doi • 10.5578/tt.66122
Tuberk Toraks 2018;66(2):144-149
Geliş Tarihi/Received: 22.11.2017 • Kabul Ediliş Tarihi/Accepted: 01.05.2018

KLİNİK ÇALIŞMA
RESEARCH ARTICLE

Clinical, radiological and prognostic features of influenza cases in the influenza epidemic during years 2016-2017

Özlem ERÇEN DİKEN[1]
Sertaç ARSLAN[1]
Özlem AKDOĞAN[2]
Derya YAPAR[2]
Özgür ÜNAL[2]
Emre DEMİR[3]
Nurcan BAYKAM[2]

[1] Department of Chest Diseases, Faculty of Medicine, Hitit University, Corum, Turkey
[1] *Hitit Üniversitesi Tıp Fakültesi, Göğüs Hastalıkları Anabilim Dalı, Çorum, Türkiye*
[2] Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Hitit University, Corum, Turkey
[2] *Hitit Üniversitesi Tıp Fakültesi, İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı, Çorum, Türkiye*
[3] Department of Biostatistics, Faculty of Medicine, Hitit University, Corum, Turkey
[3] *Hitit Üniversitesi Tıp Fakültesi, Biyoistatistik Anabilim Dalı, Çorum, Türkiye*

SUMMARY

Clinical, radiological and prognostic features of influenza cases in the influenza epidemic during years 2016-2017

Introduction: *Influenza subtypes vary by clinical, radiological, and prognostic courses and may go along with viral pneumonia. We aimed to identify clinical, radiological, and prognostic aspects of influenza epidemic during years 2016-2017.*

Materials and Methods: *Influenza cases reported to the Public Health Directorate in our city was assessed retrospectively. Clinical, radiological, and prognostic parameters were compared based on influenza subtypes.*

Results: *We analyzed samples from 197 cases with suspected influenza. Mean age of the subjects was 51.17 ± 26.74. We found influenza A/H1N1, influenza A/H3N2, and influenza B in 59 (30.0%), 29 (14.7%), and 3 (1.5%) cases, respectively. Comorbidity was present in 48 (24.4%) cases. Most common radiological finding was interstitial pattern. Seventy-one and 79 per cent of H1N1 and H3N2 cases were influenza pneumonia, respectively. The prevalence of overall mortality was 5.5% with a predominance in H1N1 over H3N2. Influenza vaccination had been performed in 6.8% and 3.4% of H1N1 and H3N2 cases, respectively. We detected no mortality in any vaccinated patient. We identified 6 pregnant women, 2 of which ended up with preterm birth, and another one with abortion.*

Conclusion: *Often manifested as lower respiratory tract infection, influenza may cause epidemics with increased mortality rate. Influenza should be suspected when interstitial pattern was seen on radiological images. H1N1 cases course worse. Since the prognosis is better in vaccinated patients, seasonal influenza vaccination among the community needs to be elevated. In addition, protective measures like vaccination should be taken in pregnancy to avoid preterm delivery or abortion.*

Key words: *H1N1; H3N2; influenza; influenza epidemic*

Yazışma Adresi (Address for Correspondence)

Dr. Özlem ERÇEN DİKEN
Hitit Üniversitesi Tıp Fakültesi, Göğüs Hastalıkları Anabilim Dalı, ÇORUM - TÜRKİYE
e-mail: oercen@hotmail.com

ÖZET

İnfluenza olgularının 2016-2017 yılı salgınında klinik, radyolojik ve prognostik özellikleri

Giriş: *İnfluenza subtiplerine göre farklı klinik, radyolojik ve prognostic seyir gösterebilir ve viral pnömoni ile seyredebilir. Amacımız, 2016-2017 yılları influenza salgınını subtiplerine göre klinik, radyolojik ve prognostic olarak incelemekti.*

Materyal ve Metod: *İlimizde halk sağlığı müdürlüğüne bildirilen olgular retrospektif olarak incelenmiştir. Klinik, radyolojik ve prognostik parametreler influenza subtiplerine göre istatistiksel olarak karşılaştırılmıştır.*

Bulgular: *İnfluenza şüphesi ile 197 olgudan örnek gönderilmişti. Yaşları 51.17 ± 26.74 idi. Olguların 59 (%29.9)'unda influenza A/H1N1, 29 (%14.7)'unda influenza A/H3N2, 3 (%1.5)'ünde influenza B mevcuttu. Kırk sekiz (%24.4) olguda ek hastalık vardı. Mikronodüler görünüm en sık radyolojik bulguydu. H1N1 olgularının %71'i, H3N2 olgularının %79'u influenza pnömonisiydi. Mortalite %5.5'di ve H1N1 olgularında H3N2'ye göre daha fazlaydı. H1N1 olgularının %6.8'i, H3N2 olgularının %3.4'ü influenza aşısı yaptırmıştı. Aşı yaptıranların hiçbirinde mortalite gözlenmedi. Altı gebe olgumuz mevcuttu ve gebeliğin 2'si erken doğum, 1'i abortusla sonlandı.*

Sonuç: *İnfluenza, sıklıkla alt solunum yolu hastalığı olarak seyreden, mortalite oranı yüksek salgınlara neden olabilen bir etkendir. Radyolojik olarak mikronodüler görünüm saptandığında influenzadan şüphelenilmelidir. H1N1 olguları daha kötü seyirlidir. Aşı yaptıranlarda prognoz daha iyi seyrettiği için, toplumda mevsimsel influenza aşılaması arttırılmalıdır. Gebelikte erken doğum ve abortusla seyredebileceğinden aşılama vb. koruyucu önlemler alınmalıdır.*

Anahtar kelimeler: *H1N1; H3N2; influenza, influenza salgını*

INTRODUCTION

Influenza is a virus that causes mortality and morbidity, and one of its leading complications is pneumonia. Influenza A and B rather lead to morbidity in human. Influenza A is often responsible for seasonal epidemics and pandemics. Pandemic influenza data showed variations among its subtypes in terms of clinical features, morbidity, and mortality (1,2). Globally, the virus has three predominant subtypes, influenza A/H1N1, influenza A/H3N2, and influenza B (3).

Rate of pneumonia and mortality was found to be higher when predominating subtype was H3N2. Although H1N1 subtype is usually more seriously associated with prognosis, frequency of complications and mortality vary among different patient populations (4).

In Turkey, the season of influenza is between November and March, when sudden onset of respiratory symptoms should make one suspect influenza. In 2009, pandemic influenza (H1N1) occurred and many countries reported disease characteristics. Some studies also examined clinical and radiological features of patients with H1N1 subtype in our country (5). However, differences regarding clinical, radiological, and prognostic course among influenza subtypes are not clearly elucidated (6).

In our study, we aimed to examine clinical, radiological, and prognostic characteristics of influenza subtypes.

MATERIALS and METHODS

Medical records of years 2016-2017 was accessed through Communicable Disease Unit of Corum Public Health Directorate. Most of 197 samples came from tertiary hospitals. Other cases included 24 samples from 2 private hospitals, 9 samples from regional chest diseases hospital, and 2 samples from district state hospital. We examined records of those cases that we, as the tertiary center, had sent to the Directorate. Approval for use of data was obtained from General Secretariat of Hitit University Training and Research Hospital. Examined parameters of cases included demographic data, influenza subtypes, symptoms and signs, radiological images on chest X-Ray (consolidation, interstitial pattern, and micronodular appearance), need for intensive care, hospitalization, stay at intensive care unit, and mortality. All data were entered into SPSS for statistical analysis. Comparisons were made between influenza subtypes, and regarded as statistically significant if p value was below 0.05.

RESULTS

Samples came from 197 suspected influenza cases, 106 (53.8%) of which were women. Mean age of the subjects was 51.17 ± 26.74. We found influenza A/H1N1, influenza A/H3N2, and influenza B in 59 (30.0%), 29 (14.7%), and 3 (1.5%) cases, respectively (Table 1). Comorbidity was present in 48 (24.4%) cases as following: diabetes mellitus (DM) in 17 patients (8.6%), hypertension (HT) in 20 patients (10.2%), heart failure in 3 patients (1.5%), renal failure in 8 patients (4.1%), chronic obstructive pulmonary disease (COPD) in 11 patients (5.6%), and asthma in 7 patients (3.6%).

While mean length of hospital stay (LOS) was 6.92 ± 4.50 days in patients with comorbid conditions, it was 7.25 ± 5.50 days in patients without (p= 1.000).

Table 1. Influenza groups

	n	%
H1N1	59	29.9
H3N2	29	14.7
hMPV	1	0.5
Influenza B	3	1.5
Negative	103	52.3
Inappropriate sample	2	1.0
Total	197	100.0

hMPV: Human metapneumovirus.

Mean LOS was 5.25 ± 2.22 days in cases with underlying pulmonary disease like COPD or asthma. While mean LOS was 6 ± 2 days in cases with history of COPD (p= 0.844), it was 3.5 ± 0.7 days in patients with history of asthma (p= 0.181). Mean LOS was 7.43 ± 5.22 days in patients without history of COPD or asthma. In patients with and without history of DM, mean LOS was 6.33 ± 3.22 and 7.18 ± 5.13 days, respectively. It was 7.67 ± 7.23 and 7.00 ± 4.73 days in patients with and without history of HT, respectively. Mean LOS was 5 ± 0 days in patients with heart failure compared with 7.26 ± 5.07 days in those with no heart failure.

Mortality was 6.2% (n= 3) in patients with comorbid conditions, whereas it was 6.0% (n= 9) in patients with no comorbidity (p= 1.000). While no mortality occurred in patients with COPD or asthma, it was seen in 12 (6.6%) patients with no COPD or asthma (p= 0.604). Mortality was seen 5.9% (n= 1) and 6.1% (n= 11) of the patients with and without DM, respectively (p= 1.000). One patient with HT (5.0%) had died of influenza versus 11 patients (6.2%) with no HT (p= 1.000). While mortality was seen in all patients with heart failure (n= 3), it was 4.6% (n= 9) in those with no heart failure (p< 0.001).

Six samples had come from pregnant cases, 5 of which were in last trimester. Two of these ended up with premature birth and one with abortion. No growth was detected in a sample of pregnant cases. Remaining samples indicated four H1N1 (80%) and one H3N2 (20%) subtypes (p= 0.661).

Eight of cases (4.1%) were asymptomatic. Most common symptom was cough (66.5%), followed by dyspnea (46.7%) and fever (43.7%). Other symptoms and signs at presentation included respiratory distress, malaise, myalgia, headache, renal failure, sore throat, tachypnea. Mean duration elapsed from symptoms till presentation was 2.45 ± 1.92 days, which was 2.53 ± 2.37 days and 2.56 ± 1.24 days for H1N1 and H3N2 subtypes, respectively.

Symptoms and signs were compared in terms of H1N1 and H3N2 subtypes. Accordingly, while cough, dyspnea, and fever was seen in 40, 32, and 27 of H1N1 cases, it was seen 22, 8, and 12 of H3N2 cases. Most common symptom in both influenza subtypes was cough (p= 0.190). On auscultation, rales and rhonchi were present in 41 and 12 of H1N1 cases compared with 16 and 3 of H3N2 cases. Most common sign in both influenza groups was rale (p= 0.730), (Table 2).

Among patients with radiological images, interstitial pattern was the most common finding, as observed in 41.5% of 41 H1N1 cases (n= 17) and 42.9% of 28 H3N2 cases (n= 12), (p< 0.001 and p< 0.024, respectively). Radiological findings were bilateral in 73.2% (n= 30) and 57.1% (n= 16) of H1N1 and H3N2 cases, respectively (p= 0.165), (Table 3).

Radiological involvement was detected in 29 (71%) and 22 (79%) patients with H1N1 and H3N2, which were regarded as influenza pneumonia. No radiological finding was present in 41 cases who had images (25%).

Table 2. Symptoms and signs by influenza groups

Symptoms	H1N1 n (%)	H3N2 n (%)
Fever	27 (45.8)	12 (41.4)
Malaise	27 (45.8)	8 (27.6)
Myalgia	17 (28.8)	8 (27.6)
Headache	13 (22)	5 (17.2)
Sore throat	17 (28.8)	2 (6.9)
Cough	40 (67.8)	22 (75.9)
Sputum	5 (8.5)	3 (10.3)
Dyspnea	32 (54.2)	8 (27.6)
Nasal discharge	1 (1.7)	3 (10.3)
SIGNS		
Rales	41 (69.5)	16 (55.2)
Rhonchi	12 (41.4)	3 (33.3)
Hyperemic pharynx	6 (22.2)	3 (33.3)

Table 3. Radiological findings in influenza groups

	Radiological finding		
	Consolidation	**Micronodular appearance**	**Interstitial pattern**
H1N1 (n= 41)	11 (26.2%)	1 (10.0%)	17 (24.6)
H3N2 (n= 28)	7 (16.7%)	3 (30.0%)	12 (17.4)
Influenza B (n= 3)	1 (2.4%)	0 (0.0%)	0 (0%)
Negative result (n= 90)	23 (54.8%)	6 (60.0%)	40 (58.0%)
p value	0.79	0.29	0.71
Total* (n= 162)	42 (100%)	10 (100%)	69 (100%)

* Out of 162 cases in total with available radiologic images, 41 cases (25%) had no radiological finding.

One hundred and ninety-four cases were hospitalized with a mean LOS of 7.08 ± 4.90 days. It was 7.11 ± 5.37 days and 7.00 ± 3.35 days in H1N1 and H3N2 cases, respectively (p= 0.514). Fifty-seven cases (26.1%) were monitored in intensive care unit, where 14 patients (6.4%) required mechanical ventilation. The need for invasive mechanical ventilation was detected in 15.3% (n= 9) and 3.6% (n= 1) of H1N1 and H3N2 cases, respectively (p= 0.158). Though not documented by growth, secondary bacterial infection was seen in 12 patients (5.5%). Fifteen cases (6.9%) developed acute respiratory distress syndrome (ARDS). Seven patients (3.2%) had influenza vaccination during current season, which was 4 (6.8%) and 1 (3.4%) among H1N1 and H3N2 cases, respectively. Mortality did not occur in patients who had been vaccinated. Overall, mortality was seen in 12 cases (5.5%), five of which had negative results. Mean age of the mortal cases and survivors did not differ significantly (p= 0.090). There was no association between mortality and gender (p= 0.746), consolidation (p= 681), nodular infiltration (p= 1.000), and interstitial involvement (p= 1.000). Mortality was significantly higher in H1N1 cases (13.6%, n= 8) compared with that in H3N2 cases (0%, n=0), (p= 0.049). Only 33 patients (16.8%) had records of antiviral treatment, which was initiated before and after 48 hours of symptoms' onset in 23 cases (11.7%) and 10 cases (5.1%), respectively. These two groups of initiation did not differ in terms of mortality (n= 4, 17.4%; n= 0, 0.0%; p= 0.29).

DISCUSSION

In our study, 30.0% and 14.7% of our cases had H1N1 and H3N2 subtypes, respectively. The most common radiological finding was interstitial pattern. Influenza pneumonia was confirmed in 71% of H1N1 and 79% of H3N2 cases. Higher in H1N1 cases, mortality was found as 5.5% overall. The percentages of cases with influenza vaccination constituted 6.8% of H1N1 and 3.4% of H3N2 cases. No patients with vaccination developed mortality.

A study with 97 patients reported mean age of cases with H1N1 subtypes to be lower than that with other subtypes (3). In our study, we did not detect age-difference between H1N1 and H3N2 subtypes. Influenza B subtype was present only in three cases, where no comparisons could be made. In the study by Ishiguro et al., 49% of patients had underlying pulmonary disease. They reported presence of at least one pulmonary disease in 61.8% of H3N2 cases and 25% of H1N1 cases. COPD was present 17.7%, 29.4% and 5% of all, H3N2, and H1N1 cases, respectively (3). In our study, 5.6% of our cases had COPD and 3.6% patients had asthma. Underlying pulmonary disease in the present study was lower than that reported by Ishiguro et al. Mean LOS and mortality was also not different in terms of presence of any underlying pulmonary disease. However, this should be carefully interpreted due to small numbers of patients within the groups.

Respiratory diseases induced by influenza had a critical hospitalization burden, which occurred in 194 of 197 cases in our study (7). Respiratory diseases have varying presentations, ranging from mild to severe or upper to lower tract involvements. In our study, lower respiratory tract disease was more frequently seen. Most common symptom and sign was cough and rales. These diseases may manifest as increased rates of cardiovascular events in adults. Attention should be sought in patients with underlying cardiac disease (8). Prognosis was worse in our cases with history of cardiac disease.

While in 20.8% of patients, antiviral treatment was begun before 48 hours of symptom's onset in the study by Ishiguro et al., it was initiated after 48 hours in 49% of patients (3). Only 16.8% of our patients had antiviral treatment, which was started before and after 48 hours in 11.7% and 5.1% of cases, respectively. These two groups did not differ in terms of mortality. The study by Ishiguro et al. reported respiratory failure in 51% of cases, with 45% in H1N1 and 58.8% in H3N2 cases. They observed need for mechanical ventilation in 7.3% of patients, with 10% in H1N1 and 8.8% in H3N2 cases (3). In our study, 6.4% of patients needed mechanical ventilation, which was similar to that reported by Ishiguro et al. Invasive mechanical ventilation was required in 15.3% of H1N1 and 3.6% of H3N2 cases, which suggests a more severe course in the former. Overall mortality reported by the study of Ishiguro et al. was 4.2% (3). A recent multi-center Turkish study reported mortality rate to be 12.2%, which was higher than that of our cases (9).

Ishiguro et al. reported the prevalence of consolidation sign in pneumonia cases as 79.2%, 60%, and 91.2% of all, H1N1 and H3N2 cases, respectively. In addition, they observed nodular appearance in 58.3% of patients overall, with 60% of H1N1 and 64.7% of H3N2 cases (3). While consolidation was rather more frequent in H3N2 cases, interstitial pattern was the most common radiological finding in our study, detected in 48.6% of H1N1 and 44.4% of H3N2 patients.

Presently, primary viral pneumonia in seasonal influenza is considered to be rare, although several groups have reported high rates of primary viral pneumonia in H1N1 (10). For instance, Perez-Padilla et al. reported primary viral pneumonia in all 18 of their cases (100%), Champunot et al. in 92%, and Cui et al. in 84% (11-13). In our study, viral pneumonia was present in 71% of H1N1 and 79% of H3N2 cases.

Oliveira et al. investigated the computed tomography (CT) findings of seasonal (H3N2, H1N1, and B) influenza and reported that bilateral diffuse interstitial/alveolar infiltrates were the most commonly observed radiographic abnormality (9 patients, 52%), followed by right lower lobe consolidation in 6 (35%) patients (14). In our study, radiological involvement was rather bilateral in both H1N1 and H3N2 subtypes, albeit statistically not significant. Interstitial pattern was most frequent.

In H1N1 pandemics of 2009, a multicenter study from Turkey assessed 264 patients and reported the most common risk factor to be comorbidity as 52%, which was higher than that we found in our study (24.4%) (5).

Okur et al. retrospectively examined characteristics of 36 pandemic influenza A (H1N1) patients and reported consolidation and interstitial alterations as the most commonly observed radiological abnormalities. They also reported mortality as 23.1% in patients with underlying diseases (15). In the present study, mortality rate was 6.2% in patients with comorbidity, which was not different than that in patients with no underlying disease. In our study, most common radiological finding was interstitial pattern.

Antiviral treatment is recommended for those having confirmed laboratory results with a high risk of complications. Oseltamivir 75 mg oral twice daily is indicated for five days. It may be administered as 150 mg twice daily for severe cases. Initiation of therapy within 48 hours of onset of symptoms was shown to improve prognosis (5). Zanamivir 10 mg twice daily by inhalation, for five days is indicated in patients with renal failure or pregnancy. Our cases only had oseltamivir as antiviral therapy. No patient received zanamivir.

In patients presenting with pneumonia, it may be difficult to differentiate viral pneumonia from bacterial pneumonia. In addition, there is possibility that a bacterial superinfection after 3-5 days may be added onto the viral pneumonia. Common infectious agents responsible for bacterial pneumonia include *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Staphylococcus aureus*. A combined use of antiviral and antibacterial medications is recommended for the management of community-acquired pneumonia or bacterial superinfections during or after influenza (16). Although we did not have records regarding site or culture results of secondary bacterial infection, it was detected 5.5% of our cases.

Our study has some limitations. Since it included past medical records just from reported cases, we could access laboratory data of only few patients and could not compare them. Another limitation is that radiological data belongs only one center, with no data from 2 private hospitals, 1 district state hospital, and regional chest diseases hospital. Nevertheless, cases from our tertiary center constituted 82% of all

cases. Our hospital has the highest number of patient visits in our study. Current study was performed just in a single province. A future nationwide study that will examine clinical and radiological appearance and frequency of pneumonia by influenza viruses would obviously produce more valuable results. Detection of no association between underlying pulmonary disease and mortality may be attributed to low number of patients to compare. Mortality was significantly higher in patients with heart failure compared with that in patients with no heart failure, yet it occurred only in three patients, which could overestimate the significance. As we have sufficient number of cases compared to the published literature, we believe that our results are remarkable.

In conclusion, viral pneumonia should be suspected in those with interstitial pattern on radiological images. In our study, the prognosis was not worse in patients having underlying pulmonary or any comorbid diseases. The disease course was worse in H1N1 subtype than in H3N2 subtype. Influenza cases frequently required hospitalization with high mortality. Absence of mortality in all vaccinated patients emphasized importance influenza vaccination. Lack of association between age and mortality indicated requirement of seasonal influenza vaccination at every age. It may be associated with abortion or premature birth if occurs during pregnancy.

REFERENCES

1. *Çiftçi E, Tuygun N, Özdemir H, Tezer H, Şensoy G, Devrim İ, et al. Clinical and epidemiological features of Turkish children with 2009 pandemic influenza A (H1N1) infection: experience from multiple tertiary paediatric centres in Turkey. Scand J Infect Dis 2011;43:923-9.*
2. *Thompson WW, Comanor L, Shay DK. Epidemiology of seasonal influenza: use of surveillance data and statistical models to estimate the burden of disease. J Infect Dis 2006;194:82-91.*
3. *Ishiguro T, Takayanagi N, Kanauchi T, Uozumi R, Kawate E, Takaku Y, et al. Clinical and radiographic comparison of influenza virus-associated pneumonia among three viral subtypes. Intern Med 2016;55:731-7.*
4. *Huang SS, Banner D, Fang Y, Ng DC, Kanagasabai T, Kelvin DJ, et al. Comparative analyses of pandemic H1N1 and seasonal H1N1, H3N2, and influenza B infections depict distinct clinical pictures in ferrets. PLoS One 2011;6:e27512.*
5. *Hacımustafaoğlu M. Pandemic H1N1 influenza infections in 2009. Turk Arch Ped 2010;45:31-6.*
6. *Ramirez A, Capuano AW, Wellman DA, Lesher KA, Setterquist SF, Gray GC. Preventing zoonotic influenza virus infection. Emerg Infect Dis 2006;12:996-1000.*
7. *Thompson WW, Shay DK, Weintraub E, Brammer L, Bridges CB, Cox NJ, et al. Influenza-associated hospitalizations in the United States. JAMA 2004;292:1333-40.*
8. *Fleming DM, Cross KW, Pannell RS. Influenza and its relationship to circulatory disorders. Epidemiol Infect 2005;133:255-62.*
9. *Özışık L, Durusu Tanrıöver M, Çıblak Akçay M, Yuntçu K, Ünal S, Badur S, et al. Mortality related factors in patients requiring hospitalization for influenza like illness. Mikrobiyol Bul 2017;51:20-31.*
10. *Treanor JJ. Influenza viruses, including avian influenza and swine influenza. In: Mandell GL, Douglas R, Bennett JE (eds). Principles and Practice of Infectious Diseases. 7th ed. Philadelphia: Churchill Livingstone, 2010:2265-89.*
11. *Perez-Padilla R, de la Rosa-Zamboni D, Ponce de Leon S, Hernandez M, Quiñones-Falconi F, Bautista E, et al. Pneumonia and respiratory failure from swine-origin influenza A (H1N1) in Mexico. N Engl J Med 2009; 361:680-9.*
12. *Champunot R, Tanjatham S, Kerdsin A, Puangpatra P, Wangsai S, Treebuphachatsakul P, et al. Impact of pandemic influenza (H1N1) virus-associated community-acquired pneumonia among adults in a tertiary hospital in Thailand. Jpn J Infect Dis 2010;63:251-6.*
13. *Cui W, Zhao H, Lu X, Wen Y, Zhou Y, Deng B, et al. Factors associated with death in hospitalized pneumonia patients with 2009 H1N1 influenza in Shenyang, China. BMC Infect Dis 2010;10:145.*
14. *Oliveira EC, Marik PE, Colice G. Influenza pneumonia: a descriptive study. Chest 2001;119:1717-23.*
15. *Okur M, Erbey F, Yazicioglu O, Celik A, Tukenmez B, Sunnetcioglu M, et al. H1N1 influenza A virus related pneumonia and respiratory failure. Indian J Virol 2013;24:85-89.*
16. *Jain S, Kamimoto L, Bramley AM, et Schmitz AM, Benoit SR, Louie J, et al. Hospitalized patients with 2009 H1N1 influenza in the United States, April-June 2009. N Engl J Med 2009;361:1935-44.*