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A retrospective look at influenza during the COVID-19 pandemic

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ABSTRACT

Aim: Influenza is the main cause of acute respiratory disease worldwide and is transmitted via the respiratory secretions of infected individuals. The aim of this study was to retrospectively investigate influenza, a virus with which we have a longer history, during a period in which the COVID-19 pandemic has dominated current events in terms of viral infections.

Material and Method: Epidemiological and laboratory data of patients over 18 years of age who tested positive for influenza infection and received inpatient treatment in the Erzurum Regional Training and Research Hospital between January 1, 2019 and December 31, 2020 according to the influenza management algorithm of the Public Health Institution of Turkey were evaluated retrospectively.

Results: Of the 164 patients included in our study, 129 were hospitalized due to influenza A and 35 due to influenza B. Procalcitonin, aspartate transaminase, alanine transaminase, creatine kinase, total bilirubin, and direct bilirubin levels were significantly higher in the influenza A group compared to the influenza B group (p=0.002, 0.005, 0.006, 0.030, 0.010, and 0.004, respectively). Ten of the patients in the study died; there was no significant difference in mortality based on influenza subtype or presence of comorbidity (p=0.999 and 0.756, respectively). Forty-one (54.7%) of the patients with comorbidities had received an influenza vaccine.

Conclusion: Although COVID-19 has dominated the global stage since the pandemic started, the effects of periodic pandemics of our old acquaintance influenza still continue. Vaccination, which is our strongest weapon against pandemics, can reduce mortality in patients with comorbidities, as seen in our study.

Keywords: Influenza, pandemic, comorbidities

INTRODUCTION

The 1918 "Spanish flu" pandemic killed more than 50 million people and is the deadliest epidemic in recorded human history. Subsequent influenza epidemics such as the Asian flu in 1957, Hong Kong flu in 1969, and swine flu in 2009 had lower mortality and morbidity. Because influenza virus is more stable at cold temperatures, outbreaks usually occur during the dry, cold winter months. Influenza viruses are enveloped RNA viruses from the Orthomyxoviridae family (1). Three different influenza viruses have been identified: influenza A, B, and C. Hemagglutinin and neuraminidase are their two main envelope glycoproteins. Due to the segmented genome structure of the genes encoding these glycoproteins, mutations and antigenic changes can lead to epidemics and pandemics (2). Influenza A shows the greatest antigenic shift and antigenic drift of the influenza viruses and is therefore the main driver of outbreaks (3).

Influenza is the leading cause of acute respiratory disease worldwide. It is transmitted via the respiratory secretions of infected people. Symptoms occur approximately 1 to 4 days after infection and patients are infectious from 1 day before to 5 to 7 days after symptom onset. The most common symptoms are chills, fever, sore throat, nasal congestion, generalized muscle aches, headache, and fatigue, with vomiting and diarrhea seen mostly in children. It can present with more severe clinical signs and symptoms in people with comorbidities, individuals over 65 years old, and pregnant female (4). In addition to the direct effect of the virus, the most

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common cause of morbidity and mortality in these patient groups is superinfections that cause pneumonia and acute respiratory distress. Therefore, vaccination is recommended for these groups before the influenza season (5).

Influenza diagnosis can be made by virus polymerase chain reaction (PCR) test or culture of respiratory secretions obtained by nose and throat swab within the first days of symptom onset. Serological testing can also be done to detect antibodies in the serum (6,7). Antiviral agents used for treatment can be effective when started within the first days of symptoms. These include the M2 protein inhibitors amantadine and rimantadine and the neuraminidase inhibitors zanamivir and oseltamivir (8,9).

The aim of this study was to retrospectively evaluate the epidemiological and clinical findings of influenza patients who presented to the infectious diseases outpatient clinic and emergency department and were treated on an inpatient basis.

MATERIAL AND METHOD

The study was carried out with the permission of Erzurum Training and Research Hospital, Noninvasive Clinical Ethics Committee (Decision No:2021/08-153) All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Design

Epidemiological and laboratory data of patients over 18 years of age who tested positive for influenza infection and received inpatient treatment in the Erzurum Regional Training and Research Hospital between January 1, 2019 and December 31, 2020 according to the influenza management algorithm of the Public Health Institution of Turkey were evaluated retrospectively. Influenza was diagnosed by real-time PCR testing of nasopharyngeal swab samples obtained from patients with consistent clinical findings.

Definitions and Treatment

Patients who presented to the emergency department or infectious diseases outpatient clinic with the following signs and symptoms were admitted for inpatient treatment: shortness of breath or difficulty breathing, change in vital signs (arterial hypotension, defined as systolic blood pressure <90 mmHg and diastolic blood pressure <60 mmHg or >40 mmHg decrease from previous blood pressure; respiratory rate above 30/min; heart rate >120/min; hypoxia, defined as oxygen saturation <92% on pulse oximetry), change in consciousness, and severe dehydration (peripheral pulse loss or attenuation, reduced skin turgor, inability to read blood pressure, and loss of more than 10% of body weight, characterized by sunken eyes). Droplet isolation precautions were implemented in the patient rooms.

During follow-up, the patients were evaluated according to intensive care admission criteria and those with indications continued treatment in the isolation intensive care unit. The following parameters were considered as criteria for admission to intensive care:

Major

1. Need for invasive mechanical ventilation
2. Septic shock requiring vasopressor therapy

Minor

1. Respiratory rate ≥30/min
2. PaO_2/FiO_2 ratio ≤250
3. Presence of multilobar infiltrates on chest x-ray
4. Confusion/disorientation
5. Uremia (blood urea nitrogen [BUN] ≥20 mg/dL)
6. Leukopenia (white blood cell count <4000/mm³)
7. Thrombocytopenia (platelet count <1 ×105/mm³)
8. Hypothermia (body temperature <36°C)
9. Hypotension requiring intensive fluid therapy

Patients with one major risk factor or three minor risk factors were treated in the isolation intensive care unit.

In addition to symptomatic treatment, inpatients in our clinic received oseltamivir, which was shown to be effective for influenza A and B, in accordance with the National Pandemic Plan guideline (10). As oseltamivir has substantial renal excretion, dose adjustments were made for patients with creatine clearance below 30 mL/min. Patients weighing more than 40 kg received oseltamivir 75 mg (capsule) twice daily for 5 days. Patients with glomerular filtration rate (GFR) of >30 to 60 mL/min received 30 mg (capsule or suspension) twice daily, and those with a GFR of >10 to 30 mL/min received a single daily dose of 30 mg (capsule or suspension). Patients undergoing hemodialysis or peritoneal received a single dose of 30 mg (capsule or suspension) after their dialysis session. The standard duration of treatment was 5 days, which was extended to 10 days for intensive care patients, immunocompromised patients, and those with severe infections. In patients whose procalcitonin level was above the upper limit (0.5 mg/dL) determined for our hospital, empirical antibiotic therapy for bacterial superinfection was started with the correlation of clinical findings. Antibiotic regimens were revised according to sputum, blood, and urine culture results.

Statistical Analysis

The data were analyzed using IBM SPSS Statistics for Windows version 20.0 (IBM Corp, Armonk, NY). Kolmogorov-Smirnov test were used to determine whether continuous variables were normally distributed. Pearson chi-square, Fisher's exact test and Mann–Whitney U test were used for comparisons of parametric data and non normally distributed numerical data, respectively, between groups. Independent-samples t test was used to compare demographic data and laboratory parameters between groups. Receiver operating characteristic (ROC) curve analysis was used to determine the diagnostic value of continuous variables and the Youden index was used to determine cut-off values. P-values lower than 0.05 were considered statistically significant.

RESULTS

The mean age of the 164 patients included in the study was 50.3±23.3 years. The mean ages of patients with influenza A and influenza B infection were 52.8±20.2 years and 41.1±18.4 years, respectively (p=0.002). Female accounted for 74 (57.4%) of the 129 patients with influenza A and 19 (54.3%) of the 35 patients with influenza B (p=0.744).

Seventy-five (45.7%) of the 164 patients in our study had comorbidities. The most common comorbidity was chronic obstructive pulmonary disease (COPD) (n=52, 69.3%), followed by coronary artery disease (n=32, 42.6%), hypertension (n=20, 26.7%), diabetes mellitus (n=13, 17.3%), and malignancy (n=12, 16%). The distribution of patients with and without comorbidities was 60 (46.5%) and 69 (53.5%) in the influenza A group and 15 (42.9%) and 20 (57.1%) in the influenza B group, respectively. There was no statistically significant difference in the frequency of comorbidity based on influenza type (p=0.700). In comparisons of age and laboratory data between patients with comorbidities compared to those without comorbidities, hemoglobin level was found to be significantly lower in patients with comorbidities (12.9±2.3 vs. 13.6±2.1, p=0.050). Other parameters showed no statistically significant differences between patients with and without comorbidities (p >0.05). The median value of hemoglobin level in surviving patients was 13.5, while it was 10 in non-survival patients. A statistically significant difference was observed between both groups (p= 0.001)

The laboratory data at time of admission in patients with influenza A and B are shown in **Table 1**. Procalcitonin, aspartate transaminase (AST), alanine transaminase (ALT), creatine kinase, total bilirubin, and direct bilirubin levels were significantly higher in influenza A group compared to influenza B group (p=0.002, 0.005, 0.006, 0.030, 0.010, and 0.004, respectively). In contrast, albumin level was significantly higher in the influenza B group (p=0.020).

The H1N1 subtype was detected in 96 (74.4%) of the patients with influenza A and the H3N2 subtype was detected in the other 33 patients (25.6%). Patients with H3N2 had a significantly higher mean age than those with H1N1 (58.2±20.9 years versus 50.4±19.7 years, p=0.050). No statistically significant differences in laboratory data were observed between the subtypes.

Ten patients died during follow-up, 8 (80%) in the influenza A group and 2 (20%) in the influenza B group. Mortality did not differ significantly between influenza A and B (p=0.999). The comparison of age and laboratory data of surviving and nonsurviving patients is shown in **Table 2**. Nonsurviving patients had significantly higher WBC count, neutrophil count, mean platelet volume, red cell distribution volume, CRP, erythrocyte sedimentation rate, procalcitonin, international normalized ratio, prothrombin time, activated partial prothrombin time, fibrinogen, D-dimer, ferritin, BUN, creatinine, AST, ALT, lactose dehydrogenase, creatine kinase, alkaline phosphatase, total bilirubin, direct bilirubin, neutrophil/lymphocyte ratio (NLR), and platelet/lymphocyte ratio (PLR) than surviving patients (p <0.050). Hemoglobin, lymphocyte count, total protein, and albumin levels were significantly lower in nonsurviving patients (p <0.001). Four of the nonsurviving patients (40%) had comorbidities and 6 (60%) did not. Statistical analysis revealed no significant association between comorbidity and mortality (p=0.756).

In the ROC curve analysis between surviving and nonsurviving patients, the areas under the curve for procalcitonin, CRP, fibrinogen, D-dimer, and ferritin were 0.886, 0.847, 0.784, 0.925, and 0.763, respectively. When these variables were evaluated based on Youden index cut-off values, sensitivity and specificity respectively were 90% and 79% for procalcitonin at a cut-off of 1.3 ng/mL; 80% and 77% for CRP at a cut-off of 53.1 mg/L; 80% and 63% for fibrinogen at a cut-off of 413.5 ng/mL; 90% and 88% for D-Dimer at a cut-off of 1630 ng/mL; and 90% and 60% for ferritin at a cut-off of 155.5 ng/ml (**Figure 1**).

Due to the global problem in influenza vaccine shipments due to the COVID-19 pandemic, only people over 65 years of age and patients with comorbidities were vaccinated in our country during the study period. The vaccination rate among the 75 patients with comorbidities in our study was 54.7% (n=41). Two of the 41 vaccinated patients died.

Table 1. Comparison of age and laboratory parameters between patients with influenza A and B

	Influenza A (n=129) Median (IQR) (min.-max)	Influenza B (n=35) Median (IQR) (min.-max)	p
Age (years)	62 (38.1-81.2) (18-94)	42 (26.4-69.5) (19-92)	0.002
WBC (/µL)	6450 (3156-14580) (2050-27780)	7300 (2630-14230) (2590-18760)	0.710
Hemoglobin (g/dl)	12.8 (9.7-15.4) (8-17)	13.6 (10.1-16.9) (7.6-18.5)	0.770
Neutrophils (/µL)	4870 (810.4-10100.4) (790-25830)	5390 (850.4-91601) (1520-14210)	0.830
Lymphocytes (/µL)	880 (954-1640) (100-3160)	1240 (765.9-1890.6) (360-3570)	0.070
Monocytes (/µL)	440 (50-890) (10-1200)	600 (98-980) (100-4680)	0.118
Eosinophils (/µL)	10 (0-140) (0-550)	10 (0-135) (0-330)	0.633
Basophils (/µL)	10 (0-30) (0-70)	20 (0-45) (0-90)	0.460
Platelets (/µL)	187000 (154000-264000) (40000-620000)	223000 (210000-286000) (27000-368000)	0.670
MPV (fL)	10.6 (8.9-12.1) (8.6-13.9)	9.9 (9.1-11.7) (9.2-12.4)	0.280
RDW	13.8 (11.7-16.4) (11.9-29.3)	13.1 (10.1-16.4) (11.6-21.2)	0.610
CRP (mg/L)	36.7 (16.9-92.4) (3-396)	13.3 (18.4-88.9)(3-231)	0.790
Sedimentation (s)	28 (5-43) (2-96)	17 (2-37) (2-90)	0.240
Procalcitonin (ng/mL)	0.63 (0.45-5.65) (0.01-32.79)	0.03 (0.06-1.14) (0-3.5)	0.002
INR	1.12 (0.95-1.14) (0.9-1.9)	1.13 (0.99-1.2) (0.8-2.0)	0.560
PT (s)	14.6 (12.1-16.7)(11.3-33)	14.2 (12.6-15.8) (13.2-19.9)	0.560
aPTT (s)	29.4 (20.8-26.4) (21.2-74.9)	31 (21.1-26.9) (21.9-43.8)	0.940
Fibrinogen (ng/mL)	410 (210-580.4) (174-735)	352 (225-590) (131-918)	0.780
D-dimer (ng/mL)	1000 (450-2560) (100-14000)	420 (340-2460) (147-4600)	0.110
Ferritin (ng/ml)	156 (80.4-456.9) (10.2-1600)	124 (76.4-637.4) (15-1289)	0.520
BUN (mg/dL)	20.1 (8.6-35.5) (4.7-104)	15 (7.9-36.1) (9.9-119)	0.200
Creatine (mg/dL)	0.96 (0.6-1.8) (0.54-8.9)	0.81 (0.55-1.89) (0.19-4.99)	0.160
AST (U/L)	35 (33.4-101.6) (11-1735)	22 (19-41.6) (14-53)	0.005
ALT (U/L)	30 (10-78.4) (6-1164)	20 (12-36.6) (6-53)	0.006
LDH (U/L)	234 (167.8-510.8) (165-2929)	303 (142.4-470.4) (183-638)	0.230
CK (U/L)	128 (45.4-468.9) (22-13649)	80 (34.4-130.4) (29-243)	0.030
GGT (U/L)	32 (19-120.9) (11-959)	21 (14-110.6) (10-121)	0.140
ALP (U/L)	77 (42-94.6) (33-633)	82 (37-95.5) (45-165)	0.370
Total bilirubin (mg/dL)	0.5 (0.3-1.2) (0.1-3.8)	0.4 (0.3-0.8) (0.25-1.72)	0.010
Direct bilirubin (mg/dL)	0.23 (0.15-0.99) (0.1-1.17)	0.17 (0.15-0.35) (0.1-0.54)	0.004
Total protein (g/dl)	6.1 (4.7-7.2) (4.5-9.3)	7.2 (4.6-7.1) (4.8-8.1)	0.790
Albumin (g/dl)	3.4 (2.34-3.6)(2.21-4.6)	4.1 (3.6-4.6) (1.8-4.8)	0.020
NLR	5.18 (3.48-7.65) (0.47-88.71)	3.42 (2.98-6,96) (0.7-34.5)	0.330
PLR	170.3 (56.8-190.6) (44.9-3100)	191.2 (55.4-110.6) (7.56-603.3)	0.280

WBC: White blood cells, MPV: Mean platelet volume, RDW: Red blood cell distribution width, INR: International normalized ratio, PT: Prothrombin time, aPTT: Activated partial prothrombin time, NLR: Neutrophil/lymphocyte ratio, PLR: Platelet/lymphocyte ratio, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, LDH: Lactate dehydrogenase, GGT: Gamma glutamyl transferase, ALP: Alkaline phosphatase, BUN: Blood urea nitrogen, CK: Creatine kinase, SD: Standard deviation, p: Comparison of parameters between groups

DISCUSSION

Our retrospective analysis of influenza patients during the COVID-19 pandemic showed that 129 of 164 patients had influenza A and 35 had influenza B infections. The mean age was higher among influenza A patients than influenza B patients. Liver function tests and procalcitonin levels were also higher among influenza A patients. Influenza A subtype analysis revealed a higher rate of H1N1 compared to H3N2, while H3N2 was more frequent in older patients. In the analysis of the 10 patients who died, the difference in mortality between patients with influenza A and B was not statistically significant. However, procalcitonin, CRP, fibrinogen, and D-dimer levels were significantly higher in nonsurviving patients than surviving patients.

The annual recurrent respiratory disease caused by influenza viruses has a significant impact on human health and the economy. Although influenza B viruses (IBV) are found almost exclusively in humans, influenza A viruses (IAVs) circulate in annual outbreaks within the human population and emerge from a large zoonotic reservoir (11). In a process called antigenic drift, IAVs can rapidly acquire adaptive mutations, enabling them evade the immune system response. In addition, their multiple RNA segments facilitate the reassortment of genetic elements from different IAVs. This process, called antigenic shift, is responsible for the increased pathogenicity and infectivity of the virus in pandemic outbreaks. In addition, studies have shown that the interaction of hemagglutinin (HA) and neuraminidase (NA) has an important place in the replication of the

Table 2. Comparison of age and laboratory parameters between surviving and nonsurviving influenza patients

	Survivors (n=154) Median (IQR) (min.-max)	Non-survivors (n=10) Median (IQR) (min.-max)	p
Age (years)	53 (22-48) (18-94)	70 (64-78) (21-92)	0.002
WBC (/µL)	6475 (4530-8210) (2050-27780)	9970 (8450-12690) (1650-19800)	0.030
Hemoglobin (g/dl)	13.5 (12.4-14.6) (8-18.5)	10 (8.8-12.1) (7.6-13.7)	0.001
Neutrophils (/µL)	4585 (2880-7140) (790-25830)	8305 (6500-9670) (2520-18090)	0.005
Lymphocytes (/µL)	985 (756-1103) (250-3570)	765 (540-910) (100-1430)	0.001
Monocytes (/µL)	515 (310-796) (70-4680)	450 (356-750) (10-870)	0.390
Eosinophils (/µL)	10 (5-90) (0-550)	0 (0-100) (0-260)	0.660
Basophils (/µL)	20 (10-40) (0-90)	15 (0-30)(0-40)	0.450
Platelets (/µL)	205000 (196000-260000) (27000-456000)	207500 (180500-250000) (9100-620000)	0.890
MPV (fL)	10.1 (8.9-11) (8.6-13.9)	11 (10.5-11.8) (10.2-12.7)	0.020
RDW	13.3 (12.1-18.6) (11.6-29.3)	15.6 (14.3-16.5) (13.2-17.1)	0.020
CRP (mg/L)	17 (10-33) (3-396)	93 (80-135) (31.1-290)	0.001
Sedimentation (s)	21 (15-33) (2-96)	48.5 (42-66) (7-90)	0.001
Procalcitonin (ng/mL)	0.1 (0-0.6) (0-12.3)	5.5 (0.9-2.4) (0.1-32.8)	0.001
INR	0.9 (0.8-1) (0.8-1.5)	1.9 (1.5-2) (1.4-2)	0.020
PT (s)	14.3 (13.5-16.4) (11.3-33)	17.7 (16.8-20.4) (13-21.9)	0.020
aPTT (s)	29.4 (28.4-35.4) (21.9-74.9)	32.5 (30.4-39.6) (21.2-73.3)	0.020
Fibrinogen (ng/mL)	373 (188-299) (131-918)	503 (430-667) (341-728)	0.006
D-dimer (ng/mL)	636.5 (225-860) (100-14000)	3185 (2456-6530) (1260-8490)	0.005
Ferritin (ng/ml)	129.3 (88-260) (10.2-1289)	249 (210-480) (130-1600)	0.001
BUN (mg/dL)	15.7 (12.6-36.4) (4.7-104)	43.3 (29.6-49.8) (9-119)	0.010
Creatine (mg/dL)	0.9 (0.8-1.4) (0.2-8.9)	1.9 (1.7-3.2) (0.6-4.99)	0.020
AST (U/L)	28 (22-45) (13-681)	49 (41-102) (11-1735)	0.001
ALT (U/L)	26.5 (20-47) (6-292)	62 (55-136) (6-1164)	0.001
LDH (U/L)	299.5 (210-350)(165-2156)	444 (360-596) (196-2929)	0.001
CK (U/L)	97.5 (80-106.5) (22-2359)	173.5 (150.6-360.6) (72-13649)	0.001
GGT (U/L)	28 (20-45) (10-242)	72 (50-96) (16-959)	0.001
ALP (U/L)	74.5 (65-95) (40-192)	150.5 (110-230) (33-633)	0.001
Total bilirubin (mg/dL)	0.5 (0.4-0.9) (0.1-3.04)	0.6 (0.5-2.2) (0.2-3.8)	0.007
Direct bilirubin (mg/dL)	0.21 (0.1-0.4) (0.1-1.17)	0.25 (0.2-0.9) (0.1-1.1)	0.040
Total protein (g/dl)	6.5 (5.1-6.8) (4.5-9.3)	5.6 (4.8-5.9) (4.6-7.7)	0.001
Albumin (g/dl)	3.7 (3.4-4.1) (2.3-4.8)	3.1 (2.7-3.3) (1.8-4)	0.001
NLR	3.6 (2.8-5.6) (0.5-34.5)	15.3 (10.2-19.8) (3.5-88.7)	0.001
PLR	171.2 (160-200.4) (7.6-854.6)	296.6 (256-410) (80.4-3100)	0.001

WBC: White blood cells, MPV: Mean platelet volume, RDW: Red blood cell distribution width, INR: International normalized ratio, PT: Prothrombin time, aPTT: Activated partial prothrombin time, NLR: Neutrophil/lymphocyte ratio, PLR: Platelet/lymphocyte ratio, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, LDH: Lactate dehydrogenase, GGT: Gamma glutamyl transferase, ALP: Alkaline phosphatase, BUN: Blood urea nitrogen, CK: Creatine kinase, SD: Standard deviation, p: Comparison of parameters between groups

virus. It has been observed that the virus mutates in order to continue its replication in host cells where balanced HA and NA activities are not realized. While these mutations facilitate the adaptation of the virus to the hosts, it also enabled it to escape from antiviral treatments. The antigenic properties of HA and NA on IAVs enable them to be divided into subtypes, the most common of which are H1N1 and H3N2 (12,13).

Influenza virus infections primarily cause uncomplicated respiratory tract infection characterized by fever, muscle aches, chills and shivering, and fatigue lasting approximately 2 to 8 days. Onset is rapid, and it may also present with gastrointestinal symptoms such as vomiting and diarrhea in the pediatric age group (14). Older patients, pediatric patients, and patients with high comorbidity can develop viral or secondary bacterial pneumonia that causes respiratory and multiple organ failure (15). Therefore, in addition to patients receiving immunosuppressive therapy, patients with obstructive pulmonary disease, congenital or acquired heart disease, chronic kidney and liver disease, and individuals over 65 years of age are risk groups for clinically severe illness (16). This increases the importance of inducing active immunity with vaccination in these populations before outbreaks occur (17-20).

Most of the patients in our study had IAV infection, and patients with IAV infection were statistically older than those with IBV infection. In addition, patients with IAV infection had higher procalcitonin levels and liver function tests at admission. These results suggest that IAV, which mutates more frequently than IBV, is

more easily transmitted to all age groups and may cause more severe illness in elderly patients in particular due to both its direct effect and the superinfections it can lead to. In the IAV subtype analysis, we observed that H1N1 was more common than H3N2.

Of the 10 patients who died, 8 had IAV infection and 2 had IBV infection. The nonsurviving patients showed significantly greater changes in nearly all studied laboratory parameters when compared with surviving patients. This may also be evidence that IAV infection leads to more severe clinical manifestations due to its high frequency among older patients and the associated superinfections that occur in this patient population. In this study, there was no statistically significant difference in mortality based on the presence of comorbidities. This result may be related to the fact that 41 of the 75 patients with comorbidities in our study with influenza vaccine priority during the pandemic (due to age and presence of comorbidities) were vaccinated. We observed with influenza the most concrete evidence of what we have experienced so bitterly during the current COVID-19 pandemic, that severe clinical illness can be prevented with vaccination. In addition, in the ROC curve analysis of nonsurviving patients, the high areas under the curve and sensitivity of procalcitonin, CRP, fibrinogen, D-dimer, and ferritin may indicate that these parameters can be used to predict mortality, as in the COVID-19 pandemic.

The main limitation of our study was the inability to observe the effect of comorbidities on mortality and laboratory parameters due to the lack of homogeneity in the vaccinated patient population. The priority given to the at-risk population in the vaccination program during the pandemic is a factor that prevented an increase in mortality in these patients. Furthermore, as superinfections cannot be predicted in advance and patients are given empiric antibiotherapy based on their laboratory results, it is not clear whether changes in laboratory parameters occurred due to influenza or superinfections that developed afterwards.

In conclusion, IAV infection occurs more frequently than IBV and may present with more severe disruptions in laboratory parameters. The IAV subtype H1N1 was found to cause infection more frequently in our region. The high procalcitonin levels observed in nonsurviving patients suggest superinfections as the likely precipitating factor of mortality in these patients. Our analysis of the relationship between comorbidity and mortality indicated that the vaccine policy prioritizing adults over 65 years of age and those with comorbidities had a favorable impact on mortality.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Erzurum Training and Research Hospital, Noninvasive Clinical Ethics Committee (Decision No:2021/08-153)

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 authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version

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