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# Determining symptoms for chest radiographs in patients with swine flu (H1N1)

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**Abstract**

Although most cases of swine-origin influenza A (H1N1) virus have been self-limited, a question arises about the chest X-ray findings and clinical symptoms in swine flu and about the most important clinical finding when correlated with the chest radiograph. Should physicians order a chest X- ray in each patient suspected of having swine flu? We described radiographic findings associated and correlated with the symptoms of swine-origin influenza A (H1N1) infection. The study was approved by hospital ethics committee. As the study was retrospective, an informed consent was waived. we retrospectively reviewed the electronic archive of the infection control department for cases of positive real-time Polymerase chain reaction (PCR) results of nasal swabs or aspirates and positive or negative results of Quick's test. Afterwards, the results were correlated with the chest radiograph performed on the day of admission. To predict the condition of patients by correlating the major symptoms and clinical outcome of the H1N1 patients. Early cases of prediction leads to minimal the severity risks and helps to get rid of the death risks. If the virus is predicted early then the suspects can be diagnosed early and can be recovered early.

**Keywords**: Swine flu, Chest X-ray, Influenza and Radiograph

## Introduction

In March 2009, a major outbreak of respiratory disease was reported by the health authorities in Mexico (1). One month later, a new influenza A virus of swine origin, H1N1, was detected in California in the United States (2). Within few weeks, the virus spread globally, and on June 11 2009, the World Health Organization declared the H1N1 influenza infection as a global pandemic (3). The majority of H1N1 influenza cases have been mild influenza-like illnesses (4). However, relatively large-scale reports of hospitalized patients with H1N1 influenza in the United States demonstrated that the current strain of H1N1 virus can cause severe illness, including sepsis, pneumonia, and acute respiratory distress syndrome (5,6). Although underlying medical conditions were common among these patients, severe illness was also prevalent among young, previously healthy persons (6). In a series of 272 U.S. patients (6), 40% of the hospitalized patients who underwent chest radiography at admission had radiographic findings consistent with pneumonia (there were no descriptions of the nature of the radiologic findings). In the largest series of patients published (5), which included 1088 cases of hospitalization or death in California, 833 (66%) patients who underwent chest radiography during their hospitalization had opacities suggestive of pneumonia or acute respiratory distress syndrome. Similar findings were described in a few reports (6–9) that focused solely on severely ill patients who were admitted to intensive care units or required mechanical ventilation. To date, the largest series that described imaging findings in H1N1 influenza patients (10) Consisted of 66 patients, only 38% of whom were given a definite diagnosis. The reported radiologic findings included patchy consolidation and ground-glass opacities, most commonly detected in the lower and central lung zones (10, 11).

We postulated that the identification of radiologic characteristics on the chest radiograph obtained at admission, which are related to poor clinical outcome, may contribute to the patient's triage during the current influenza pandemic. The purpose of our study was to retrospectively evaluate whether findings on initial chest radiographs obtained from influenza A (H1N1) patients can help predict clinical outcome.

Chest radiographs were obtained for the following indications: fever, dyspnea, cough, desaturation, tachycardia, or auscultatory findings suspicious for pneumonia. All chest radiographs that were obtained within 24 hours of admission to the department of emergency medicine were included. At our institution, poster anterior chest radiography is routinely performed and a lateral view is added when requested.

The findings that were likely to be related to the current influenza infection were then described according to the pattern of opacity: Ground-glass opacity was defined as an area of hazy increased lung opacity within which definition of lung structures is usually preserved; this opacity is less opaque than is consolidation (14). Consolidation was defined as a homogeneous increase in pulmonary parenchyma attenuation that obscures the margins of vessels and airways (14). Further description of the opacities was recorded as (a) nodular (a rounded opacity measuring ≤3 cm in diameter) (14), (b) patchy (no homogeneous airspace consolidation in the anatomic distribution of a bronchial lung segment, such as described in bronchopneumonia) (14–16), and (c) confluent nodular (collections of poorly defined, discrete, or partly confluent opacities) (15).

The question arises about the chest X-ray findings and clinical symptoms in swine flu and about the most important clinical finding when correlated with the chest radiograph. Should physicians order a chest X-ray in each patient suspected of having swine flu?

There were 179 patients with a high suspicion of swine flu. All 179 patients had an initial chest radiograph. As many as 65 males (representing 56% of the projected study population) had a normal chest radiograph, while 35 males (representing 55.6% of the study population) had an abnormal chest X-ray. As many as 51 females (representing 44% of the population) had a normal chest X-ray, while 20 females (representing 44% of the study population) had abnormal chest X-rays.

Polymerase chain reaction (PCR) was not a determining factor for normal vs. abnormal chest X-ray (CXR). Rapid antigen test was not a determining factor for normal vs. abnormal CXR. Fever was not a determining factor for normal vs. abnormal CXR. Cough appears to be a determining factor for normal vs. abnormal CXR. Sore throat appears to be a determining factor for normal vs. abnormal CXR. Chest pain was not a determining factor for normal vs. abnormal CXR. Presence of cough with PCR was statistically significant.

## MATERIAL AND METHODS

This method revealed 179 patients with a high suspicion of swine flu. All 179 patients had an initial chest radiograph, in the postero-anterior projection. In 150 out of 179 patients, a follow-up radiograph was performed within 1–2 days after the initial visualization: 5 patients had a bedside antero-posterior projection. Postero-anterior radiographs were obtained using a General Electric X-ray unit (GE Healthcare) Milwaukee, USA.

All the patients should be 18 years or older, have clinical evidence of acute respiratory tract infection, have radiological findings consistent with pneumonia, and have confirmed laboratory diagnosis of H1N1 influenza virus infection. The radiological studies were plain chest X-ray (CXR) and/or computerized tomography (CT) scan of the chest. The radiological studies were done within 24 h of hospital arrival. The laboratory diagnosis was based on the detection of the virus with real-time reverse transcriptase polymerase chain reaction (RT-PCR) in the nasopharyngeal swab or in the lower respiratory tract secretion collected within 24 h of hospital arrival.

**The exclusion criteria were:**

1. Patients younger than 18 years old.

2. The radiological studies and/or the sample collection for RT-PCR were delayed for more than 24 h of hospital arrival.

3.The presence of a known major immune compromising condition such as HIV, hematologic malignancy, post organ transplant, active chemotherapy utilization, and/or regular use of steroid of more than 15 mg Prednisolone (or equivalent) daily for more than one month.

4.The presence of other radiological features that obscure, enhance, and/or conflict with the pneumonia opacity.

## IMAGE ANALYSIS

I. the CXR was assessed for

1. Pattern of opacities: The nature of the opacities was categorized as confluent consolidation, alveolar consolidation, ground glass opacities (GGO), nodular opacities, and/or reticular opacities. The presence of other opacities will be accepted if they did not interfere with the assessment of the pneumonia opacities and will be inferred.

2. Distribution of opacities: The distribution of opacities was assessed for two variables:

•Focal, multifocal unilateral, or bilateral.

•Upper zones, middle zones, and/or lower zones.

3. Extension of opacities: The extension of opacities was calculated as the number of the involved lung zones out of six.

II. The Chest CT images were assessed for

1. Pattern of opacities: The nature of opacities was categorized as for CXR.

2. Distribution of opacities: The distribution of opacities was assessed for three variables:

•Focal, multifocal unilateral, or bilateral.

•Upper zones, middle zones, and/or lower zones.

•Central, peripheral, and/& peribronchovascular.

3. Extension of opacities:

## STATISTICAL ANALYSIS

The statistical analysis was performed with an SPSS software package (version 16.0; SPSS, Chicago. IL). Student's t-test was used to analyze the relationship between chest X-rays (CXR) and age. Chi-squared test was used to analyze the relationship between CXR and gender, CXR and PCR, CXR and rapid antigen test, CXR and cough, as well as CXR and sore throat. Fisher's exact test was used to analyze the relationship between CXR and fever, CXR and dyspnea, CXR and hemoptysis, as well as CXR and chest pain.

All data were summarized and displayed as the mean ± standard deviation or the median and interquartile range for the continuous variables and as a number of individuals plus the percentage in each group for the categoric variables. All analyses were considered significant at P values of less than .05 (two-tailed).

## RESULTS

A total number of 179 patients was enrolled and labeled with the diagnosis of swine flu. Their age ranged from 2 to 89 years. One hundred of them were males with a mean age of 26.2 ± 17.2 years. There were 79 females with a mean age of 27.19±24.4 years. Age was not a determining factor (P- value = 0.777) according to the student's t-test for independent groups. Chest X-rays were obtained in all these patients: 65 males representing

56% of the study population had a normal chest X-ray (CXR), while 35 males, representing 55.6% of the study population, had abnormal chest X- rays. As many as 51 females, representing 44% of the population, had a normal CXR, while 28 females (44% of the study population) had an abnormal CXR. Sex was not a determining factor (with a P-value of 0.999 according to the chi-squared test). From among patients with a normal CXR, 79 (73.1%) had a positive PCR, while 29 patients (26.9%) had a negative PCR. Among those with an abnormal chest X-ray, 44 patients (74.6%) had a positive PCR and 15 patients (25.4%) had a negative PCR. PCR, therefore, was not a determining factor for normal vs. abnormal CXR as the P-value was 0.98, according to the chi-squared test. From among patients with a normal CXR, 29 (25%) had a positive rapid antigen test, while 87 (75%) had a negative rapid antigen test. Among those with an abnormal CXR, 12 patients (19%) had a positive rapid antigen test, while 51 patients (81%) had a negative rapid antigen test.

Once again, rapid antigen test was not a determining factor for normal vs. abnormal CXR, as the P-value was 0.472 according to the chi- squared test. Of those patients with a normal CXR, 109 (94%) had a fever, and 7 (6%) had no fever. Among those with an abnormal CXR, 96.8% had a fever and only 2 (3.2%) had no fever. Fever was not a determining factor for normal vs. abnormal CXR, as the P-value was 0.327.

Of the patients with a cough, 94 (81%) had a normal CXR, while 22 (19%) had no cough. Among those with an abnormal CXR, 59 (93.7%) had a cough and only 4 (6.3%) had no cough (Figure 1). Therefore, cough appears to be a determining factor, with a P-value of 0.039, according to the chi-squared test. Among those with a normal CXR, 27 (23.3%) had a sore throat, while 89 (76.7%) had no sore throat. Among those with an abnormal CXR, 25 (3%) had a sore throat, while only 38 patients had no sore throat (Figure 2). Therefore, sore throat appears to be a determining factor, with a P-value of 0.33, according to the chi-squared test. There were 7 (6%) patients with a normal CXR and dyspnea, and 109 (94%) with a normal CXR and without dyspnea. Among patients with an abnormal chest X-ray, there were 3 (4.8%) with dyspnea and 60 (95.2%) without dyspnea. The correlation between dyspnea and chest X-ray was not statistically significant (P=0.507 according to the Fisher's exact test). None of the patients with a normal CXR had hemoptysis, while only 1 (1.6%) had an abnormal CXR. The remaining 62 patients (96%) had no hemoptysis. Hemoptysis was not a determining factor (P-value =0.352 according to the Fisher's exact test). Only 6 patients with a chest pain had a normal CXR

(5.2%) while the majority – 110 (94.8%) had no chest pain. Two patients with a chest pain (3.2%) had an abnormal CXR, while 61 patients (96.8%) had no chest pain at all. Chest pain was not a determining factor, as the P- value was 0.420 according to the Fisher's exact test. Of the patients with a positive PCR (123), 112

(91.1%) had a cough, while only 11 (8.9%) had no cough. Among patients with a negative PCR (44), 32 (72.7%) had a cough, while only 12 (27.3%) had no cough (Table 2 and Figure 3).

Fig. 1: graph showing cough and sore throat symptoms in H1N1 patients vs. Chest X-rays (CXR) in H1N1 patients

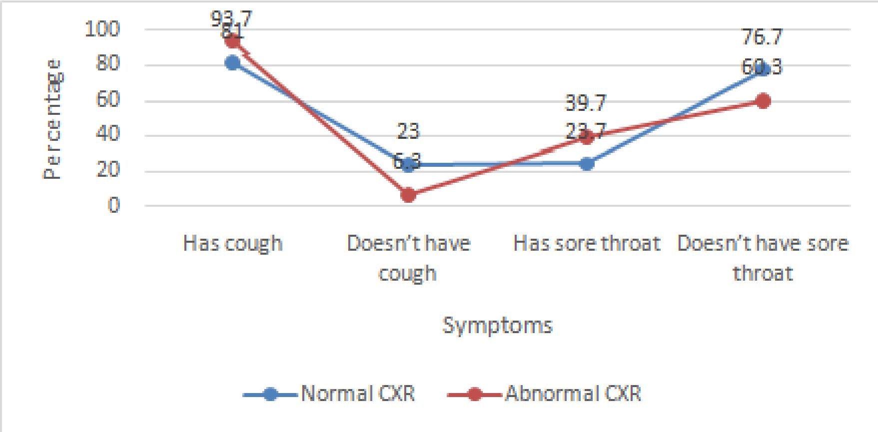



Table 1: Statistical relation between CXR and symptoms in percentage according to chi-squared test

| | **CXR** | | |
|---|---|---|---|
| | **Normal(n=116)** | **Abnormal(n=63)** | **P-Value** |
| Age | 26.21±17.21 | 27.19±24.44 | 0.777*** |
| **Gender** | | | |
| Male | 65 (56%) | 35 (55.6%) | 0.999* |
| Female | 51 (44%) | 28 (44.4%) | |
| **PCR** | | | |
| + ve | 79 (73.1%) | 44 (74.6%) | 0.987* |
| – ve | 29 (26.9%) | 15 (25.4%) | |
| **Rapid Ag test** | | | |
| + ve | 29 (25%) | 12 (19%) | 0.472* |
| – ve | 87 (75%) | 51 (81%) | |
| **Fever** | | | |
| Yes | 109 (94%) | 61 (96.8%) | 0.327** |
| No | 7 (6%) | 2 (3.2%) | |
| **Caugh** | | | |
| Yes | 94 (81%) | 59 (93.7%) | 0.039* |
| No | 22 (19%) | 4 (6.3%) | |
| **Soar throat** | | | |
| Yes | 27 (23.3%) | 25 (39.7%) | 0.033* |
| No | 89 (76.7%) | 38 (60.3%) | |
| **Dyspnea** | | | |
| Yes | 7 (6%) | 3 (4.8%) | 0.507** |

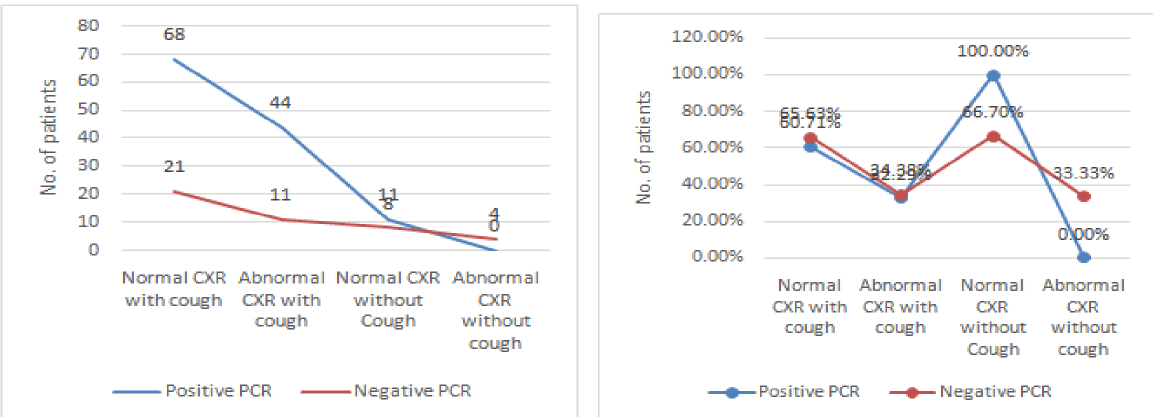
| | | | |
|---|---|---|---|
| No | 109 (94%) | 60 (95.2%) | |
| **Hemoptysis** | | | |
| Yes | 0 (0%) | 1 (1.6%) | 0.352** |
| No | 116 (100%) | 62 (98.4%) | |
| **Chest pain** | | | |
| Yes | 6 (5.2%) | 2 (3.2%) | 0.420** |
| No | 110 (94.8%) | 61 (96.8%) | |

Table 2: Statistical relation between cough and Polymerase chain reaction (PCR) in percentage according to chi-squared test

| **PCR** | | | |
|---|---|---|---|
| | **+ ve** | **– ve** | |
| Cough | 112 (68/44) | 32 (21/11) | 0.006* |
| No Cough | 11 (11/0) | 12 (8/4) | |

The correlation between cough and PCR is statistically significant (P-value = 0.006, according to the chi-squared test) (Table 1). From among 123 patients with a positive PCR, 112 had a cough. Out of those 112, 68 had a normal CXR, while 44 patients had an abnormal chest X-ray. There were 11 patients who had no cough and a normal CXR. None of the patients without cough had an abnormal CXR. There were 44 patients with a negative PCR. As many as 32 of them had a cough, and out of those who had a cough, 21 had a normal CXR and 11 had an abnormal CXR (Table 3 and Figure 4A, B). There were 12 patients with a negative PCR and no cough. Eight of them had a normal CXR and 4 had an abnormal CXR (Table 1).

Fig.2: graph representing PCR vs. CXR and cough in H1N1 Patients and graph representing the percentage of PCR vs. CXR and cough in H1N1 Patients




Based on the readings of PCR values graphs are designed. Graph represent the positive PCR and Negative PCR reading of normal CXR with without cough and Abnormal CXR with and without cough values in percentage and also in the normal values. H1N1 radiologic findings are observed in order to identify the abnormal values for abnormal chest radiographs. 39 patient's readings like opacity, Lung zone, Distribution are taken and are tabulated.

Table 3: H1N1 patient's radiologic findings with abnormal chest radiograph.

| **characteristic** | **No of patients (n= 39)** |
|---|---|
| Opacity | |
| Ground glass | 27(69) |
| Consolidation | 23(59) |
| Patchy | 16(41) |
| Nodular | 11(28) |
| Confluent | 2(5) |
| Air bronchogram | 13(33) |
| Lung zone | |
| Right upper | 4(10) |
| Right middle | 26(66.7) |
| Right lower | 13(33) |
| Left upper | 1(3) |
| Left middle | 24(62) |
| Left lower | 16(41) |
| Distribution | |
| Central | 24(62) |
| peripheral | 30(77) |
| No. of Zones | |
| Single | 11(28) |
| Multiple | 28(72) |
| No. of sides involved | |
| Unilateral | 15(38) |
| Bilateral | 24(62) |
| Central | 21(54) |
| Peripheral | 8(21) |
| Pleural infusion | 3(8) |

The most frequently observed opacity was that of ground glass (n = 27, 69%), predominantly at a central location (n = 21, 78%) (Fig 1), and slightly less frequently seen in peripheral locations (n = 18, 67%). Consolidation was also frequent (n = 23, 59%), and it was accompanied by ground-glass opacities in almost one-half of the patients (n = 11, 48%). Consolidation appeared in either patchy distribution (n = 11, 48%) (Fig 2), or as rounded nodular opacities (n = 10, 43%) (Fig 3), while it was seldom confluent (n = 2, 9%). In one-third of the patients, air bronchogram could be detected.

Mid-lung zones were the most frequently involved sites, followed by lower-lung zones. More than one-half of the patients had bilateral opacities, mostly central, with involvement of multiple lung zones. Three (8%) patients had pleural effusion; one of whom had a medium-size effusion, the other two had small effusions that were bilateral in one of them.

Figure 3: Initial chest radiograph of 45-year-old woman after gastric banding who presented 48 hours after onset of fever and sore throat. Bilateral central ground-glass opacities are seen in perihilar region. Patient discharged 3 days later after clinical improvement.

Figure 4: Initial posterior anterior chest radiograph of 21-year-old woman who presented with dyspnea and fever 48 hours after onset of symptoms. Patchy consolidation, some with air bronchogram is distributed in multiple lung zones, accompanying central ground-glass opacities. Patient required mechanical ventilation 6 days later but slowly recovered and was discharged following 20 days of hospitalization.

Figure 5: Initial posterior anterior chest radiograph of pregnant 37-year-old woman who presented with muscular pain and fever 72 hours after onset of symptoms. Nodular consolidation and patchy ground-glass opacities are visible in mid and central zones of left lung. After initial worsening of status, unilateral involvement improved after 5 days of treatment.

Table 4: Outcome of Patients with Abnormal First Chest Radiograph

| Characteristic | No Mechanical ventilation/Death(n=34) | Mechanical ventilation/Death(n=5) | P-value |
|---|---|---|---|
| **Opacity** | | | |
| Ground glass | 23(67.6) | 4(80) | 0.665 |
| Consolidation | 18(52.9) | 5(100) | 0.066 |
| Air Bronchogram | 10(29.4) | 3(60) | 0.31 |
| Patchy | 13(38.2) | 3(60) | 0.631 |
| Nodular | 11(32.4) | 0 | 0.296 |
| Confluent | 1(2.9) | 1(20) | 0.243 |
| Lung Zone | | | |
| Right Upper | 3(8.8) | 1(20) | >.999 |
| Right Middle | 21(61.8) | 5(100) | 0.149 |
| Left Upper | 0 | 1(20) | 0.128 |
| Left Middle | 21(61.8) | 3(60) | >.999 |
| Left Lower | 13(38.2) | 3(60) | 0.631 |
| Distribution | | | |
| Central | 19(55.9) | 5(100) | 0.136 |
| Peripheral | 25(73.5) | 5(100) | 0.318 |
| Bilateral | 21(61.8) | 3(60) | >.999 |
| Central | 18(52.9) | 3(60) | >.999 |
| Peripheral | 5(14.7) | 3(60) | 0.049 |
| Four or more Zones | 2(5.9) | 3(60) | 0.01 |

Table 4 presents the frequency of findings among the 39 patients with abnormal initial chest radiographs stratified by the endpoint of mechanical ventilation. Five (13%) patients required mechanical ventilation; four (80%) of these died. Radiologic findings in four or more lung zones and distributed bilaterally peripherally were significantly more often seen on the chest radiograph obtained at admission of these five patients with poor outcome compared with the other 34 patients who had a good clinical outcome (multizonal opacities: 60%, n = 3 vs 6%, n = 2, respectively, P = .01; bilateral peripheral opacities: 60%, n = 3 vs 15%, n = 5, respectively, P =.049). In the receiver operating characteristic curve analysis, involvement of four or more zones had a sensitivity of 60% and a specificity of 94% for the prediction of requiring mechanical ventilation. The area under the receiver operating characteristic curve was 0.8 (95% confidence interval: 0.58, 1.0, P = .031).

## CONCLUSIONS

The chest radiographs in patients with suspected H1N1 should only be obtained if there is a cough or sore throat. Other symptoms associated with H1N1 do not warrant chest radiograph unless absolutely necessary. In our study, we have tried to identify specific parameters at admission that are associated with the outcome and length of stay. We found that 2009 H1N1 affects relatively younger age groups (21-50 years) in the sub population affected severely enough to require admission. In comparison to the discharged group, increased duration of dyspnoea prior to admission(in other words, early onset of dyspnoea), presence of bilateral pneumonia, a low $PaO_2$ /$FiO_2$ ratio at admission and 24 hours later, higher $PaCO_2$ values at admission, higher oxygen requirement and number of organ failures have been found to be associated with a poorer outcome. A lower PaO2 /FiO2 ratio at admission and 24 hours, organ failure and delay in specialized treatment were found to prolong the course of illness among survivors.

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