8.9% (8)	4.3% (1)	0.473
Submandibular tenderness	56.7% (51)	26.1% (6)	0.009
Postauricular LAP	4.4% (4)	0% (0)	0.303
Pharyngeal petechiae	2.2% (2)	4.3% (1)	0.571
Throat Kx strep	6.7% (6)	0% (0)	p<0.001

* All categorical data were analyzed with the chi-square test. All data were given as n (percent).

DISCUSSION

It was exciting that leukocyte was lower in the influenza test positive group, while the PDW and monocyte counts were higher in the positive influenza group. While those with a history of cough were significantly higher in the group with positive test results, the influenza swab test was not positive in any patient with tonsillar crypt. As a remarkable result, antibiotic use in the last week was significantly higher in those with positive test results. Our results in diagnosing patient differentiation may benefit physicians.

Depending on the virus and host characteristics, Influenza typically consists of malaise, fever, chills, headache, and myalgia, with clinical presentation ranging from asymptomatic infections to severe illness (8, 9). Headache and myalgia involving the extremities or back muscles are often the most bothersome symptoms, and Respiratory symptoms are also present at the onset of the disease (10, 11). Although dry cough, pharyngeal pain, and runny nose are prominent, they are usually overshadowed by the systemic symptoms that distinguish Influenza from other upper respiratory tract infections (12). Fever usually lasts for three days continuously but may remain high for up to 8 days, and systemic symptoms subside upon remission (13). Additional findings on physical examination are a flushed face, warm, moist skin, clear runny nose, hyperemic nasal and throat mucosa, and small, tender cervical lymphadenopathies. In our study, while headache scores were higher and close to significant, there was no difference between vital clinical signs and those with positive or negative swab tests. White blood cells in complete blood count parameters were lower in the Influenza positive group, and platelet distribution width and monocyte were higher in Influenza positive than in the negative ones.

Leading cause of influenza-related mortality, two pulmonary complications are frequently associated with Influenza (14). Primary influenza pneumonia begins with typical influenza symptoms and is followed by rapid respiratory decompensation with severe dyspnea, cyanosis, and hypoxemia (15, 16) a. Secondary bacterial pneumonia develops biphasic; symptoms resolve after the first presentation of typical Influenza and are associated with shortness of breath, productive cough, and consolidation in chest imaging (17). The similarities in these upper respiratory tract infections increase the importance of the distinction. In our study, a history of cough was higher in the group with a positive test result. The influenza swab was not positive in patients with tonsillar crypt. Submandibular tenderness was found less in the group with a positive Influenza test.

High creatinine was observed in more than 50% of hospitalized Influenza A patients. While symptoms usually resolve after 4-6 weeks, CNS involvement causes higher morbidity in adult patients (18). Influenza can also be complicated by altered kidney function, including acute kidney injury, glomerulonephritis, and tubulointerstitial nephritis (19). Liver damage has also been associated with Influenza, as patients may experience elevated AST and ALT, more commonly exacerbating underlying cardiac disorders (20). Our study found no significant difference between the two groups when comparing kidney function tests, electrolytes, and CRP levels.

Research results indicate that the preferred methods for influenza B antigen detection exhibit lower sensitivity than those for Influenza A detection (21). Influenza B virus-associated antigen and secretion levels are lower than for A virus infections. This may explain the low diagnostic levels for the influenza B virus due to the prevalence of anti-influenza antibodies in nasal secretions, as nasal secretions in influenza A and B virus infections likely contain similar amounts of anti-influenza virus immunoglobulins (22). Influenza swab test was positive in 23 of them (8 Influenza-A / 15 Influenza-B). There was no difference between vital clinical signs and those with positive or negative swab tests. The essential part is that antibiotic use in the last week was significantly higher in those with positive test results.

In primary health care, identifying the pathogen causing respiratory diagnosis should preferably be made during the visit. An integrated multianalyte testing panel is needed to make the laboratory diagnosis cost-efficient. Such a testing panel would comprise reagents for six to nine different bacterial and viral pathogens, sufficient to cover a significant proportion of respiratory infection cases. The use of such a diagnostic product in primary health care would enable the differentiation between bacterial and viral infections, promote correct treatment, and decrease the unnecessary use of antibiotics.

The study's main limitations are its retrospective design with limited cases and the routine variability of physiological conditions. Overcoming the limitations and making generalizable presentations will only be possible with a large population in a prospective design.

CONCLUSION

In a remarkable conclusion, antibiotic use in the last week was significantly higher in those with positive test results. Leukocyte was lower in the influenza-positive group, while the PDW and monocyte were higher in the influenza-positive group. While those with a history of cough were significantly higher in the group with positive test results, the influenza swab test was not positive in any patient with tonsillar crypt. Influenza infections should be examined in detail in terms of costs to both public health and social security institutions, considering the burdens of diagnosis and treatment on the patient and society. The fact that health institutions collect polyclinic and emergency service data healthily and present them to the authorized units for interpretation will contribute to the work and long-term planning of health policies, social services, and social security institutions on a regional basis, regionally, and on a country basis in general.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of İstinye University Clinical Researches Ethics Committee (Date: 07.11.2022, Decision No: 3/2022.K-85).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author has no conflicts of interest to declare.

Financial Disclosure: The author declares that this study has received no financial support.

Author Contributions: The author declares that he has participated in the design, execution, and analysis of the paper, and he has approved the final version.

REFERENCES

1. Choi N, Edginton HD, Griffin CE, Angus JC. Comparison of two ear cytological collection techniques in dogs with otitis externa. Veterinary Dermatol 2018; 29: 413-e136.
2. Duvignaud A, Lhomme E, Pistone T, et al. Home Treatment of Older People with Symptomatic SARS-CoV-2 Infection (COVID-19): A structured Summary of a Study Protocol for a Multi-Arm Multi-Stage (MAMS) randomized trial to evaluate the efficacy and tolerability of several experimental treatments to reduce the risk of hospitalisation or death in outpatients aged 65 years or older (COVERAGE trial). Trials 2020; 21: 846.
3. Hirsch A, Katz MA, Laufer Peretz A, et al. Study of Healthcare Personnel with Influenza and other Respiratory Viruses in Israel (SHIRI): study protocol. BMC Infect Dis 2018; 18: 550.
4. McDaniel T, Wilson DK, Coulon MS, Sweeney AM, Van Horn ML. Interaction of neighborhood and genetic risk on waist circumference in African-American adults: a longitudinal study. Ann Behav Med 2021; 55: 708-19.
5. Maignan M, Viglino D, Hablot M, et al. Diagnostic accuracy of a rapid RT-PCR assay for point-of-care detection of influenza A/B virus at emergency department admission: A prospective evaluation during the 2017/2018 influenza season. PloS one 2019; 14: e0216308.
6. McIlwain DR, Chen H, Apkarian M, et al. Performance of BioFire array or QuickVue influenza A + B test versus a validation qPCR assay for detection of influenza A during a volunteer A/California/2009/H1N1 challenge study. Virol J 2021; 18: 45.
7. Marshall HS, McMillan M, Koehler A, et al. B Part of It School Leaver protocol: an observational repeat cross-sectional study to assess the impact of a meningococcal serogroup B (4CMenB) vaccine programme on carriage of Neisseria meningitidis. BMJ Open 2019; 9: e027233.
8. Abadoğlu O, Mungan D, Paşaoglu G, Celík G, Misirligil Z. Influenza vaccination in patients with asthma: effect on the frequency of upper respiratory tract infections and exacerbations. J Asthma 2004; 41: 279-83.
9. Anar C, Bicmen C, Yapicioglu S, Unsal I, Halilcolar H, Yilmaz U. Evaluation of clinical data and antibody response following influenza vaccination in patients with chronic obstructive pulmonary disease. New Microbiologica 2010; 33: 117-27.
10. Benson ER, Alphin RL, Rankin MK, Caputo MP, Hougentogler DP, Johnson AL. Mass emergency water-based foam depopulation of poultry. Avian diseases 2012; 56: 891-6.
11. Beran J, Abdel-Messih IA, Raupachova J, Hobzova L, Fragapane E. A phase III, randomized, open-label study to assess the tolerability and immunogenicity of an H5N1 influenza vaccine administered to healthy adults with a 1-, 2-, 3-, or 6-week interval between first and second doses. Clinical therapeutics 2010; 32: 2186-97.
12. Cuhaci Çakir B, Beyazova U, Kemaloğlu YK, Özkan S, Gündüz B, Özdek A. Effectiveness of pandemic influenza A/H1N1 vaccine for prevention of otitis media in children. European journal of pediatrics 2012; 171: 1667-71.
13. Desrosiers M, Ferguson B, Klossek JM, Drugeon H, Mösges R. Clinical efficacy and time to symptom resolution of 5-day telithromycin versus 10-day amoxicillin-clavulanate in the treatment of acute bacterial sinusitis. Current medical research and opinion 2008; 24: 1691-702.
14. Sener M, Gürsel G, Türktaş H. Effects of inactivated influenza virus vaccination on bronchial reactivity symptom scores and peak expiratory flow variability in patients with asthma. The Journal of asthma : official journal of the Association for the Care of Asthma 1999; 36: 165-9.
15. McLean HQ, Levine MZ, King JP, Flannery B, Belongia EA. Serologic response to sequential vaccination with enhanced influenza vaccines: Open label randomized trial among adults aged 65-74 years. Vaccine 2021; 39: 7146-52.

16. Oğuz F, Unüvar E, Süoğlu Y, et al. Etiology of acute otitis media in childhood and evaluation of two different protocols of antibiotic therapy: 10 days cefaclor vs. 3 days azitromycin. International journal of pediatric otorhinolaryngology 2003; 67: 43-51.
17. Zengin E, Sarper N. Humoral immunity to diphtheria, tetanus, measles, and hemophilus influenzae type b in children with acute lymphoblastic leukemia and response to re-vaccination. Pediatric blood & cancer 2009; 53: 967-72.
18. Havasi A, Visan S, Cainap C, Cainap SS, Mihaila AA, Pop L-A. Influenza A, influenza B, and SARS-CoV-2 similarities and differences - a focus on diagnosis. Front Microbiol 2022; 13: 908525-32.
19. Cheng A, Riedel S, Arnaout R, Kirby JE. Verification of the Abbott Alinity m Resp-4-Plex assay for detection of SARS-CoV-2, influenza A/B, and respiratory syncytial virus. Diagnostic microbiology and infectious disease 2022; 102: 115575.
20. Zhen W, Manji R, Smith E, Wuitschick J, Lucic D, Berry GJ. Evaluation of the alinity m Resp-4-Plex assay for the detection of severe acute respiratory syndrome coronavirus 2, influenza A virus, influenza B virus, and respiratory syncytial virus. Microbiol Spectrum 2022; 10: e0109021.
21. Reina J, Padilla E, Alonso F, Ruiz De Gopegui E, Munar M, Mari M. Evaluation of a new dot blot enzyme immunoassay (directigen flu A+B) for simultaneous and differential detection of influenza a and B virus antigens from respiratory samples. J Clin Microbiol 2002; 40: 3515-7.
22. Brokstad KA, Cox RJ, Eriksson JC, Olofsson J, Jonsson R, Davidsson A. High prevalence of influenza specific antibody secreting cells in nasal mucosa. Scand J Immunol 2001; 54: 243-7.