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FACTORS ASSOCIATED WITH LETHAL OUTCOME IN PATIENTS WITH SEVERE FORM OF INFLUENZA

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Abstract

Introduction: Clinical manifestations of influenza range from relatively mild and self-limiting respiratory infections to severe clinical manifestations with significant morbidity and mortality. The awareness of predictive indicators for the lethal outcome of influenza is of particular significance in making timely and exact decision for adequate treatment. The *aim* of this study was to identify the factors in patients with a severe form of influenza, resulting in lethal outcome.

Materials and methods: The investigation was a prospective group comparison conducted at the University Clinic for Infectious Diseases in Skopje, R. Macedonia in the period from January 01, 2012 to January 01, 2015. The study included adult patients with a severe form of influenza who were further categorized into a group of either survived patients or a group of deceased patients. Demographic, clinical and biochemical data were noted in all patients included in the study on admission. The variables of the univariate analysis that showed a significant difference in terms of the outcome were used for creating multivariate logistic and regression analysis of the outcome as dependent factors. The independent predictors for lethal outcome in severe cases of influenza were identified by using logistic regression.

Results: The study included 87 patients with a severe form of clinical and laboratory confirmed influenza. The patients were divided in two groups: survived (n = 75) and deceased (n = 75). The overall mortality was 13.79%. Multivariate analysis conducted on admission to hospital identified cardiovascular comorbid diseases (p = 0.014), urea values higher than 8.3 U/L (p = 0.045) and SAPS score (p = 0.048) as independent predictors of the outcome in patients with severe form of influenza. Influenza patients with cardiovascular diseases had 2.024 times greater risk of death from influenza in comparison to the patients having influenza without history of such a disease (OR = 2.024 95% CI 1.842–17.337). Patients with serum urea values higher than 8.3 U/L had 1.89 times higher chance of death compared to patients with normal values (OR = 1.89 95% CI 1.091–11.432). The increase of the SAPS score in one point increased the chance of death in patients with influenza by 1.2% (OR = 1.12 95% CI 1.01–2.976). The ROC analysis indicated that cardiovascular diseases, increased urea values and SAPS score in combination act as a good prognostic model for the fatal outcome. The global authenticity of this predictive model to foresee lethal outcome amounts to 80%, sensitivity being 82%, and specificity 70%.

Conclusion: Cardiovascular diseases, increased values of urea over 8.3 mmol/l and SAPS score are independent predictive indicators for lethal outcome in severe influenza. Early identification of the outcome predictors in patients with severe influenza will allow implementation of adequate medical treatment and will contribute to decreasing of mortality in patients with severe form of influenza.

Keywords: severe influenza, predictive indicators, lethal outcome

Introduction

Clinical manifestations of influenza range from relatively mild and self-limiting respiretory infections to severe clinical manifestations with significant morbidity and mortality [1]. During seasonal epidemics from 3 to 5 million severe cases and about 250.000–500.000 lethal cases are registered worldwide [2]. Until now there has not been a laboratory test which has served as a potential marker for identification of patients with a high risk of developing severe clinical forms of influenza and lethal outcome [3, 4]. It is known that patients with different comorbid conditions such as diabetes mellitus, chronic cardiovascular and pulmonary diseases, immunosuppressive conditions, adult patients and other conditions are at higher risk of developing severe clinical course of the disease and lethal outcome [5]. Although the influenza virus is primarily a respiratory pathogen, the severe clinical forms of the disease are manifested as systemic infections with multisystem organ affection, and even 10–30% of the diseased need intensive treatment [6, 7]. Pneumonia, delayed antiviral treatment, severe hypoxemia and multisystem organ failure are most commonly referred as leading risk factors for lethal outcome [8]. The largest number of studies has evaluated isolated risk factors leading to lethal outcome and only a few of them have been focused on the complete palette of predictors for development of a severe form of the disease and lethal outcome [9–12]. From the clinical practice point of view, the awareness/recognition of the risk factors and predictors for lethal outcome of influenza is of particular importance in bringing timely and exact decision for hospitalization, treatment or undertaking special measures for intensive monitorring of these patients.

Severe influenza is defined by signs for respiratory weakness (dyspnea, tachypnea, hypoxia, cyanosis) that is arterial PaO2 < 70 mmHg (< 9.0 kPa) and/or need of mechanical ventilation or signs of ARDS (PaO2/FiO2 ≤ 200), intensive care, severe complications, exacerbation of the existing chronic disease.

The aim of this study was to identify the risk factors that lead to lethal outcome in patients with severe form of influenza.

Materials and methods

The study was designed in accordance with the ethics principles of the Declaration of Helsinki for patients and their rights, and was approved by the Ethics Committee of the Medical Faculty of Ss. Cyril and Methodius University in Skopje.

The study was clinical, prospective, group comparison and it was performed at the Clinic for Infectious Diseases and Febrile Conditions in a three-year-period (01.01.2012–01.01.2015).

A total of 87 patients with severe forms of clinically and laboratory confirmed influenza were analyzed. The patients were divided into two groups:

Group 1 contained 75 patients who survived and

Group 2 contained 12 patients who had lethal outcome

Criteria for inclusion in the study:

All patients with clinical and laboratory confirmed severe form of influenza.

- Age ≥ 16 years

Criteria for exclusion of the study:

- Patients were excluded if they died in the first 24 hours of their inclusion in the study. Those that did not receive approval for inclusion

On admission of patients, the following parameters were noted: demographic characteristics, comorbidities, clinical signs of the disease and laboratory-biochemical characteristics.

For determining the presence of the influenza virus nasopharyngeal smear was used. In the Laboratory of virology and molecular diagnosis at the Institute for Public Health from the previously isolated RNA (ribonucleic acid) real time **RT-PCR** (**reverse transcriptase/ion-polymerase chain reaction in real time**) was performed on the apparatus IQ (BioRad) for detection of matrix gene of influenza A and influenza B. The samples positive to influenza A were subtyped by the same method, by RT-PCR, with a specific set of primers for highly conserved regions of X1, X3 and X1 pdm (pandemic).

The data were statistically analyzed with the program SPSS for Windows 13.0, using relevant statistical methodologies. Distribution of frequencies (absolute and relative incidence) was used for qualitative parameters. Descriptive methods such as mean, median and mode were used for mean and typical values of data as well as measures of declination, standard deviation and standard error. For testing the significance of the difference between certain analyzed factors para-

metric tests (t-test for independent samples, Analysis of Variance) were also used non-parametric tests for independent samples (Mann-Whitney U test, Chi-square test, Fisher-exact test).

Regarding the determination of the prognostic factors of death in patients with influenza the method of multivariate analysis was used (Logistic Binary Regression), by which the relation of probability of exposure (OR) was determined as an approximate value of the real risk (RR). The statistical precision of (OR) was obtained by calculation of the confidence intervals (CI) about the estimated values.

The value of $p < 0.05$ was considered to be statistically significant, and the value of $p < 0.01$ highly significant.

Results

The study included 87 patients with a severe form of clinically and laboratory confirmed influenza, who were treated at the Clinic for Infectious Diseases and Febrile Conditions in the period from 01.01.2012 to 01.01.2015. Twelve (13.79%) of them died.

Our results showed that women died insignificantly more often than men (16.13% vs 12.5% ($p = 0.64$).

The age had significant influence on the disease outcome ($p = 0.019$). The mean age of the deceased patients was 65.58 ± 17.5 years, opposite the mean age of the survived patients which was 53.04 ± 16.8 years.

The place of living of the patients had no significant influence on the outcome ($p = 0.44$), that is, patients from the rural environment died insignificantly more often than patients from the urban environment (22.22% vs 12.82%) (Table 1).

Table 1

Demographic characteristics of patients regarding outcome

variable	Severe influenza			p value
	Total n = 87	Survived n = 75	Deceased n = 12	
Sex [n (%)]				
women	31(35.63)	26(83.87)	5(16.13)	[a]0.64
men	56(64.37)	49(87.5)	7(12.5)	
Age (mean ± SD)				
	54.77 ± 17.3	53.04 ± 16.8	65.58 ± 17.5	[b]0.019*
Place of living [n (%)]				
city	78(89.65)	68(87.18)	10(12.82)	[a]0.438
village	9(10.34)	7(77.78)	2(22.22)	

[a]p (Chi-square test) [b]p (Student's t- test) [c](Fisher exact test) *p < 0.05

The patient who was vaccinated against influenza overcame the disease whereas 13.95% of the patients who were not vaccinated died. ($p = 1.0$).

Prior to hospitalization 77.78% of survived patients 22.22% of patients who died were treated with osaltamivir ($p = 0.6$). The duration of health problems prior to hospitalization differed significantly between the survived and deceased patients ($p = 0.05$). The mean duration of symptoms prior to hospitalization was 5 days in the group of survived patients and 7 days in the group of deceased patients (Table 2).

Table 2

Vaccination, use of osaltamivir, days prior to admission in relation to outcome

variable	Influenza			p value
	Total n = 87	Survived n = 75	Deceased n = 12	
Vaccine [n (%)]				
yes	1(1.5)	1(100)	0	[c]1.0
no	86(98.85)	74(86.05)	12(13.95)	
Use of osaltamivir prior to admission [n (%)]				
no	78(89.65)	68(87.18)	10(12.82)	[c]0.6
yes	9(10.34)	7(77.78)	2(22.22)	
Days prior to admission (median IQR)				
	5 (3–7)	5 (2–7)	7 (4–7)	[d]0.05

[a]p (Chi-square test) [c](Fisher exact test) [d](Mann-Whitney U test)

The highest mortality rate of influenza was registered at the Intensive Care Unit (22.5%) (p < 0.001). Statistically significant difference was also registered in the outcome of patients who were and who were not treated with mechanical ventilation where significantly dominated the deceased patients who underwent mechanical ventilation (41.67% vs 9.33% p = 0.01) The results of our study have demonstrated that patients with comorbid conditions died more often than those without these diseases (15.38% vs 9.09%) (p = 0.72). The cardiovascular diseases had a significant impact on the outcome of influenza (p = 0.011). All other analyzed comorbid conditions such as: chronic pulmonary diseases (survived 92.31% vs deceased 7.69%) (p = 0.68), neurological diseases (80% vs 20%) (p = 0.62), renal diseases (60% vs 40%) (p = 0.14), endocrinological diseases (88.24% vs 11.76%) (p = 1.0), hematological diseases (83.33% vs 16.67%) (p = 1.0) were insignificantly associated with outcome in patients with influenza. Small number of patients who had previous immunological disease (1), hepatic diseases (1) and obesity (2) survived in spite of being presented with severe form of influenza. Two pregnant patients also survived. SAPS 2 score which was calculated in the first 24 hours of admission, was significantly associated with lethal outcome (Table 3).

Table 3

Stay at the Intensive care unit, days on intensive care and mechanical ventilation, comorbid conditions, SAPS 2 score in relation to outcome

variable	Total n = 122	Influenza Survived n = 75	Deceased n = 12	p value
Intensive [n (%)]				
no	47(54.02)	46(97.87)	1(2.13)	[a]0.0006
yes	40(45.98)	29(72.5)	11(27.5)	
Days at intensive (median IQR)				
	7 (3–11)	6 (3–10)	8 (2–12)	[d]0.72
Mechanical ventilation [n (%)]				
no	75(86.21)	68(90.67)	7(9.33)	[c]0.01
yes	12(13.79)	7(58.33)	5(41.67)	
Comorbid conditions [n (%)]				
no	22(25.29)	20(90.91)	2(9.09)	[c]0.72
yes	65(74.71)	55(84.62)	10(15.38)	
Cardiovascular disease [n (%)]				
no	44(50.57)	42(95.45)	2(4.55)	[a]0.011
yes	43(49.42)	33(76.74)	10(23.26)	
SAPS 2 score (mean ± SD) median (IQR)				
	36.4 ± 29.1 med 26(17–42)	33.7 ± 28.9 med 23(16–37)	53.4 ± 24.9 med 46.5(40–53)	[d]0.00038**

[a]p (Chi-square test) [c](Fisher exact test) [d](Mann-Whitney U test)

Out of all the laboratory–biochemical analyses conducted on admission, only urea > 8,3 mmo/l, showed significant association with a lethal outcome (survived 25.33% vs deceased 66.67%) (p = 0.007).

Tables 4 and 4a present the results from Univariate Logistic Regression analysis in determining the analyzed demographic, clinical and biochemical variables that have confirmed to be predictors of the lethal outcome.

The results of the multivariate analysis as independent predictors of lethal outcome, from the analyzed demographic, clinical and biochemical parameters have confirmed the following: cardiovascular comorbidities (p = 0.014), urea values higher than 8.3 U/L (p = 0.045) and SAPS 2 score (simplified acute physiology score) (p = 0.048).

Patients with influenza and cardiovascular diseases had 2.024 times higher risk of death by influenza when compared to patients with influenza without history of cardiovascular comorbidity (OR = 2.024 95% CI 1.842–17.337).

Table 4

Univariate Logistic regression analysis for prediction of lethal outcome in patients with influenza

variable	**Crude OR 95% CI for OR**	**p value**
Demographic variables		
age	1.05 (1.006– 1.095)	0.025*
Men vs women	0,743 (0.214– 2.573)	0.639
Village vs town	1.943 (0.353–10.698)	0.445
Tamiflu prior to admission	0.515 (0.093– 2.834)	0.445
Comorbidity	1.818 (0.366– 9.025)	0.465
Number of comorbidities	3.167 (0.903– 11.102)	0.072
cardiovascular	6.364 (1.304– 31.055)	0.022**
Clinical variables (symptoms)		
temperature >37.8°	0.364 (0.105–1.259)	0.11
dyspnea	1.067 (0.292–3.859)	0.928
cyanosis	1.056 (0.258–4.324)	0.94
Chest pain	1.109 (0.303–4.057)	0.876
pulse >80	1.313 (0.149–11.555)	0.806
SAP <120	0.8 (0.076–8.474)	0.853
SAP >120	1.077 (0.112–10.369)	0.949
respirations >20	1.25 (0.247–6.318)	0.787
SAPS	1.15 (1.07–3.18)	0.039*
RTG finding		
consolidation	1.091 (0.268–4.438)	0.903

Table 4a

Univariate Logostic regression analysis for prediction of lethal outcome in patients with influenza

variable	**Crude OR 95% CI for OR**	**p value**
Biochemical variables		
leukocytes > 9	1.027 (0.304–3.474)	0.966
thrombocytes <140	2.0 (0.492–8.129)	0.333
thrombocytes > 250	0.737 (0.136–3.992)	0.723
glycemia > 6.3	1.891 (0.473–7.569)	0.368
urea > 8.3	5.89 (1.593–21.807)	0.008**
creatinine > 110	2.222 (0.627–7.87)	0.216
potassium < 3.5	0.429 (0.05–3.672)	0.492
potassium > 5.5	1.714 (0.306–9.599)	0.54
sodium < 135	0.653 (0.126–3.372)	0.611
sodium > 145	1.175 (0.216–6.388)	0.852
ALT > 52	1.706 (0.457–6.362)	0.426
AST > 47	1.885 (0.552–6.431)	0.312
LDH > 618	3.152 (0.644–15.422)	0.156
CPK > 170	1.083 (0.32–3.655)	0.898
bilirubin > 17	1.05 (0.204–5.407)	0.953
bicarbonates	1.893 (0.583–6.653)	0.32

Patients with serum urea levels higher than 8.3 U/L had 1.89 times greater chance for dying compared to patients with normal values (OR = 1.89 95% CI 1.091–11.432).

The increase of SAPS score for one score increases the chance of death in patients with influenza by 1.2% (OR = 1.12 95% CI 1.01–2.976).

Table 5

Multivariate Logistic regression analysis for prediction of lethal outcome in patients with influenza

variable	**Adjusted OR 95% CI for OR**	**p value**
Cardiovascular	2.024 (1.842–17.337)	0.014*
urea > 8.3	1.89 (1.091–11.432)	0.045*
SAPS score	1.12 (1.01–2.976)	0.048*

ROC analysis has demonstrated that the combination of cardiovascular diseases, the increased urea values and the SAPS score are a good prognostic model of the lethal outcome. The area under the ROC curve, that is, AUC was 0.755, with 95% confidence interval from 0.587–0.923 suggesting that the probability of combination of these two predictors for death in influenza patients was 75.5%.

The global precision of this predictive model to foresee the lethal outcome was 80%, sensitivity 82%, and specificity 70%.

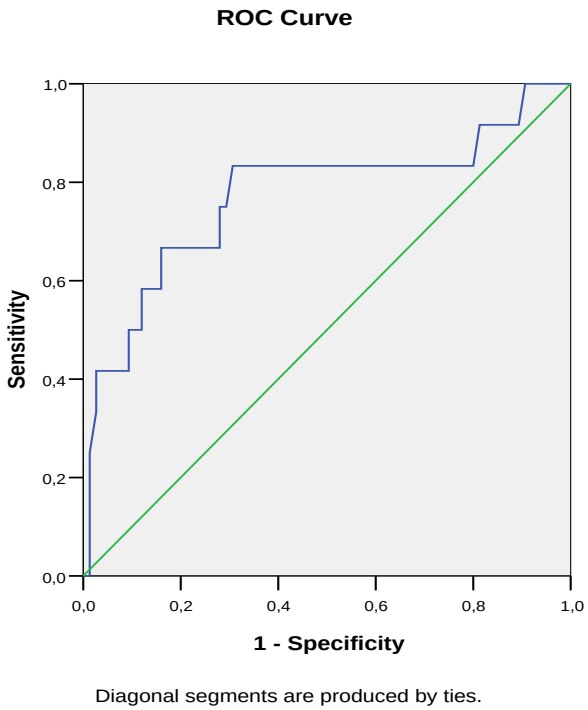

Figure 1 – ROC curve for the influence of cardiovascular diseases, urea and SAPS score in prediction of lethal outcome from influenza

Discussion

The mortality rate of the hospitalized patients with severe influenza infection amounted to 13.79% in our study. The percentage of lethality varies among published studies and it ranges from 10% to extreme 59%, which certainly depends on the various conditions and criteria according to which the patients are analyzed as well as on the criteria for admission to intensive care units [13–15]. Thus, the study performed in China showed that from 60 patients with severe form of influenza 44% were treated at Intensive care unit and the lethality was 14.7% [16].

There was no a significant difference regarding the mortality between male and female patients in our study, although in most of the studies the male sex was identified as a risk factor associated with lethal outcome. [17, 18]. Our results have demonstrated that from the total number of 12 lethal outcomes 5 or (16.1%) were women and 7 (12.5%) were men. Our study is similar to that conducted in Canada where from the total number of 29 lethal out-

comes, 27.6% were men, whereas 72.4% were women [17]. The age had significant influence on the disease outcome in our study. The mean age of patients that died was 65.58 (p = 0.019). The mortality was the highest in patients at the age over 65 (27.2%). These results coincide with almost all studies in the world that identify the old age as an important risk factor for mortality in patients with influenza [19]. The place of living of the patients was not significant in relation to the outcome. Patients from the rural environment exited as patients from the urban environment, 22.2% vs 12.8%.

According to many studies the use of neuraminidase inhibitor within 48 hours from the beginning of the symptoms decreases the risk of progression into a severe form and death of patients with influenza. In addition, the guidelines of the WHO recommend early treatment with oseltamivir for suspected influenza cases and warn that delayed medical attention increases the mortality rate [20]. In our study, 89.6% of patients did not use osaltamivir prior to admission, whereas only 10.35% of them used this medication. In the first group the mortality rate was 12.8% vs 22.2% in the second group (p = 0.06). The answer probably lies in two important issues. The first one is the small group of patients and the second one arises from the existence of resistant forms of the virus [21, 22].

The results of our study have shown that in the group of patients with severe influenza without comorbidity the mortality rate was 9.09% whereas in the group of patients with associated comorbid diseases the mortality rate was higher than in the first one (15.38%) (p = 0.72). The analysis of identified associated chronic conditions have shown that cardiovascular diseases had significant influence on the outcome from influenza (p = 0.011). While patients with a negative history of cardiovascular comorbidity yielded a mortality rate of 4.55%, the patients who did have cardiovascular disease present, yielded a significantly higher mortality rate of 23.26% [5].

All 87 patients with severe influenza in our study had higher body temperature than 37.8º. The mean body temperature between the group of survived and deceased patients showed no statistically significant correlation (38.7 ± 0.7 vs 38.4+ 0.8) p = ns. The other clinical symptoms that were analyzed did not differ among themselves in the group of survived patients and those that died, although the latter group complained on cough, dizziness, dyspnea and chest pain [23–25].

In all of the patients where the diagnostic protocol included chest radiologic procedures in our study, the statistical analysis indicated that 60% of patients that had diffuse bilateral consolidation died contrary to 10.9% of patients who did not have this type of radiologic finding (p = 0.017) [26].

Laboratory and biochemical analyses were performed in patients on their admission to the Clinic, 24 and 48 hours after admission. The statistical analysis showed significantly decreesed values of erythrocyte the second day of the hospitalization (p = 0.009), higher mean value of sedimentation rate (p = 0.02) as well as higher percentage of neutrophils in the group of deceased patients opposite to the survived patients (p = 0.0005). In relation to the remaining biochemical parameters the glycemia was with higher values in the group of deceased patients but statistical significance was confirmed only 48 hours after admission (p = 0.001). In all three measurements the level of urea higher than 8.3 mmol/l was significantly more often in the group of deceased patients (p = 0.007, p = 0.0027 and p = 0.017).

The creatinine level higher than 110 micromol/l demonstrated statistically significant difference between the two groups only in the period of 24 hours after hospitalization. These findings correlate with most of the studies where the increased level of serum createnine was confirmed as a significant statistical factor that had influence on the outcome.

With reference to the mean values of bilirubin, CRP, ALAT, ASAT, CPK, LDH albumins and total proteins analyzed on admission, 24 and 48 hours after admission, the following parameters were statistically significant in the group of patients who died: bilirubin 48 hours after admission (p = 0.038), CRP after 24 and 48 hours (p = 0.01), p = 0.0004), ASAT after 24 hours (p = 0.006) albumins after 48 hours (p = 0.019) and total proteins on admission, 24 and 48 hours (p = 0.007, p = 0.002 and p = 0,002). All these results are in agreement with

a large number of studies that have analyzed the lab-biochemistry parameters [14, 18, 19].

As independent predictors for lethal outcome in patients with influenza, we have identified the following variables: cardiovascular diseases ($p = 0.014$), urea levels higher than 8.3 ($p = 0.045$) and SAPS score ($p = 0.048$). Patients with influenza and cardiovascular diseases had 2.024 times higher risk of death of influenza compared to influenza patients without history of cardiovascular comorbidity. The confidence interval was 98%. Those patients that had urea levels higher than 8.3 had 1.89 times bigger chance for lethal outcome compared to patients with normal values of urea. The increase of SAPS score for one score raises the risk of death in patients with influenza by 1.2%.

Conclusion

In our study the mortality rate was 13.9%. Cardiovascular diseases, the increased urea level over 8.3 mmol/l and SAPS score have been identified as independent variables, which have predicted the outcome in patients with severe influenza on the very admission to the Clinic demonstrating precision of this predictive model of 80%.

The early identification of the outcome predictors in patients with severe influenza will ensure implementation of adequate medical procedures, and also, it will contribute to decreasing the mortality of this disease.

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Р е з и м е

ФАКТОРИ АСОЦИРАНИ СО СМРТЕН ИСХОД КАЈ ПАЦИЕНТИ СО ТЕШКА ФОРМА НА ИНФЛУЕНЦА

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Вовед: Клиничките манифестации на инфлуенца се движат во дијапазон од релативно лесни и самолимитирачки респираторни инфекции до тешки клинички манифестации со сигнификантен морбидитет и морталитет. Познавањето на предикторите за смртен исход од инфлуенца е од посебно значење за донесување навремена и правилна одлука за соодветен третман.

Цел на оваа студија е да се идентификуваат факторите кои укажуваат на смртен исход кај пациентите со тешка форма на инфлуенца.

Материјал и методи: Истражувањето е проспективно групно споредбено и е изведено на Универзитетската клиника за инфективни болести во Скопје, Р. Македонија, во период од 1 јануари 2012 до 1 јануари 2015 година. Во студијата се вклучени возрасни пациенти со тешка форма на инфлуенца кои понатаму се поделени на група преживеани и група починати пациенти. При вклучување во студијата се бележени демографски, клинички и биохемиски податоци. Варијаблите од униваријантната анализа кои покажаа значајна разлика во однос на исходот се употребени за изработка на мултиваријантна логистичка регресивна анализа за исходот како зависни фактори. Со логистичката регресија се добиени независни предиктори за смртен исход од тешка форма на сезонска инфлуенца.

Резултати: Во студијата беа вклучени 87 пациенти со тешка форма на клинички и лабораториски потврдена сезонска инфлуенца. Болните беа поделени во две групи: преживеани (н = 75) и починати (н = 12). Вкупната смртност изнесуваше 13,79%. Мултиваријантната анализа при приемот ги издвои кардиолошките коморбидитетни болести (п = 0,014), вредностите на уреа повисоки од 8,3 У/Л (п = 0,045) и САПС скорот (п = 0,048) како независни показатели кои го предвидуваат исходот кај болните со тешка инфлуенца. Пациентите со инфлуенца и кардиолошки заболувања имаат за 2,024 пати поголема шанса за смрт од инфлуенца, компарирано со пациентите со инфлуенца без историја за кардиолошки коморбидитет (OR = 2,024 95% CI 1,842 – 17.337). Пациентите со вредности на уреа во серум повисоки од 8,3 U/L имаа за 1.89 пати поголема шанса за егзитирање, компарирано со пациентите со нормални вредности (OR = 1,89 95% CI 1.091 – 11,432). Зголемувањето на САПС-скорот за еден скор ја зголемува шансата за смрт кај пациентите со инфлуенца за 1,2% (OR = 1,12 95% CI 1.01 – 2,976).

ROC-анализата покажа дека кардиолошките заболувања, покачени вредности на уреа и САПС скорот како комбинација претставуваат сигурен прогностички модел за летален исход. Глобалната точност на овој предиктивен модел да предвиди летален исход изнесува 80%, сензитивноста е 82%, специфичноста е 70%.

Заклучок: Кардиолошките заболувања, покачените вредности на уреа над 8,3 ммол/л и

САПС-скорот се независни предиктори за смртен исход кај тешка инфлуенца. Раната идентификација на показателите на исходот кај болните со тешка инфлуенца ќе овозможи имплементација на адекватни медицински постапки и ќе придонесе за намалување на морталитетот на болните со тешка форма на сезонска инфлуенца.

Клучни зборови: тешка инфлуенца, предиктори, смртен исход