CLINICAL, SUBCLINICAL CHARACTERISTICS AND TREATMENT OUTCOMES OF ADULT INFLUENZA A AND B PATIENTS AT TAM ANH GENERAL HOSPITAL IN 2022

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Influenza is an acute respiratory infectious disease caused by the influenza virus. Studies on influenza patients' incidence, complications, and treatment outcomes vary. The COVID-19 pandemic has shown changes in circulating influenza strains.

Objectives: The study aims to describe the clinical, subclinical characteristics and treatment outcomes of influenza patients to help physicians improve prognosis and treatment outcomes for patients.

Subjects and methods: This cross-sectional descriptive study was conducted on 224 adult influenza patients admitted to Tam Anh General Hospital. The sample was conveniently collected from January 2022 to January 2023.

Result: 61 patients with influenza B (27.2%) and 163 patients with influenza A (72.8%). Clinical characteristics: The average age of the patients was 33.3 years. The most common symptoms were fever, body aches, headache, and productive cough. Biochemical characteristics: Patients had elevated Creatinine levels (0.9%). 45 patients had mildly elevated AST levels (20.1%), and 9 patients had significantly elevated AST levels (2.7%). 30 patients had mildly elevated ALT levels (13.3%), and 10 patients had significantly elevated ALT levels (4.5%).

Treatment outcomes: The average treatment duration for patients in the study was 3.50 ± 1.19 days. Patients with CRP > 2.5 mg/dL had longer treatment durations, higher complication rates, and higher antibiotic use compared to those with CRP ≤ 2.5 mg/dL. 87.5% of patients had good treatment outcomes, with symptoms improving and being discharged from the hospital; 12.5% of patients requested early discharge. Common complications included secondary bronchitis (11.6%), rhinosinusitis (4.4%), and pneumonia (2.2%).

Conclusions: Influenza A predominates among the cases. Patients with CRP > 2.5 mg/dL have a longer average treatment duration, higher complication rates, and increased antibiotic use compared to those with CRP ≤ 2.5 mg/dL.

Keywords: Influenza, complications of influenza, thrombocytopenia, virus.

INTRODUCTION

The COVID-19 pandemic has emphasized the importance of effectively managing respiratory diseases with pandemic potential. Influenza viruses not only cause high annual morbidity and mortality rates seasonally but also pose a significant global health security threat. The World Health Organization estimates that there are 3 to 5 million cases of influenza annually worldwide, leading to an estimated 500,000 deaths[1]. In Vietnam, from 2006 to 2015, the rate of severe pneumonia due to influenza A was 16.9%, with 50.2% of severe pneumonia cases caused by the A/H1N1/09 subtype. Severe pneumonia due to A/H5N1

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influenza has the highest mortality rate, at 66.7%.2 To date, influenza B has received less attention than influenza A, partly because influenza B is often considered less virulent, less likely to cause severe illness, and does not cause pandemics. However, its clinical significance is increasingly recognized. A study by Yogesh and colleagues indicated a higher rate of septic shock in influenza B patients compared to influenza A patients (3.8% versus 0.5%, $p < 0.001$)[3]. Given the unpredictable variations of influenza viruses, the high infection rates, lingering complications, and mortality, studies and reports on pathogenic influenza strains and their complications differ. To contribute to early prediction and appropriate treatment approaches, thereby improving treatment prognosis, we conducted a study on adult influenza patients at Tam Anh General Hospital in 2022. The objectives were to describe clinical, subclinical characteristics and analyze the treatment outcomes of adult patients with influenza A and B at Tam Anh General Hospital from January 2022 to January 2023.

SUBJECTS AND METHODS

Subjects: From January 2022 to January 2023, 224 adult influenza patients were treated at Tam Anh General Hospital.

- Patient Selection Criteria: Patients receiving medical treatment at Tam Anh General Hospital from January 2022 to January 2023 who agreed to participate in the study.

• Positive test results for influenza A or B by PCR or rapid test (SD BIOLINE Influenza Ag A/(H1N1)/B Pandemic at Tam Anh General Hospital or other medical facilities).

- Exclusion Criteria: Individuals under 16 years of age.

Method: Cross-sectional descriptive study.

Data processing techniques: Descriptive statistical analysis. Quantitative variables are expressed as number/percentage, and continuous variables as mean/standard deviation. Chi-square ($\chi 2$) or Fisher's Exact test is used to compare the proportions of qualitative variables..

RESULTS

Proportion of influenza A and B patients in the study

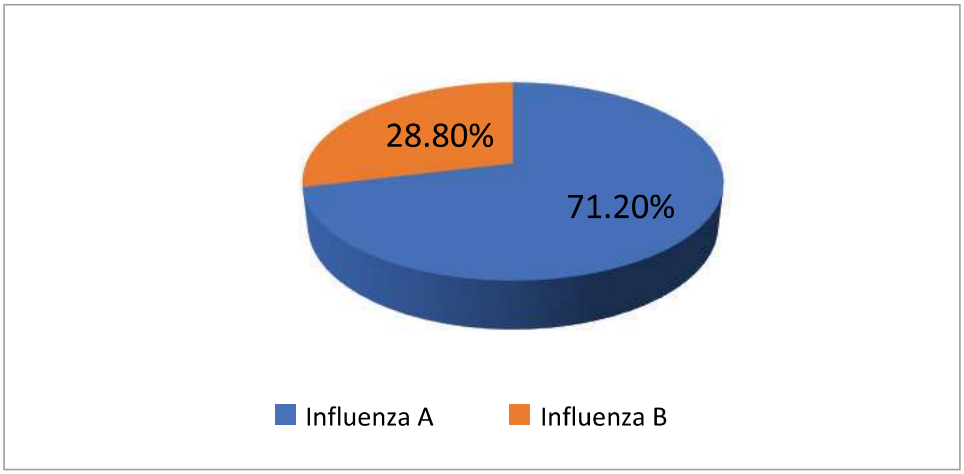

Chart 1. Proportion of adult influenza A and patients

Observation: Among the study patients, there were 163 patients with influenza A (71.2%) and 61 patients with influenza B (28.8%).

Distribution of patients by age group

Table 1. Distribution of patients by age group (n = 224)

Age group (year)	Number of patients (n = 224)	Percentage (%)
16 - 25	38	17%
26 - 35	129	57.6%
36 - 45	29	12.9%
46 - 55	17	7.6%
56 - 65	5	2.2%
> 65	6	2.7%
X ± SD	33.3 ± 11.3	

Observation: The majority of patients in the study were in the 26 - 35 age group, accounting for 57.6%. This was followed by the 16 - 25 age group (17%), 36 - 45 age group (12.9%), 46 - 55 age group (7.6%), > 65 age group (2.7%), and the 56 - 65 age group (2.2%).

Common clinical symptoms in influenza patients

Table 2. Common clinical symptoms in influenza patients (n = 224)

Clinical Symptoms	n (%)	Influenza A	Influenza B	p
		n	n	
Fever	222 (99.1)	162	60	0.471**
Body aches	185 (82.6)	135	50	0.881
Headache	142 (63.4)	99	43	0.177
Sore throat	124 (55.4)	92	32	0.594
Nasal congestion	106 (47.3)	74	32	0.346
Dry cough	95 (42.4)	66	29	0.342
Productive cough	89 (39.5)	65	24	0.942
Shortness of breath	8 (3.6)	6	2	1.000
Nausea	6 (2.7)	5	1	1.000

Observation: The most common symptoms among the patients were fever (99.1%), body aches (82.6%), headache (63.4%), sore throat (55.4%), nasal congestion (47.3%), dry cough (42.4%), productive cough (39.5%), shortness of breath (3.6%), and nausea (2.7%). There was no significant difference in clinical symptoms between the influenza A and B groups (p > 0.05).

Hematological characteristics at admission

Table 3. Hematological test characteristics at admission (n = 224)

Chỉ số		n	%
White blood cell count	< 4 G/L	13	5.8
	4 - 10 G/L	183	81.7
	> 10 G/L	28	12.5
Platelet count	< 150 G/L	16	7.1
	> 150 G/L	208	92.9

Observation: There were 13 patients with a white blood cell count below 4 G/L (5.8%) and 28 patients with a white blood cell count above 10 G/L (12.5%). The average white blood cell count was 7.27 ± 2.19 G/L. There were 16 patients with a platelet count below 150 G/L (7.1%).

Biochemical characteristics at admission

Table 4. Biochemical tests at admission

Xét nghiệm		n	%
Creatinin (n = 222)	Normal	220	99.1
	Elevated	2	0.9
AST (n = 224)	Normal	173	77.2
	Midly elevated	45	20.1
	Highly elevated	6	2.7
ALT (n = 224)	Normal	184	82.2
	Midly elevated	30	13.3
	Highly elevated	10	4.5

Observation: 2 patients had elevated Creatinine levels (0.9%). 45 patients had mildly elevated AST levels (20.1%), and 9 patients had significantly elevated AST levels (2.7%). 30 patients had mildly elevated ALT levels (13.3%), and 10 patients had significantly elevated ALT levels (4.5%).

Treatment outcomes

Table 5. Treatment outcomes of patients in the study (n = 224)

Outcome	n	%	X ± SD (Min - Max) (days)
Improved, discharged	196	87.5	3,50 ± 1,19 (1 - 10)
Requested discharge	28	12.5	

Observation: 96 patients showed symptom improvement and were discharged (87.5%), while 28 patients requested discharge (12.5%). The average treatment duration for patients in the study was 3.50 ± 1.19 days, ranging from 1 to 10 days.

Proportion of complicated and uncomplicated influenza cases in the study.

Table 6. Proportion of complicated and uncomplicated influenza cases (n = 224)

Condition (n = 224)		n	%
No complications		183	81.7
With complications	Bronchitis	26	11.6
	Sinusitis	10	4.4
	Pneumonia	5	2.2
	Laryngitis	2	0.8
	Otitis media	1	0.4

Observation: There were 26 patients with bronchitis (11.6%), 10 patients with sinusitis (4.4%), 5 patients with pneumonia (2.2%), 2 patients with laryngitis (0.8%), and 1 patient with otitis media (0.4%).

Comparison of treatment duration between patients with CRP levels below and above 2.5 mg/dL

Table 7. Treatment outcomes of patients in the study (n = 224)

CRP	n	%	X ± SD (days)	p
CRP ≤ 2.5 mg/dL	157	74.1	3.39 ± 1.15	0.013
CRP > 2.5 mg/dL	55	25.9	3.85 ± 1.28	

Observation: The treatment duration for patients with CRP > 2.5 mg/dL was statistically significantly longer than for those with CRP ≤ 2.5 mg/dL ($p < 0.05$, T-test).

Comparison of complication rates between patients with CRP levels below and above 2.5 mg/dL

Table 8. Comparison of complication rates between patients with CRP levels below and above 2.5 mg/dL (n = 212)

	CRP ≤ 2,5 mg/dL n (%)	CRP > 2,5 mg/dL n (%)	p
Flu with complications	23 (59.0)	16 (41.0)	0.017
Flu without complications	134 (77.5)	39 (22.5)	

Observation: The proportion of patients with CRP > 2.5 mg/dL is higher in the group with complications than in the group without complications ($p < 0.05$; Chi-square test).

DISCUSSION

Some laboratory test results of patients in the study

Among the 224 patients, the majority had influenza A with 163 patients (71.2%), and 61 patients had influenza B (28.8%). This result aligns with studies by Torgun Wæhre et al. in Norway and Tadashi Isida et al. in Japan[4,5]. Influenza activity was unusually low during the 2020 - 2021 flu season both in the United States and globally, despite high levels of testing. The Centers for Disease Control and Prevention reports that between Sept. 28, 2020 to May 22, 2021 in the United States, 1,675 (0.2%) of 818,939 respiratory specimens tested by U.S. clinical laboratories were positive for an influenza virus. The low flu activity in the past season contributed significantly to reduced influenza cases, hospitalizations, and deaths compared to previous flu seasons[1].

For comparison, in the three seasons before the pandemic, the proportion of respiratory samples testing positive for influenza peaked from 26.2% to 30.3%. In terms of hospitalizations, the cumulative hospitalization rate related to lab-confirmed influenza during the 2020 - 2021 season was the lowest recorded since this type of data collection began in 2005. In 2020 - 2021, COVID-19 mitigation techniques such as wearing face masks, staying at home, hand washing, school closures, reduced travel, increased ventilation of indoor spaces, and avoiding the crowded places, close contacts, and closed spaces (3Cs) and physical isolation were expected to have contributed to a drop in flu incidence, hospitalizations, and deaths[1]. Our study did not record any hospitalized influenza cases from January to May 2022.

The average age of the patients in the study was 33.3 ± 11.3 years. The three most common age groups were 26 - 35 years (57.6%). The average age in our study was lower compared to some studies such as that of Yogesh Sharma et al. at two tertiary hospitals in Australia from 2016 - 2020, which reported an average age of 66.5 years, or the study by Torgun Wæhre from 2014 - 2018 at Oslo University Hospital, Norway, which reported an average age of 70 years[3,7]. The average age of patients in our study was lower, and the proportion of patients over 65 was low. This is due to the small sample size in our study and differences in study timing and location. Additionally, Tam Anh General Hospital is a high-cost medical service hospital; patients aged 16 - 45 often have fewer underlying conditions and a higher rate of private insurance use, leading to a higher hospitalization rate. The common symptoms among patients in our study were fever (99.1%), body aches (82.6%), headache (63.4%), productive cough (60.7%), sore throat (55.4%), nasal congestion (47.3%), and dry cough (39.3%). The study by Cohen et al. from 2015 - 2018 on 759 influenza patients noted common clinical symptoms of fever (82%), cough (75%), and shortness of breath (41%)[8].

In the study, at the time of hospitalization, there were 28 patients with leukocytosis (12.5%) and 13 patients with leukopenia (5.8%). Durani et al.'s study from 2005 to 2013 on 673 influenza patients recorded leukopenia within one week after influenza diagnosis in 40 patients (5.9%)[9]. This rate is nearly equivalent to our study, but Durani's study had a larger sample size. Our complete blood count tests were taken at hospital admission, before antiviral medication oseltamivir was administered, and none of the patients had hematopoietic system diseases, so the leukopenia was related to influenza. However, due to the overall low number of patients in our study, with only 13 patients having leukopenia and most having a short average hospital stay (3.5 days), we did not track neutrophil changes in the following days in this group of patients. Thrombocytopenia can occur in some viral infections, including influenza. Our study found 16 patients with platelet counts below 150 G/L (7.1%), with the lowest being 119 G/L. Thrombocytopenia was reported in 14% of hospitalized cases worldwide during the 2009 influenza pandemic. Jansen et al.'s 2020 study indicated that thrombocytopenia is a common complication of influenza virus infection[10]. In patients with influenza A/H1N1, there is an inverse correlation between viral load and platelet count during the acute infection phase. Studies on ferrets infected with influenza showed that platelet counts decreased with the virus's pathogenicity, varying from 0% in animals infected with influenza A/H3N2 to 22% in animals infected with influenza A/H1N1 and up to 62% in animals infected with influenza A/H5N1.

Increased AST, ALT in influenza patients has also been indicated in studies such as Özge et al., which found significantly higher AST, ALT levels in the influenza-positive group.11 Neven et al.'s 2011 study on liver injury during the 2009 A/H1N1 influenza pandemic compared to seasonal influenza showed a significant increase in AST, ALT levels in the blood correlated with hypoxia.12 In the pandemic group, liver enzyme levels were often higher than normal compared to the seasonal group: AST (35.78% vs. 18.60%, $p = 0.01245$), ALT (26.31% vs. 7.36%, $p = 0.0016$). Most patients had mild liver injury. In patients with abnormal liver enzymes, transaminase

levels increased 2-5 times and normalized quickly within a few days.

Treatment outcomes

Among 196 patients, symptoms improved, and they were discharged (87.5%), while 28 patients requested discharge (12.5%). This may be due to the generally young average age of patients in the study, with the predominant age group being 26 - 35 years, and fewer underlying health conditions.

CRP is a non-specific biomarker of acute inflammation produced mainly in the liver and also in the lungs. In influenza pandemics, systemic inflammatory response syndrome (SIRS) is often more severe than in seasonal influenza. SIRS eventually causes tissue perfusion disorders, contributing to liver cell damage and increased transaminase levels. Patients with CRP ≤ 2.5 mg/dL had a shorter average treatment duration than those with CRP > 2.5 mg/dL. The proportion of patients with CRP > 2.5 mg/dL was higher in the group with complications than in the group without complications. Haran et al.'s study also indicated that influenza patients with CRP levels greater than 2.5 mg/dL had longer-lasting symptoms compared to those with CRP levels below 2.5 mg/dL[13]. Rongbao et al.'s study suggested that CRP might be related to the severity and fatality risk in patients infected with influenza A/H5N1, A/H7N9, or A/H10N8[14]. CRP also correlates with complement activation in patients with severe avian influenza (H5N1, H7N9). However, 100% of the patients in our study were diagnosed with influenza using rapid tests, which only excluded influenza A/H1N1 and did not type the virus, making it impossible to analyze the correlation between CRP and influenza strains.

CONCLUSIONS

Our research draws some conclusions as follows:

- There were 61 patients with influenza B (27.2%) and 163 patients with influenza A (72.8%).

- The average age of the patients in the study was relatively young (33.3 years), with the most common age group being 26 - 35 years.

- The common symptoms were fever (99.1%), body aches (82.6%), headache (63.4%), productive cough (60.7%), sore throat (55.4%), nasal congestion (47.3%), and dry cough (39.3%).

- The average treatment duration for patients in the study was 3.50 ± 1.19 days. Patients with CRP > 2.5 mg/dL had longer treatment durations, higher complication rates, and higher antibiotic use compared to those with CRP ≤ 2.5 mg/dL. 87.5% of patients had good treatment outcomes, with symptoms improving and being discharged from the hospital; 12.5% of patients requested early discharge.

- Common complications included secondary bronchitis (11.6%), rhinosinusitis (4.4%), and pneumonia (2.2%).

RECOMMENDATION

After the COVID-19 pandemic, there was a resurgence of influenza towards the end of 2022, with influenza A predominating. Further research is needed to determine whether CRP can be used to predict hospitalization needs, the necessity of prescribing antiviral medication, the development of influenza-related complications, and the presence of concurrent bacterial infections.

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