

## ETIOLOGIC TREATMENT OF PANDEMIC INFLUENZA

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### Abstract

**Introduction:** Oral oseltamivir administration is effective treatment for influenza in adults. This study was conducted to determine the efficacy, safety and tolerability of oseltamivir in adults with influenza.

**Objectives:** To access the effect of antiviral treatment of the patients admitted with pandemic A(H1N1) infection.

**Patients and method:** Medical records of patients with confirmed influenza A(H1N1) 2009 were reviewed retrospectively for this study after their admission to the Infectious Diseases Hospital at UHC "Mother Theresa", Tirana between May 2009 and January 2010.

**Results:** Of 182 patients were enrolled in the study. A significant correlation was found between the time of disease onset and radiologic diagnosis of pneumonia,  $\rho=2.6$ ,  $p<0.01$ . Patients who presented early at disease onset did not develop severe disease. The mean duration of hospitalization among patients presented with co-morbidities was 7.9 days ( $SD\pm 4.9$ ) which was significantly higher compared to patients without co-morbidities with a mean of 5.8 days ( $SD\pm 2.8$ ),  $t=3.5$   $p<0.01$ . Patients who received oseltamivir had a significant reduction in the median duration of symptoms such as fever,

cough and coryza than did the untreated patients (Log-rank = 4.2  $p=0.04$ ).

**Conclusions:** Oral oseltamivir administration is an efficacious and well-tolerated therapy for influenza in adults when given within 48 h of onset of illness.

**Key words:** A(H1N1) virus, co-morbidities, oseltamivir, treatment.

### Introduction

Pandemic influenza is a respiratory infection that caused substantial morbidity, including upper and lower respiratory complications, and it increased health care contacts (12,3,4). The very young patients and those with underlying health problems, particularly those immune-compromised, patients with chronic heart and lung disease, diabetes, obesity and pregnant women should be considered to be at high-risk in the event of an influenza pandemic (5,6,7,8). Fortunately the virus and the pandemic were milder than many had initially feared. Bacterial co-infection in the lungs often occurred when pandemic influenza was accompanied by pneumonia. Among patients with 2009 pandemic influenza A (H1N1), we found significant differences in clinical and laboratory manifestations between patients with lung involvement and those without (9,10,11,12,13,14). On the basis of data from this study and the existing literature, early

treatment with oseltamivir is recommended for patients with 2009 pandemic influenza A(H1N1), regardless of age (15,16,17,18,19,20,21).

#### Patients and method

Medical records of patients with confirmed influenza A(H1N1)2009 were reviewed retrospectively for this study after their admission to the Infectious Diseases Hospital at UHC "Mother Theresa", Tirana between May 2009 and January 2010. A physical examination was performed, and blood samples were taken for standard hematologic and clinical biochemistry assays at baseline.

The results were analyzed using SPSS version 20. Categorical variables were compared using Pearson  $\chi^2$  test and

continuous variables were compared using the Student's t-test. Non parametric Spearman correlation coefficient ( $\rho$ ) was used to assess the correlation between variables. Survival analysis was used to estimate the differences in median time of illness resolution. All tests of significance were two-tailed and a P value of 0.05 was considered significant.

#### Results

A total of 182 patients were enrolled into the study. The characteristics of patients are presented in (Table nr.1). The mean age of patients was 35 years (SD $\pm$ 16.6), range 14-79 yrs. 85 were females (46.7%) and 97 males (53.3%),  $p=0.02$ . The median time of disease onset was 3 days.

**Table nr.1. Socio-demographic and clinical features of patients**

Characteristics of study patients	N	(%)	p
<b>Gender n (%)</b>			0.02
Female	85	(46.7)	
Male	97	(53.3)	
Age mean (SD)	35 (16.6)		
Days from onset	4.2 (2.8)		
Hospital stay (days)	7.9 (4.9)		
<b>Underlying condition n (%)</b>			<0.01
Pneumopathy	15	(8.2)	
Arterial Hypertension	9	(4.9)	
Cardiopathy	7	(3.8)	
Pregnancy	6	(3.3)	
Anaemia	3	(1.6)	
Diabetes	3	(1.6)	
Chronic Atria Fibrillation	3	(1.6)	
Acute Renal Failure	3	(1.6)	
Rheumatoid Arthritis	2	(1.1)	
Epilepsy	2	(1.1)	
Prostate adenoma	1	(0.5)	
Depression	1	(0.5)	

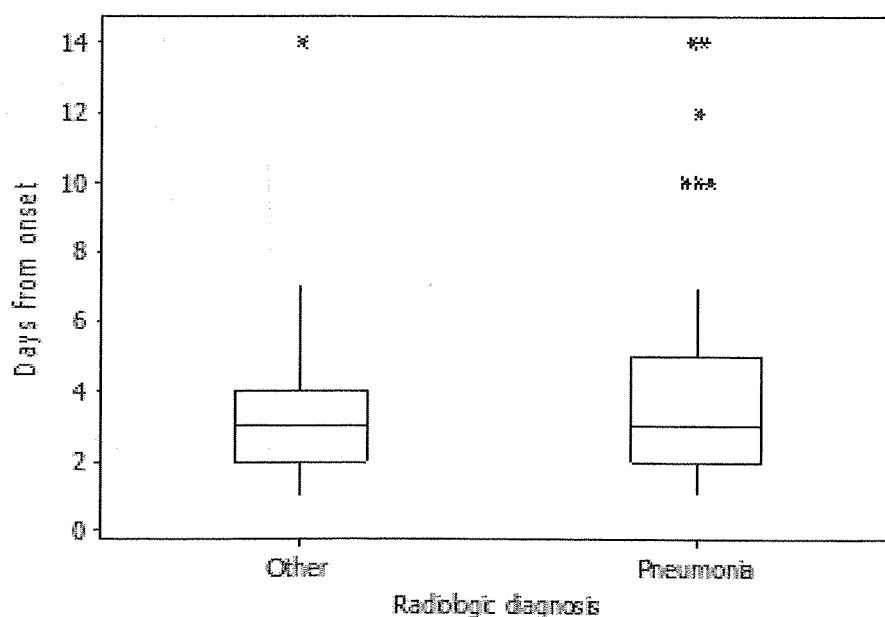
Visceral leishmaniasis	1	(0.5)	
Paralysis	1	(0.5)	
Parkinson	1	(0.5)	
Mental retardation	1	(0.5)	
Allergic rhinitis	1	(0.5)	
Renal transplant	1	(0.5)	
<b>Radiologic diagnosis n (%)</b>			<b>&lt;0.01</b>
Bilateral bronchopneumonia	32	(17.6)	
Bilateral tracheitis	12	(6.6)	
Tracheobronchitis	8	(4.4)	
Pulmonary congestion	4	(2.2)	
Pleuritis	3	(1.6)	
<b>Treatment n (%)</b>			
Oseltamivir & antibiotics	100	(54.9)	<b>&lt;0.01</b>
Antibiotics	81	(44.5)	
Non-invasive O <sub>2</sub> ventilation	37	(20.3)	

The radiologic examination revealed bilateral bronchopneumonia in 32 patients (17.6%), bilateral tracheitis in 12 patients (6.6%), tracheobronchitis in 8 patients (4.4%), pulmonary congestion in 4 patients (2.2%) and pleuritis in 3 patients (1.6%).

The proportion of patients with bronchopneumonia was significantly higher compared to other radiologic findings,  $\chi^2=47.5$   $p<0.01$ . The mean time of disease

onset of patients with pneumonia was 4.2 days ( $SD\pm 2.8$ ) which was significantly higher compared to 2.9 days ( $SD\pm 1.9$ ),  $t=-3.3$ ,  $p<0.01$ .

Also, a significant correlation was found between the time of disease onset and radiologic diagnosis of pneumonia,  $\rho=2.6$ ,  $p<0.01$ . Patients who presented early at disease onset did not develop severe disease (Figure nr1).



**Figure nr.1. Time from disease onset and radiologic findings**

Out of patients admitted, 61 patients (33.5%) of them were presented with underlying condition. Pneumopathy was the most frequent co-morbidity in 15 patients (8.2%), followed by Arterial Hypertension in 9 patients (4.9%), cardiopathy in 7 patients (3.8%) and 6 patients (3.3%) were pregnant,  $\chi^2=69.7$   $p<0.01$ . Anaemia, diabetes, chronic atria fibrillation and acute renal failure were

each of them found in 3 patients (1.6%) respectively, followed by rheumatoid arthritis and epilepsy in 2 patients (1.1%) respectively. The mean age of patients with underlying condition was 43.9 years ( $SD\pm 17.3$ ) which was significantly higher compared to the mean age 43.9 years ( $SD\pm 17.3$ ) of other patients,  $t=5.5$ ,  $p<0.01$  (Figure nr.2).

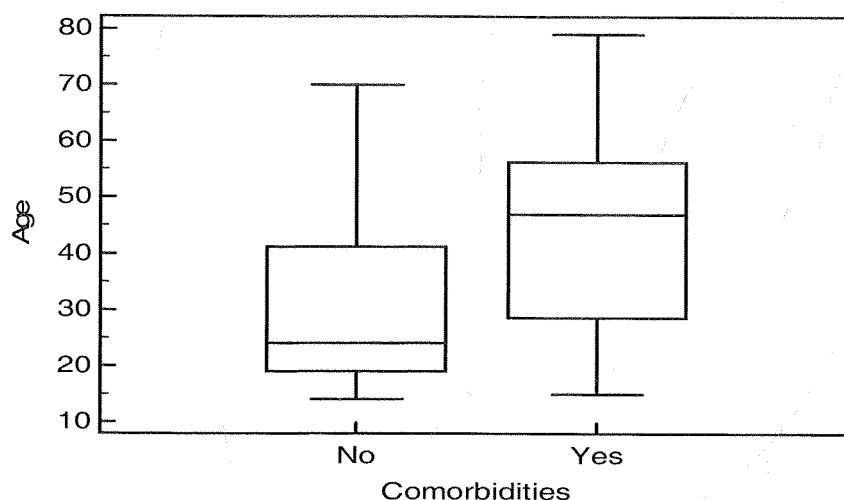


Figure nr.2. The mean age of patients with regard to co-morbidities

The mean time of hospitalization was 6.5 days ( $SD\pm 3.7$ ), range 1-26 days.

The mean duration of hospitalization among patients presented with co-morbidities was 7.9 days ( $SD\pm 4.9$ ) which was significantly higher compared to patients without co-morbidities with a mean of 5.8 days ( $SD\pm 2.8$ ),  $t=3.5$   $p<0.01$ . Oseltamivir and antibiotics were used for the treatment of influenza patients. Antibiotics were used for the treatment of physician-diagnosed complications and also for their prevention. 100 of patients (55%) received oseltamivir

and antibiotics while 81 patients (44.5%) received only antibiotics. Estimates of the difference in median time of alleviation of all influenza symptoms in regard the treatment choice were obtained from the Kaplan-Meier curves. The efficacy endpoint was the time to resolution of illness including mild/absent cough and coryza mild/absent, return to normal activity. Patients who received oseltamivir had a significant reduction in the median duration of symptoms such as fever, cough and coryza than did the untreated patients (Log-rank = 4.2,  $p=0.04$  (Figure nr.3).

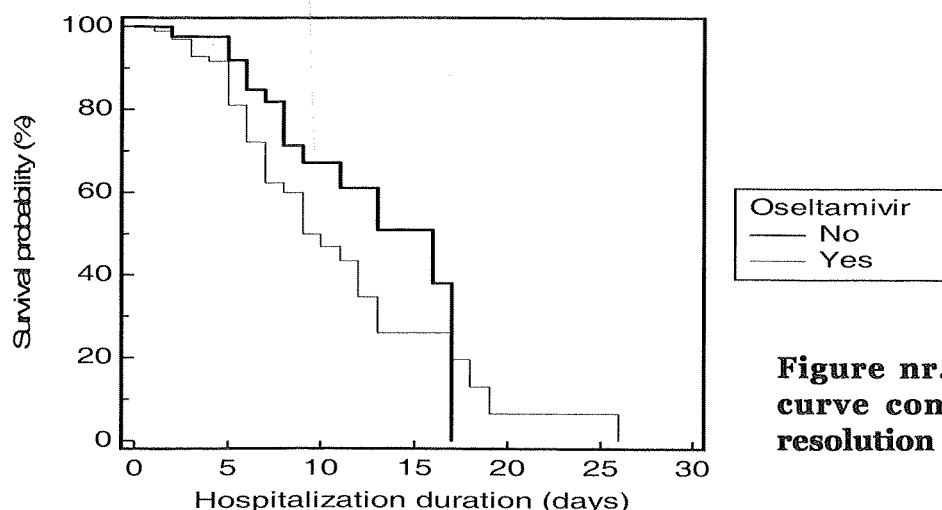


Figure nr.3. Kaplan-Meier curve comparing times to resolution of illness

The mean O<sub>2</sub> saturation was 0.93 (SD± 0.06) range 0.70 – 0.99. Non-invasive ventilation with oxygen was used in 37 patients (20.3%).

### Discussion

Because influenza infections are an important cause of illness during the winter months and increase the burden of the primary health care provider, attempts at both prevention and treatment would be of significant value to the health care system (22). To this end oseltamivir therapy significantly improved outcome. In particular, our results underscore the impact of admission delays and underlying medical conditions within the last 12 months in increasing the risk and the time of hospitalization (23,24).

Treatment with oseltamivir adults (75 mg twice a day) shortened the duration of hospitalization and severity of symptoms, such as cough or coryza, and caused a rapid decline in viral shedding (25). Oseltamivir treatment was well-tolerated and no adverse events were reported during treatment.

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