Pneumonia in patients with novel influenza A (H1N1) virus in Southeastern Turkey

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swine, human, avian, and Eurasian swine genetic components, which combine to form a single influenza virus [1]. The first human infections with the new swine-origin influenza A virus (S-OIV) were confirmed in April 2009 in Mexico and the United States. Since then, Turkey and several other countries experienced outbreaks of respiratory illness caused by S-OIV. On 11 June 2009, WHO announced a global 2009 influenza pandemic [2]. On 16 May 2009, the first infection by S-OIV in Turkey was reported. Outbreak spread throughout the country during the winter wave; the first death due to S-OIV infection in Turkey occurred on 24 October 2009.

Previous studies have reported that a prominent clinical feature of S-OIV infection is severe pneumonia [3–5]. In this report, we aim to describe the clinical characteristics and the radiological and laboratory findings of patients with H1N1 virus pneumonia who lived in the southeastern region of Turkey. Attempts to define specific clinical or laboratory parameters to distinguish S-OIV from other types of pneumonia might facilitate early suspicion of S-OIV infection.

Methods

This study was performed at Şanlıurfa Education and Research Hospital, which is located in the southeastern region of Turkey. We retrospectively reviewed medical charts and radiological and laboratory findings of the patients who were followed up at the hospital between 27 October 2009 and 26 December 2009. We enrolled all hospitalised patients with pneumonia for whom nasopharyngeal swab specimens were collected due to suspected S-OIV infection. We separated the patients into two groups. In the positive group, 33 patients had laboratory-confirmed S-OIV infection. Twenty-three patients without an S-OIV infection (confirmed by laboratory tests) were used to document the differences between the patients with or without S-OIV infection.

Microbiological studies

Nasopharyngeal swab specimens were collected upon admission and kept at a temperature ranging from 4 to 8°C. Specimens were sent to a Turkish government health ministry laboratory centre called “Refik Saydam Hıfsızsıhha Center Presidency” (RSHCP). Specimens were tested using real-time reverse-transcriptase-polymerase-chain-reaction (rRT-PCR), in accordance with the guidelines provided by the WHO. At the national influenza centre of RSHCP, diagnosis of influenza and viruses-forming influenza-like illness was achieved using primers and probe sequence provided by the U.S. Centers for Disease Control (CDC) [6].

Statistical analysis

Data analysis was conducted using SPSS 11.5 statistical software. Continuous variables were summarised as means (± SD) or medians (with interquartile ranges). A P value of less than 0.05 was considered statistically significant. Mann–Whitney U-test, Chi-square test, or Fisher’s exact test was used as appropriate. All values were two-sided.

Results

Demographic characteristics of the patients with S-OIV infection are shown in Table 1. The minimum and maximum ages of the positive group were 13 and 70 years, respectively, with a median age of 30 years. The median age of the negative group was 34 years, with a range of 15–80 years; 57.6% of the positive group and 69.6% of the negative group had no comorbidities. In the positive group, 9 of 33 patients had pulmonary disease, such as chronic obstructive pulmonary disease (COPD) or asthma, 3 patients were pregnant, 2 patients had type 2 diabetes mellitus and 1 patient was postpartum. Other comorbidities in the positive group were Down syndrome (n = 1), hypertension (n = 1) and congestive heart failure (n = 1). There were no pregnant or postpartum patients in the negative group, and 4 of 23 patients had pulmonary disease, such as chronic obstructive pulmonary disease (COPD) or asthma.

Fourteen patients (42.4%) in the positive group and 8 patients (34.8%) in the negative group were followed up in the intensive care unit (ICU). The duration of hospital stay was 6.42 ± 4.56 days in the positive group and 6.0 ± 6.0 days in the negative group. The duration of symptoms onset to admission was 43 ± 2.31 days in the positive group and 4.3 ± 2.31 days in the negative group.

Table 1. Characteristics of the patients with pneumonia who had S-OIV infection

| Variable                          | Value                        |
|-----------------------------------|------------------------------|
| Gender – no (%)                   | Male 20 (60.6) Female 13 (39.4) |
| Age – year                        | Median 30 Range 13–70        |
| Occupation – no (%)               | Housewife 12 (36.4) Unemployed 8 (24.2) Freelancer 5 (15.2) Farmer 4 (12.1) |
| Comorbidities – no (%)            | *14 (42.42)                  |
| Hospital stay – in days           | Mean 6.42 ± 4.56 Range 1–24  |
| ICU stay – in days                | Mean 6.0 ± 6.0 Range 1–24    |
| Duration of symptoms onset to admission – in days | Mean 43 ± 2.31 Range 2–10 |

*The number of patients who had at least one comorbidity.

Table 2. Comparison of the symptoms during admission in the positive group and negative groups

| Symptom     | Positive group n (%) | Negative group n (%) | p*   |
|-------------|----------------------|----------------------|------|
| Dyspnoea    | 32 (97.0)            | 17 (73.9)            | 0.015|
| Cough       | 31 (93.9)            | 22 (95.7)            | 1    |
| Sputum      | 25 (75.8)            | 19 (82.6)            | 0.743|
| Hemoptysis  | 6 (18.2)             | 2 (8.87)             | 0.449|
| Fever       | 32 (97.0)            | 20 (87.0)            | 0.295|
| Runny nose  | 17 (51.5)            | 9 (39.1)             | 0.361|
| Headache    | 26 (78.8)            | 18 (78.3)            | 0.962|
| Sore throat | 27 (81.8)            | 13 (56.5)            | 0.039|
| Myalgia     | 29 (87.9)            | 19 (82.6)            | 0.704|

*Pearson chi-squared test and Fisher’s exact test were performed.
stay (6.42 ± 4.56 days) and ICU stay (6.0 ± 6.0) in the positive group was lower than in the negative group (8.0 ± 5.50 days, 7.37 ± 7.55 days, respectively), but this difference was not statistically significant (p = 0.296 and 0.810, respectively).

A comparison of the symptoms between the groups during admission is shown in Table 2. The most common symptom was dyspnea in the positive group. Dyspnea and sore throat were more common in the positive group (p = 0.015 and 0.039, respectively).

In auscultation, crackles were identified in 63.6% (n = 21) of the positive group. 54.5% of the crackles were bilateral. Cyanosis and mental confusion were seen more frequently in the positive group (n = 11, 33.3% and n = 15, 45.5%, respectively) than in the negative group (n = 3, 13.0% and n = 7, 30.4%, respectively) but this difference was not statistically significant (p = 0.258 and 0.120, respectively). The mean highest body temperature during the hospital stay of the positive group (39.42 ± 0.70) was higher than that of the negative group (38.51 ± 1.05) (p = 0.001).

The frequency of mechanical ventilation (MV), Acute Respiratory Distress Syndrome (ARDS) and death was higher than in the negative group, but this difference was not statistically significant (p = 0.496, 1 and 0.172, respectively) (Table 3). Neither patients in the positive group with ARDS nor those who underwent MV survived.

### Laboratory results

A complete blood cell count was performed on all 33 patients and on the negative group. The results of the blood

### Table 3. Frequency of MV, ARDS and exitus in both groups

| Variable | Positive group n (%) | Negative group n (%) | p* |
|----------|----------------------|-----------------------|----|
| MV       | 8 (24.2)             | 3 (13.0)              | 0.496 |
| ARDS     | 7 (21.2)             | 4 (17.4)              | 1   |
| Exitus   | 8 (24.2)             | 2 (8.7)               | 0.172 |

*p* Fisher’s exact test was performed.

### Table 4. Laboratory findings of the patients with S-OIV infection and negative group*

| Variable                          | Positive group | Negative group | p** |
|-----------------------------------|----------------|----------------|-----|
| Hemoglobin                        |                |                |     |
| Mean value in patients with anemia| 10.96 ± 1.0    | 10.12 ± 1.49   | 0.562 |
| Anemia – no (%)                   | 11 (33.3)      | 6 (26.1)       |     |
| Leucocyte count                   |                |                |     |
| Mean count in patients with leucocytosis – cells/mm³ | 19,458 ± 14,132 | 17,433 ± 7,484 | 0.240 |
| Leucocytosis – no (%)             | 12 (36.4)      | 12 (52.2)      |     |
| Lymphocyte count                  |                |                |     |
| Mean count in patients with lymphopenia – cells/mm³ | 600.0 ± 299.8  | 600.0 ± 238.1  | 0.819 |
| Lymphopenia – no (%)              | 11 (33.3)      | 7 (30.4)       |     |
| Platelet count                    |                |                |     |
| Mean count in patients with thrombocytopenia – cells/mm³ | 108,285 ± 31,555 | 131,500 ± 20,506 | 0.007 |
| Thrombocytopenia – no (%)         | 14 (42.4)      | 2 (8.7)        |     |
| Alanine aminotransferase (ALT)    |                |                |     |
| Mean value in patients with elevated ALT – U/l | 99.4 ± 71.56   | 99.24 ± 29.90  | 0.190 |
| Elevated ALT – no (%)             | 5 (15.6)       | 7 (30.4)       |     |
| Aspartate aminotransferase (AST)  |                |                |     |
| Mean value in patients with elevated AST – U/l | 72.68 ± 52.37 | 90.69 ± 58.72  | 0.874 |
| Elevated AST – no (%)             | 16 (50)        | 11 (47.8)      |     |
| Gamma-glutamyl transpeptidase (GGT)|               |                |     |
| Mean value in patients with elevated GGT – U/l | 124.89 ± 61.27 | 113.49 ± 71.48 | 0.770 |
| Elevated GGT – no (%)             | 9 (31)         | 6 (27.3)       |     |
| Lactate dehydrogenase (LDH)       |                |                |     |
| Mean value in patients with elevated LDH – U/l | 649.68 ± 421.47 | 680.0 ± 325.97 | 0.019 |
| Elevated LDH – no (%)             | 28 (90.3)      | 13 (61.9)      |     |
| Creatine kinase (CK)              |                |                |     |
| Mean value in patients with elevated CK – U/l | 516.47 ± 409.84 | 586.28 ± 527.75 | 0.014 |
| Elevated CK – no (%)              | 15 (60)        | 5 (23.8)       |     |
| Serum creatinin                   |                |                |     |
| Mean value in patients with elevated serum creatinin – mg/dl | 1.77 ± 0.32    | –              | 0.504 |
| Elevated serum creatinin – no (%)| 2 (6.3)        | 0 (0)          |     |
| Blood urea                        |                |                |     |
| Mean value in patients with elevated blood urea – mg/dl | 68.88 ± 13.45 | 69.33 ± 11.72  | 1    |
| Elevated blood urea – no (%)      | 5 (15.6)       | 3 (13.0)       |     |
| C-reactive protein (CRP)          |                |                |     |
| Mean value in patients with positive CRP – mg/l | 17.65 ± 10.43  | 18.18 ± 10.72  |     |
| Positive CRP – no (%)             | 13 (61.9)      | 8 (50)         | 0.469 |

*p* Plus-minus values are means ± SD; **Pearson chi-squared test and Fisher’s exact test were performed.
cell count and other biochemical parameters are shown in Table 4. Thrombocytopenia, increased creatine kinase and elevated lactate dehydrogenase levels were observed in the patients with S-OIV infection ($p=0.007$, $0.014$ and $0.019$, respectively). The mean value of platelet count was $202.575 \pm 129.600$ and $283.608 \pm 133.290$ in the positive group and negative group, respectively ($p=0.002$). The mean value of creatine kinase and serum creatinin was higher in the positive group ($337.40 \pm 385.14$ and $0.82 \pm 0.31$, respectively) than in the negative group ($191.89 \pm 327.63$ and $0.67 \pm 0.19$, respectively) ($p=0.033$ and $0.026$, respectively).

The mean arterial PO$_2$ of the patients with S-OIV and the S-OIV negative group was $50.5 \pm 8.81$ ($n=11$) and $56.8 \pm 11.06$ ($n=6$), respectively ($p=0.262$). The mean pH of arterial blood was $7.34 \pm 0.06$ ($n=11$) and $7.34 \pm 0.18$ ($n=6$) in the positive group and negative group, respectively ($p=0.288$).

In 11 patients with S-OIV infection, bacterial cultures of sputum or bronchial aspirate samples were obtained during the hospital stay. Specimens were negative, with the exception of two samples, which were positive for Pseudomonas aeruginosa. Each of the blood specimen cultures taken from 10 patients was negative. Each of the blood specimen cultures, bronchial aspirate samples or bacterial cultures of sputum taken from 11 of 23 patients belonging to the negative group was also negative.

**Radiology**

All patients had opacities on a chest radiograph. Bilateral infiltration was seen more frequently in the patients with S-OIV infection ($n=19$, 57.6%) as compared to the negative group ($n=7$, 30.4%) ($p=0.044$). In 27.3% ($n=9$) of the positive group, bilateral expansive infiltration on upper, medial and lower zones was observed, but there were no patients in whom infiltration extended throughout the lung zones in the negative group ($p=0.007$). Pneumothorax and pleural effusion were seen in two different patients.

**Treatment**

All of the patients received oseltamivir upon admission, at a dose of 75 mg twice a day. Oseltamivir treatment was maintained for 5 days in the patients with S-OIV infection, but in the negative group, the duration of oseltamivir treatment was limited by the time required to obtain negative laboratory test results for S-OIV. After admission, 17 patients with S-OIV received ceftriaxone and others received ceftriaxone combined with other antibiotics (13 received clarithromycin, 1 received levofloxacine, 1 received moxifloxacin). Other initial treatments were imipenem or meropenem for 7 patients (one combined with vancomycin), moxifloxacin for 2 patients, piperacillin-tazobactam combined with ciprofloxacin for 2 patients, sulbactam-ampicillin for 2 patients, cefazolin sodium for 2 patients and sulbactam-cefoperazon for 1 patient. Additional antibiotics were prescribed for several patients, on the basis of their clinical course: four were given imipenem or meropenem (combined with vancomycin in two patients); one, piperacillin-tazobactam + vancomycin and one, sulbactam-cefoperazon + vancomycin.

**Discussion**

We describe the clinical, radiological and laboratory features of pneumonia that developed in the patients with S-OIV infection. The most common symptom was dyspnea. The mean peak body temperature during hospital stay amongst patients with S-OIV infection was higher than in the negative group ($p=0.001$). Thrombocytopenia, increased creatine kinase and elevated lactate dehydrogenase levels were observed in the patients with S-OIV infection. Bilateral infiltration was seen more frequently in the patients with S-OIV infection ($p=0.044$).

Swine influenza pneumonia was seen in 66% of hospitalised patients with S-OIV infection [7]. This number varied in some studies [3, 8–12], as did the number of hospitalised patients associated with patient characteristics.

All of the patients were living in the Şanlıurfa province of Turkey and were followed at Şanlıurfa Education and Research Hospital, located in the southeastern region of Turkey. The mean age of the patients with swine influenza pneumonia was lesser than the patients with community-acquired pneumonia. The frequency of comorbidity in the patients with swine influenza pneumonia was similar to that reported by Perez-Padilla et al. [4]. Most of the studies suggest that some younger and healthy people, especially middle-aged adults and pregnant women, were severely affected by S-OIV infection [3–5, 13–16]. One study showed that the new H1N1 virus causes pneumonia in ferrets, which is moderate in severity compared to that caused by seasonal H1N1 virus [17]. If we assume that the severity is the same as observed for patients admitted to the ICU in our study, there is no difference between healthy and comorbid patients with regard to severity. Extremes in age and multiple and debilitating underlying medical conditions might be contributing to the severity of illness in these patients.

Primary viral pneumonia is the most common finding in the patients with severe S-OIV infection [11]. The onset of swine influenza pneumonia is often abrupt. In adults with S-OIV, pneumonia presents as an influenza-like illness with a temperature higher than 39°C (102°F) accompanied by prominent myalgia [1]. The most consistent symptoms were cough, sore throat, sputum, dyspnea and fever that varied in different studies [4, 13, 18, 19]. In our study, dyspnea and sore throat were most common in swine influenza pneumonia.

The most consistent laboratory characteristics in our patients with S-OIV infection were thrombocytopenia, increased creatine kinase and elevated lactate dehydrogenase levels. Venkata et al. [20] demonstrated that thrombocytopenia was common in ICU patients. In the reports from Chile [21] and Italy [12], 20% and 27% of the patients with S-OIV had thrombocytopenia, respectively. More commonly reported in children, myositis associated with influenza A and B has been well documented and appears to occur most often during the convalescent phase of illness [22]. The elevation of lactate dehydrogenase and
Creatine kinase levels in swine influenza pneumonia is consistent with previous reports of pneumonia associated with S-OIV in Mexico, most likely due to myositis [4].

In our study, the mortality rate of swine influenza pneumonia (24.2%) was higher than in the negative group (8.7%), but this finding was not statistically significant ($p=0.172$). We do not currently know whether our patients had coinfection with other respiratory viruses. During the 1918 pandemic, a large number of deaths were associated with bacterial infection [23], but concurrent bacterial infection does not appear to be a major contributing factor to the severity of illness in our patients, possibly in part because most received antibiotics during hospitalisation. Delayed admission, delayed initiation of oseltamivir therapy and coinfection with other respiratory viruses could be contributing factors for death in our patients. Higher mortality rates and higher frequency of ARDS and MV as well as lower mean PO2 values in the patients with swine influenza pneumonia show that there was a tendency towards severe illness, as compared with community-acquired pneumonia.

In a study from California, 102 of 227 mechanically ventilated patients with S-OIV infection died [7]. In our study, the small number of mechanically ventilated patients may have skewed the results. In a report from Mexico, most deaths occurred in patients with S-OIV pneumonia who required MV on admission [4]. Another possible cause of high mortality amongst our patients who required MV could be that 8 of 8 patients had transitioned to MV on the first day of admission.

Perez-Padilla et al. [4] reported the clinical and epidemiological features of the first 18 patients with laboratory-confirmed S-OIV in Mexico. All 18 patients had radiologically confirmed pneumonia with bilateral patchy alveolar opacities (predominantly basal), affecting three or four lung quadrants in 11 patients. Bilateral infiltrates were seen in 66% (66/100) of the patients in a report from the United States [3], 94% (64/68) of the patients in a report from China [24] and 59% (10/17) of the patients in a report from Korea [25]. Prachi et al. [26] demonstrated that 71% (20/28) of the patients with S-OIV infection had bilateral involvement on chest radiograph. In this report, 93% of patients that required ICU admission had extensive disease involving ≥ 3 lung zones and all of them had bilateral opacities. Champunot et al. [13] reported that 79.2% (19/24) of the patients had multilobular or bilateral diffuse infiltrate on chest X-ray. The report from New Zealand showed that 48% of the patients had multi-lobar infiltrates [27]. One of the remarkable findings in our study was that 27% of the patients with swine influenza pneumonia had infiltration extending throughout the lung zone, whereas there was not any infiltration of the entire lung zone in the negative group. Bilateral infiltration (Fig. 1) was seen more frequently in swine influenza pneumonia than in the negative group ($p=0.044$). Based on these findings, widespread infiltrations should alert physicians about distinguishing swine influenza pneumonia from community-acquired pneumonia.

Our study has several limitations. Firstly, most of the patients were adult (only 3 patients were less than 16 years of age). Secondly, the numbers of patients with and without S-OIV infection were too small to acquire strong statistical data.

S-OIV pneumonia is a complication of S-OIV infection and can cause serious illness. Although our radiological or clinical data show significant differences between the patients with S-OIV pneumonia and the negative group, we suggest that no specific constellation seems to be typical of H1N1-associated pneumonia. In conclusion, each patient presenting with signs of pneumonia during pandemia should be tested for Influenza A.

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Conflict of interest

No financial or other potential conflicts of interest exist.
References

1. Cunha BA. Swine Influenza (H1N1) pneumonia: clinical considerations. Infect Dis Clin North Am 2010;24:203–28.

2. World Health Organization. Updated: June 11, 2009. World events at start of 2009 influenza pandemic. http://www.who.int/mediacentre/news/statements/2009/h1n1_pandemic_phase6_20090611/en/index.html. Accessed: September 4, 2010.

3. Jain S, Kamimoto L, Bramley AM, et al. 2009 Pandemic Influenza A (H1N1) Virus Hospitalizations Investigation Team. Hospitalized patients with 2009 H1N1 influenza in the United States, April–June 2009. N Engl J Med 2009;361:1935–44.

4. Perez-Padilla R, de la Rosa-Zamboni D, Ponce de Leon S, et al. Pneumonia and respiratory failure from Swine-Origin Influenza A (H1N1) in Mexico. N Engl J Med 2009;361:680–9.

5. Chowell G, Bertozzi SM, Colchero MA, et al. Severe respiratory disease concurrent with the circulation of H1N1 influenza. N Engl J Med 2009;361:674–9.

6. World Health Organization. Updated: October 6, 2009. CDC protocol of realtime RTPCR for influenza A (H1N1). http://www.who.int/csr/resources/publications/swineflu/CDCRealtimeRTPCR_SwineH1Assay-2009_20090430.pdf. Accessed: September 4, 2010.

7. Louie JK, Acosta M, Winter K, et al. Factors associated with death or hospitalization due to pandemic 2009 influenza A (H1N1) infection in California. JAMA 2009;302:1896–902.

8. Cao B, Li XW, Mao Y, et al. National Influenza A Pandemic (H1N1) 2009 Clinical Investigation Group of China. Clinical features of the initial cases of 2009 pandemic influenza A (H1N1) virus infection in China. N Engl J Med 2009;361:2507–17.

9. Gildsof G, Agyeman P, Duppenthaler A, Heininger U, et al. Influenza-A associated myositis in children. Infection 2004;32:199–203.

10. Torres JP, O’Ryan M, Herve B, et al. Impact of the novel Influenza A (H1N1) virus and highly pathogenic avian influenza H5N1 virus. J Infect Dis 2010;201:993–9.

11. Lee CS, Lee JH. Dynamics of clinical symptoms in patients with pandemic influenza A (H1N1). Clin Microbiol Infect 2010;16:389–90.

12. Venkata C, Sampathkumar P, Afessa B. Hospitalized patients with 2009 H1N1 influenza infection: The Mayo Clinic Experience. Mayo Clin Proc 2010;85:798–805.

13. Grijalva-Otero I, Talavera JO, Solorzano-Santos F, et al. Critical analysis of deaths due to atypical pneumonia during the onset of the influenza A (H1N1) virus epidemic. Arch Med Res 2009;40:662–8.

14. Presanis AM, De Angelis D; New York City Swine Flu Investigation Team, Hagy A, et al. The severity of pandemic H1N1 influenza in the United States, from April to July 2009: a Bayesian analysis. PLoS Med 2009;6(12):e1000207.

15. New South Wales public health network. Progression and impact of the first winter wave of the 2009 pandemic H1N1 influenza in New South Wales, Australia. Euro Surveill 2009;14(42): pii:19365.

16. Poggensee G, Gildsof G, Buda S, et al. RKI Working Group Pandemic Influenza, Krause G, Haas W. The first wave of pandemic influenza (H1N1) 2009 in Germany: From initiation to acceleration. BMC Infect Dis 2010;10:155.

17. van den Brand JM, Stittelaar KJ, van Amerongen G, et al. Severity of pneumonia due to new H1N1 influenza virus in ferrets is intermediate between that due to seasonal H1N1 virus and highly pathogenic avian influenza H5N1 virus. J Infect Dis 2010;201:993–9.

18. Grijalva-Otero I, Talavera JO, Solorzano-Santos F, et al. Critical analysis of deaths due to atypical pneumonia during the onset of the influenza A (H1N1) virus epidemic. Arch Med Res 2009;40:662–8.

19. Lee CS, Lee JH. Dynamics of clinical symptoms in patients with pandemic influenza A (H1N1). Clin Microbiol Infect 2010;16:389–90.

20. Venkata C, Sampathkumar P, Afessa B. Hospitalized patients with 2009 H1N1 influenza infection: The Mayo Clinic Experience. Mayo Clin Proc 2010;85:798–805.

21. Ugarte S, Arancibia F, Soto R. Influenza A pandemics: clinical and organizational aspects: the experience in Chile. Crit Care Med 2010;38:133–7.

22. Aygeman P, Duppenthaler A, Heininger U, et al. Influenza-associated myositis in children. Infection 2004;32:199–203.

23. Reissens MF, Taubenberger JK, Faucci AS. Predominant role of bacterial pneumonia as a cause of death in pandemic influenza: implications for pandemic influenza preparedness. J Infect Dis 2008;198:962–70.

24. Choi WI, Kim WY, Kim SH, et al. Clinical characteristics of pneumonia in hospitalized patients with novel influenza A (H1N1) in Korea. Scand J Infect Dis 2010;42:311–4.

25. Agarwal PP, Cinti S, Kazerooni EA. Chest radiographic and CT findings in novel swine-origin influenza A (H1N1) virus (S-OIV) infection. Am J Roentgenol 2009;193:1488–93.

26. Dee S, Jayathissa S. Clinical and epidemiological characteristics of the hospitalised patients due to pandemic H1N1 2009 viral infection: experience at Hutt Hospital, New Zealand. N Z Med J 2010;123:45–53.