Original Article

DOI: 10.7860/IJARS/2021/44765:2633

Radiology Section

Chest Multi Detector Computed Tomography Findings among Patients with H1N1 Influenza A Infection: A Retrospective Study

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ABSTRACT

Introduction: The first cases of H1N1 Influenza A occurred in Mexico in 2009, thereafter the infection rapidly spread worldwide. Seasonal epidemics and unpredictable pandemics had been declared by the World Health Organisation (WHO), since then.

Aim: To describe the Thoracic Multi-Detector Computed Tomography (MDCT) findings in moderate to severely ill, H1N1 patients during epidemic spread.

Materials and Methods: A retrospective observational study was done in which evaluation of 155 hospitalised patients confirmed to have H1N1 Influenza A epidemic infection between October 2018-December 2018, through the radiologic and clinical aspects. About 56 moderate to severely ill patients, who failed to improve with through treatment, underwent thoracic cross-sectional MDCT and their scans available on picture archiving and communication system (PACS) were assessed and radiological findings were evaluated with respect to clinical condition. Descriptive statistics were used for representation of data.

Results: About 56 moderate to severely ill H1N1 patients who underwent chest MDCT, consisted of 30 males and 26 females ranging in age from 20 to 86 years with median age of 55.19 years. Ground glass opacities was found in 34 (60.71%) patients, Consolidation in 33 (58.93%) patients, combined Ground glass pattern and Consolidation in 18 (32.14%) patients and Acinar nodules in 21 (37.50%) patients. Combined Peripheral & Central distribution of lesions was found in 47 (83.92%) patients and central lesions in 6 (10.71%) patients. The lesions were multifocal in 51 (91.07%) patients and diffuse in 25 (44.64 %) patients. Lesions seen in bilateral all lobes in 25 (44.6%) patients and unilateral in 7 (12.5%) patients. Small mediastinal Lymphnodes were detected in 42 (75%) patients, pleural effusion was associated in 18 (32.14%) patients and pericardial effusion in 4 (7.14%) patients. In nonvulnerable group, 53 (94.6%) patients showed full recovery as in those patients therapy was started earlier while in vulnerable group 3 (5.35%) died immediately after infection.

Conclusion: Unilateral or bilateral ground-glass opacities may or may not be linked with focal or multifocal areas of consolidation in the peribronchovascular and subpleural distribution that resembled the appearance of organising pneumonia is the main finding which was observed.

Keywords: H1N1 pneumonia, Swine flu, Swine-origin influenza

INTRODUCTION

Influenza viruses are common and important pathogens affecting human. The novel swine-origin influenza (H1N1) virus generally known as the “swine flu” was first identified in Mexico in April 2009 [1]. Seasonal epidemics and unpredictable pandemics associated with influenza A (“swine” influenza or H1N1) virus had been declared by the WHO, last one on June 11, 2009 [2]. It was observed by Amorim VB et al that even though there was a substantial decrease in H1N1 infection since 2009 but still it is possible that this virus may be present and circulating with other viruses [3]. It has covered 214 countries and more than 18000 deaths were noted by august 2010 [4].

This condition is generally mild but due to various conditions like old age, pregnancy, diabetes, cardiac diseases, asthma, immunosuppression it may progress and leads to high morbidity and mortality [5]. Diagnostic imaging based on Chest Computed Tomography (CT) is very useful in the study of disease because it allows to assess the extent of lung parenchymal damage. The early diagnosis of pneumonia and the rapid initiation of the proper empirical antimicrobial therapy are mandatory to improve the outcome of the patients [6,7]. The purpose of the present study was to retrospectively evaluate, MDCT chest scans of moderate to severely ill, confirmed H1N1 infection patients, the most common computed tomographic findings and the characteristics of their distribution in the lung parenchyma.

MATERIALS AND METHODS

A retrospective observational MDCT study was performed so informed consent and Hospital ethics committee approval was waived. The three months (October-December) study period was in the year 2018 H1N1 epidemic and was conducted at Velammal Medical College Hospital and Research Institute (VMCH and RI), Madurai, Tamil Nadu. The study population of 155 patients admitted at VMCH and RI with symptoms of flu and tested positive for the influenza A viral infection by Real-Time reverse transcriptase Polymerase Chain Reaction (RT-PCR), consisted of 79 males and 76 female ranging in age from 1 month to 86 years (median age, 47 years). All patients were subjected to thorough history taking and clinical examination as well as laboratory workup.

The MDCT chest imaging study group included only 56 moderate to severely ill patients out of total 155 H1N1 patients, who were not showing improvement with treatment. Mild to moderate influenza A is clinically impossible to differentiate from illnesses caused by other respiratory viruses that present as Influenza Like Illnesses (ILIs). Severe influenza A has a distinctive clinical presentation in adults with abrupt onset, accompanied by fever higher than 39°C/102°F and chills, dry cough with or without haemoptysis, severe myalgia especially of the neck and lower back, debilitating fatigue with profound prostration [8]. Winthrop-University Hospital Infectious Disease department devised a modified point system for diagnosing severe influenza A in adults based on the symptoms, signs and laboratory findings [8]. According to the point system >20=Severe

influenza A highly probable, 10-20=Mild/moderate influenza A likely and <10=Influenza A unlikely [8].

The vulnerable group of patients for H1N1 A pneumonia included old age, pregnancy, diabetes, cardiac problem, chronic cardiopulmonary conditions such as asthma and immune-suppression [5]. Rest of the patients without above co-morbid conditions constituted the non-vulnerable group.

Inclusion criteria: Viral culture or PCR confirmed cases and moderate to severe diseased patients whose condition is not improving even after treatment. Other inclusion criteria was the availability of chest MDCT scans of each study patient on PACS, performed during the acute moderate to severe phase of the disease. These CT examinations were performed 1-7 days after the onset of illness.

Exclusion criteria: Exclusion criteria included patients who did not undergo MDCT chest examination.

Thin-section cross-sectional MDCT was done on a 128 Slice General Electric Optima CT 660 Scanner model in spiral mode and mediastinal and lung windows viewing was done in the PACS work station.

The CT procedure parameters were as follows: End-inspiratory acquisition, 120 kV, 150-200 mAs, thickness of 0.625 mm. Both the lung and mediastinal settings were used to analyse the images. IV contrast was given to three patients as there was clinical uncertainty of pulmonary embolism. All the other CT studies were unenhanced. The chest MDCT cross-sectional images were reviewed by experienced radiologists on a PACS workstation. Each of them were analysed and identified as normal or abnormal.

The pulmonary findings described below are consistent with the Fleischner Society glossary [9]. Ground-Glass Opacity (GGO) on CT is defined as hazy increased opacity of lung, with preservation of underlying bronchial and vascular margins, and may be caused by subtotal displacement of air in the alveoli. Consolidation on CT is defined as increased opacity of lung, with obscuration of underlying bronchial and vascular margins, caused by total replacement of alveolar air [10].

Nodular opacities were defined as focal rounded opacities measuring <3 cm in diameter. Reticular opacities were defined as linear opacities forming a mesh like pattern [11]. The involvement was categorised as unilateral or bilateral. If the involvement was deemed bilateral, the process was categorised as symmetric or asymmetric in nature. The radiological appearances were characterised as ground glass pattern, consolidation, tree-in-bud pattern, septal lines, reticular opacities or nodular opacities [11].

The presence of associated hilar, mediastinal or pleural abnormalities was also assessed. The dominant location was determined i.e., whether in upper, middle and lower lobe. It is also determined as predominantly central or peribronchovascular or subpleural. If the shortaxis diameter was >1 cm at the hilum, mediastinum, paratracheal region, and any other sites then the lymph node was called as enlarged [11]. If there was only one focus of anomaly, it is called as focal and if more than one focus, it multifocal and if it involves volume of one lung, it is called as diffuse [12].

The presence of associated hilar, mediastinal or pleural abnormalities was also assessed. Presence of pericardial effusion and bronchiectasis was also documented.

STATISTICAL ANALYSIS

Descriptive statistics were used for representation of data.

RESULTS

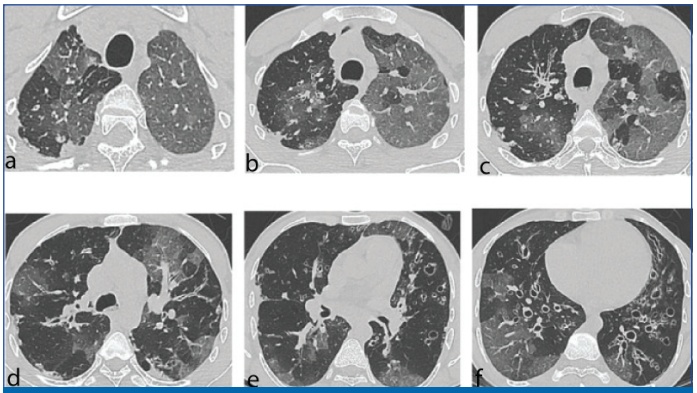
Fifty-six patients, who underwent chest MDCT during the acute moderate to severe phase of H1N1 disease, consisted of 30 males and 26 females ranging in age from 20 to 86 years with median age of 55.19 years. The male patients aged 24-86 years with mean age of 56.73 years and female patients in the age group of 20-76 years with mean age of 53.42 years.

Fever, cough, dyspnoea or chest pain as well as generalised fatigue and bone aches were documented in all examined patients.

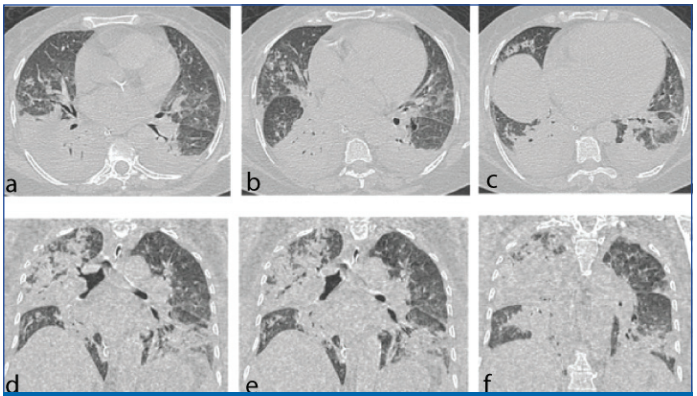
The numeric distribution of the pulmonary patterns of the H1N1 disease in decreasing order in this study were as follows ground glass opacities in 34 patients (60.71%) [Table/Fig-1,2], Consolidation in 33 patients (58.93%) [Table/Fig-1,3,4], combined Ground glass pattern and Consolidation in 18 patients (32.14%) [Table/Fig-1,5-7]. Bronchiectasis in 8 patients (14.28%) [Table/Fig-8].

Serial no.	Pattern of parenchymal lesions	Male	Female	Total	Percentage (%)
1	Ground glass opacities (GGO)	17	17	34	60.71
2	Consolidation	17	16	33	58.93
3	GGO+Consolidation	9	9	18	32.14
4	Acinar nodules (tree in bud)	11	10	21	37.50
5	Reticulo-nodular densities (ILD)	1	3	4	7.14
6	Bronchiectasis	4	4	8	14.28
Serial no.	**Associated findings**	**Male**	**Female**	**Total**	**Percentage (%)**
7	Pleural effusion	10	8	18	32.14
8	Pericardial effusion	2	2	4	7.14
9	Small mediastinal lymphnodes	25	17	42	75
Serial no.	**Pre-existing disease**	**Male**	**Female**	**Total**	**Percentage (%)**
10	Fibrosis/old TB	4	2	6	10.71
11	Pulmonary hypertension	2	3	5	8.92
12	Cardiomegaly	4	3	7	12.5
13	COPD	3	1	4	7.14

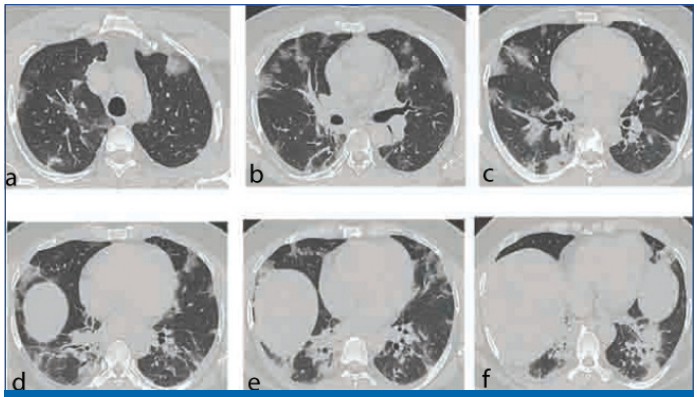
[Table/Fig-1]: Characteristic MDCT Chest imaging findings in 56 acute moderate to severely ill H1N1 Influenza A infection patients.



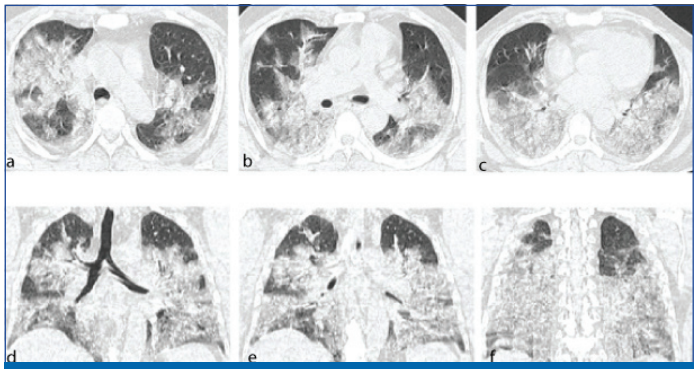
[Table/Fig-2]: H1N1 positive 28-year-old male. Chest CT Axial (a-f) performed, demonstrates bilateral bronchiectasis, lobular groundglass opacities in a peribronchovascular and subpleural distribution.



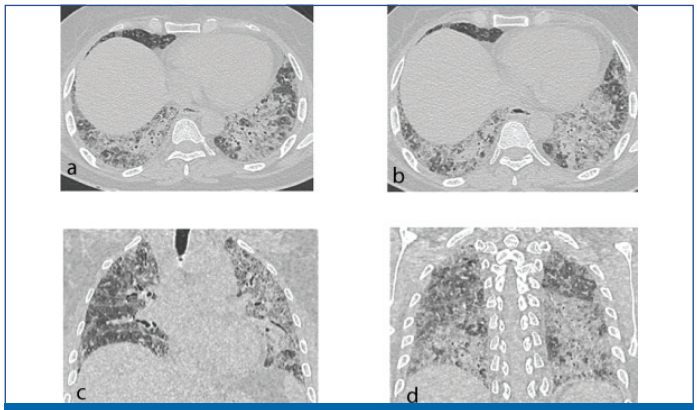
[Table/Fig-3]: A 60-year-old female presenting with fever and chills, positive H1N1. CT chest performed Axial (a-c) & reformatted coronal (d-f) images shows large right upper lobe and bilateral lower lobe consolidation.



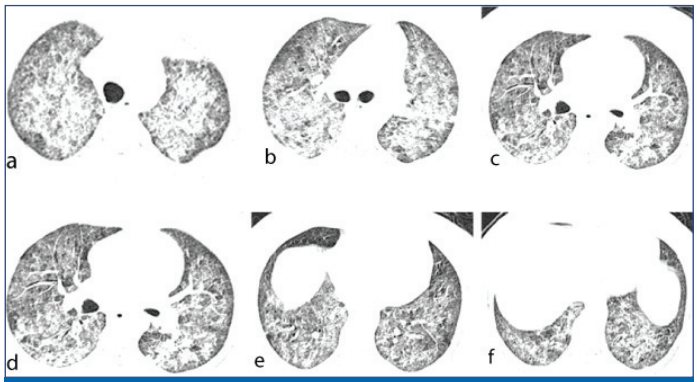
[Table/Fig-4]: A 37-year-old H1N1 positive male, who presented to the ER with cough, fever, and shortness of breath. Chest CT Axial sections (a-f) performed on the day of presentation, demonstrated patchy peribronchovascular and subpleural consolidations.



[Table/Fig-5]: A 50-year-old H1N1 positive male, who developed Acute Respiratory Distress Syndrome (ARDS), CT Chest done Axial (a-c) and reconstructed coronal (d-f) images show bilateral central and subpleural consolidations and ground glass opacities.

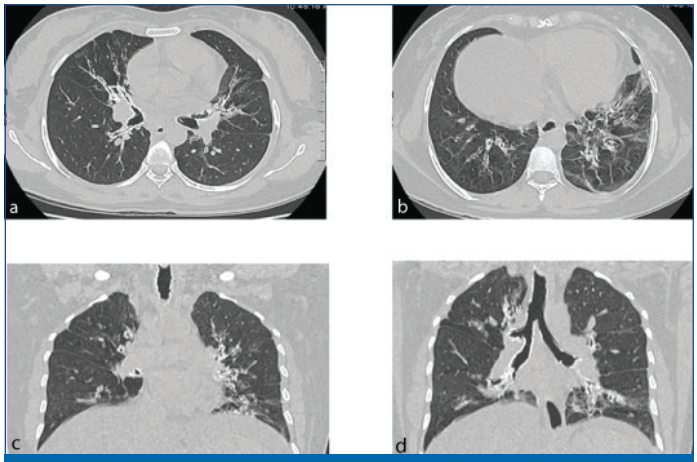


[Table/Fig-6]: A 52-year-old H1N1 positive female, who developed ARDS, CT chest done Axial (a,b) and Reformatted coronal (c,d) images show bilateral central and subpleural mixed consolidation and ground glass opacity.



[Table/Fig-7]: A 45-year-old female with H1N1 infestation who developed rapidly progressive Acute Respiratory Distress Syndrome (ARDS) requiring mechanical ventilation. Chest CT performed Axial (a-f) on the day of presentation, revealed confluent perihilar consolidations and ground glass opacities.

Thoracic MDCT examinations revealed that; combination of central and peripheral pulmonary involvement was observed in 83.92% patients, while only central pulmonary involvement was observed in 10.71% patients and only peripheral pulmonary involvement was observed in 1.78% patients [Table/Fig-9].



[Table/Fig-8]: A 36-year-old female with H1N1 positive infection, CT Chest Axial (a,b) and reconstructed coronal (c,d) images showing bilateral bronchial wall thickening and bronchiectasis.

Serial no.	Distribution of lesions	Male	Female	Total	Percentage (%)
1	Peripheral	1	0	1	1.78
2	Central	5	1	6	10.71
3	Peripheral + central	25	22	47	83.92
4	Focal	3	1	4	7.14
5	Multifocal	26	25	51	91.07
6	Diffuse	13	12	25	44.64
Serial no.	**CT lesions Lobe wise**	**Male**	**Female**	**Total**	**Percentage (%)**
7	Right Upper Lobe (RUL)	5	6	11	19.64
8	Right Middle Lobe (RML)	5	6	11	19.64
9	Right Lower Lobe (RLL)	12	9	21	37.5
10	Left Upper Lobe (LUL)	6	6	12	21.43
11	Lingular Lobe (LL)	3	1	4	7.14
12	Left Lower Lobe (LLL)	9	9	18	32.14
13	All Lobes (Bilateral)	13	12	25	44.64
14	Unilateral	2	5	7	12.5

[Table/Fig-9]: Chest MDCT frequency distribution of parenchymal lesions.

All lobes 44.64%, unilateral 12.5%, right lower lobe 37.5%, insignificant mediastinal lymphnodes seen in 42 (75%) of patients [Table/Fig-9].

Complete recovery was the natural outcome in 53 patients (94.6%) who were nonvulnerable and received proper clinical care with early onset of therapy, while three patients (5.35%) among vulnerable groups died shortly after infection. Similarly, among total 155 admitted H1N1 patients, 9 (5.8%) patients died and 146 (94.2%) survived.

DISCUSSION

Patients with H1N1Influenza A infection typically present with fever, cough, sore throat, chills, headache, rhinorrhea, shortness of breath, myalgias, arthralgias, fatigue, vomiting, or diarrhoea [13]. Most patients have mild illness, but a small percentage of patients have a severe course that may result in respiratory failure and death [13,14]. The high-risk group includes children younger than 5 years, 65-year-old or older patients with chronic underlying conditions and immuno-suppressed patients [1,14]. The most common laboratory findings include: Elevated serum lactate dehydrogenase (>1,000 IU/L), CRP, serum creatine kinase, lymphopenia and thrombocytopenia. Increased lactate dehydrogenase levels are significantly associated with disease severity and Intensive Care Unit (ICU) admission [15,16], Elevated D-dimer and transaminase levels can occur in some patients [1,17,18]. A confirmed H1N1 case is determined

when a patient demonstrates influenza-like illness and positive RT-PCR or positive viral culture [19]. Reticular or reticulo-nodular pattern may occur due to spread of infection and inflammatory exudate along the bronchovascular bundles. Spreading along the air spaces will cause multifocal areas of airspace opacities [2,20], which are represented radiologically by poorly defined nodules (air-space nodules of 4-10 mm in diameter), patchy peribronchial ground-glass opacities and airspace consolidation [21]. Progressive confluent form occurs in virulent viruses infection or in elderly and immune-compromised patients [21,22], represented by rapid confluence of ground glass opacities and air space consolidations leading to diffuse alveolar damage and Acute Respiratory Distress Syndrome (ARDS). Thoracic CT plays an important role in characterising the lesions and establishing the extent of the involvement, predicting the prognosis, planning the treatment and follow up of patient [23]. Several authors have described CT imaging findings in adults with 2009 influenza A H1N1 virus of varying severity [17,24-27]. Findings ranged from unilateral to bilateral predominant peribronchovascular and subpleural GGO with or without associated focal or multifocal areas of consolidation, predominantly in the basal lung zones, resembling organising pneumonia. The bilateral lower segment and central area are typically involved. Generally, the lung findings first appeared in the lower zones and then rapidly progressed to the middle and upper zones and the patchy areas progressed to consolidation. In present study group, young to middle aged patients were more commonly affected, which always occurred in novel influenza A infection [25].

In the current study, the most common MDCT findings were ground-glass opacities, consolidations, and a combination of ground-glass opacities and consolidations in the same patient. These data is in concordance with these studies [17,21,24-27]. In accordance with the literature [17,21,24-27], the most common radiological findings in present study group were ground glass opacities (60.71%) and multifocal patchy consolidations (58.93%). In present study, patients with influenza A pneumonia, the axial distribution was more often multifocal (91.07%) and diffuse (44.64%). In a study by Tanaka N et al., and Lin L et al., of the CT manifestations of H1N1 influenza A virus pneumonia, diffuse and random axial distributions were commonly seen, which is consistent with present findings [28,29]. In the published literature, the majority of HRCT findings is bilateral multifocal involvement mainly in the lower lobes [30,31]. In the present study, bilateral lower lobes involved in 69.6%, bilateral upper lobes involved in 41%, all lobes involved in 44.64% and unilateral in 12.5% which correlates with previous studies [30,31]. In a study by Amorim VB et al., parenchymal involvement was bilateral in 89% and unilateral in 11% which is near similar to present study [32]. Another important finding in present study was pleural effusion in 18 patients (32.14%). In a High Resolution Computed Tomography (HRCT) study of 71 patients by Amorim VB et al., minimal pleural effusion was observed in 19 patients (27%), being bilateral in 10 (52%) which nearly correlates with present study [30]. Even though pleural effusion in viral pneumonia is comparatively uncommon, influenza virus pneumonia with pleural effusion has been seen in previous studies [30,31], perhaps reflecting secondary bacterial infection or succession of the disease.

Acinar nodules were found in 21 patients (37.5%) in present study which is similar to study by Rodrigues RS et al., in which it was observed in 25% of the cases [30]. Few studies have noted the presence of airspace nodules in patients with H1N1 infection [30,31]. Bronchial wall thickening and Bronchiectasis was observed in 8 patients (14.28%) in present study. Bronchial wall thickening was found in 18 of patients (25%) in a study by Amorim VB et al., [32]. There may be a relationship between fulminant myocarditis and swine influenza cardiovascular complications, consequential from swine Influenza A infection, but are very rare [33]. Recently, cases of acute transient constrictive pericarditis in a healthy adult [34] and fulminant myocarditis in a child [34] infected with swine influenza A has been reported. Acute pericarditis as a complication of H1N1 influenza infection is a very rare event [33]. However, pericardial effusion was found in 7.14% cases in present study. When PCR is negative in patients as the laboratory marker, radiological (MDCT) findings can influence the definite diagnosis and avoid any delays in the treatment protocol [35].

Limitation(s)

First, it is a retrospective study that includes only a small number of cases in a short span of 3 months. Secondly, none of the patients underwent lung biopsy or autopsy that would have allowed radiographic histopathologic correlation. Finally, we could not follow-up the patients who survived. Therefore, we could not detect when the pathological findings on radiological imaging resolved.

CONCLUSION(S)

The most common MDCT findings in patients with H1N1 infection are unilateral or bilateral ground-glass opacities with or without associated focal or multifocal areas of consolidation, predominantly in the peribronchovascular and subpleural distribution, that likely represents the sequelae of diffuse alveolar damage in the immediate peribronchiolar regions. Organising pneumonia may occur as a complication of H1N1 infection and should be considered in the event of a prolonged hospital course, as the patient's management may change with this diagnosis.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Apr 23, 2020
- Manual Googling: Oct 23, 2020
- iThenticate Software: Feb 02, 2021 (25%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? NA
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Apr 22, 2020**
Date of Peer Review: **Jun 08, 2020**
Date of Acceptance: **Oct 23, 2020**
Date of Publishing: **Apr 01, 2021**