Pulmonary Sequelae in Treated Swine Flu Patients

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ABSTRACT

BACKGROUND
We wanted to assess the pulmonary sequelae in patients (without any underlying respiratory disease previously) with swine flu after treatment.

METHODS
This is a retrospective follow up study conducted in the Department of Respiratory Medicine, Jawahar Lal Nehru Medical College, Ajmer, Rajasthan. 50 patients were enrolled in the study who reported to Respiratory Medicine OPD, with a history of swine flu in the past for which they got treated and recovered from the illness but were symptomatic on follow up. They were assessed clinically, and functionally by doing Pulmonary Function Test (PFT - Spirometry and DLCO) and radiologically (by doing HRCT Chest). With the results of these parameters, we assessed the long-term sequelae after swine flu attack.

RESULTS
Out of the total of 50 patients, 32 were males and 18 were females. The mean age of the study group was 40 years. The most common symptom reported by the patients was dry cough (72%) and breathlessness (60%). PFT showed restrictive pattern in 16 patients (62%), obstructive pattern in 6 patients (23%), and mixed pattern in 4 patients (15%). DLCO was done in patients with abnormal spirometry findings (26 patients); 14 (54%) patients had normal diffusion function and 12 (46%) showed reduced diffusion. 32 (64%) patients had abnormal HRCT pattern.

CONCLUSIONS
Pulmonary sequelae are more common after swine flu attack. But studies and literatures are lacking in this regard. This study shows that abnormal PFT and abnormal radiological features are seen even after the swine flu attack on follow up. So, our present study shows the importance of the follow up of all symptomatic swine flu patients on long term even after recovery from the illness.

KEYWORDS
Swine Flu (H1N1), Pulmonary Sequelae, Follow Up

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BACKGROUND

Swine flu (H1N1) is a viral infection caused by an RNA virus belonging to orthomyxovirus group which results in clinical spectrum of mild respiratory illness to severe illness like pneumonia, ARDS and sometimes death. First pandemic was reported in 1918 which resulted in high morbidity and mortality. After that in 2009 WHO declared a H1N1 pandemic, around 214 countries were notified with confirmed cases of H1N1.[1] From then to till date every year morbidity and mortality due to H1N1 continued to increase. According to the recent data given by National Centre for Disease Control, in India total number of cases of H1N1 in 2018 was around 15266 which was still more increased to 28798 in 2019. The number of deaths due to H1N1 in 2018 was 1128 and 1218 in 2019. A significant number of cases were reported from Rajasthan in 2019 (5092 cases and 208 deaths).[2]

H1N1 is a type of influenza a virus. There are four types of influenza viruses: A, B, C and D. Human influenza A and B viruses cause seasonal epidemics of disease (known as the flu season) almost every winter. Influenza A viruses are the only influenza viruses known to cause flu pandemics, i.e., global epidemics of flu disease. A pandemic can occur when a new and very different influenza. A virus emerges from a process called re-assortment that both infects people and has the ability to spread efficiently between people. Influenza type C infections generally cause mild illness and are not thought to cause human flu epidemics. Influenza D viruses primarily affect cattle and are not known to infect or cause illness in people.

Influenza A viruses are divided into subtypes based on two proteins on the surface of the virus: hemagglutinin (H) and neuraminidase (N). There are 18 different hemagglutinin subtypes and 11 different neuraminidase subtypes (H1 through H18 and N1 through N11, respectively). While there are potentially 198 different influenza A subtype combinations, only 131 subtypes have been detected in nature. Current subtypes of influenza A viruses that routinely circulate in people include: A (H1N1) and A (H3N2).

A common severe clinical manifestation of patients infected with H1N1 is severe ARDS. During recovery, pulmonary fibrosis is the major pathological change observed during recovery. In addition, abnormal pulmonary function like restrictive pattern on spirometry and decreased diffusion were observed. Even some studies showed during the recovery phase of swine flu illness patients had developed signs of small airway obstruction in addition to the above findings. In a study including pulmonary fibrosis three other pathological changes i.e., diffuse alveolar lesion, necrotizing obliterans and alveolar hemorrhage were observed which results in abnormal pulmonary function. Till now many studies have reported the long-term sequelae in patients of H1N1 who presented with severe pneumonia and ARDS. But very few studies in literature have mentioned the long-term sequelae in non ARDS and non-ventilated patients of H1N1. After recovery, even patients with mild illness due to H1N1, had persisting clinical symptoms, radiological lesions and some functional impairment was observed. So we have planned a retrospective follow up of patients who presented with persisting respiratory symptoms after recovery from H1N1 illness. Patients who were symptomatic even after recovery from H1N1 illness were assessed clinically, radiologically (HRCT) and functionally (by doing spirometry and DLCO) and long-term complications in non ARDS and non-ventilated patients of H1N1 were observed. The results of this study showed the significance of follow up of H1N1 patients after recovery from the illness. This study also provides a valuable information for future treatment and rehabilitation process in treated swine flu (H1N1) patient.

METHODS

A retrospective follow-up study was conducted in the Department of Respiratory Medicine at JLN Medical College and Hospital, Ajmer, Rajasthan, involving 50 individuals who got treated for H1N1 infection and discharged from our institution after clinical improvement but had some persisting clinical symptoms. The study was conducted from November 2018 to November 2019.

Inclusion Criteria

1. Confirmed cases of H1N1 by RTPCR and got treated for the same with oxygen, antibiotics and oseltamivir.
2. Those who are willing for the study.
3. Age group between 20 to 60 years.

Exclusion Criteria

1. Patient who got treated with ventilatory support for H1N1 infection.
2. Patients with known underlying respiratory illness like bronchial asthma, COPD and bronchiectasis.
3. Pregnant women.

After getting informed consent from the subjects, they were assessed clinically, radiologically (HRCT) and functionally (by doing spirometry and DLCO) when they presented with persisting clinical symptoms within the period of 6 to 12 months after recovery from swine flu. Detailed clinical history obtained, and a complete clinical examination done in patients present with clinical symptoms. They also underwent radiological assessment by doing HRCT to look for persisting lesion after recovery from H1N1 infection. All 50 patients underwent functional assessment by doing spirometry and DLCO to look for functional impairment.

RESULTS

50 individuals who had swine flu and who were treated for the same but had persisting clinical symptoms were assessed. The mean age of the population was 40 years.

Among 50 cases, 32 (64%) were males and 18 (36%) were females. In that 32 cases of males 8 (25%) were smokers. Most of the cases were from urban population, 36 cases (72%). Patients presented with persisting clinical symptoms within 6 to 12 months after swine flu illness were assessed. The mean duration of presentation with persisting clinical symptoms after swine flu illness was 7 months. Around 36 (72%) patients had dry cough, 30 (60%) patients had breathlessness, 14 (28%) patients had chest pain and 10 (20%) patients had chest tightness. 16 (32%) patients presented with associated co-morbidities in which most of the patients were hypertensive 6 (12%).

Total No. of Study Population	50
Mean age of Study Population	40 years
Male: Female	32:18
Smokers: Non–smokers	8:42
Urban Population: Rural Population	36:14
Mean duration of Presentation	7 months
No. of patients with Comorbidities	16

Table 1. Demographic Statistics

Clinical Symptoms	No. of Patients (n=50)
Dry cough	36 (72%)
Breathlessness	30 (60%)
Chest pain	14 (28%)
Chest tightness	10 (20%)

Table 2. Clinical Symptoms

Comorbidities	No. of Patients (n = 16)
Hypertension	6 (12%)
Diabetes mellitus	4 (8%)
Ischaemic heart disease	4 (8%)
hypothyroidism	2 (4%)

Table 3. Comorbidities

HRCT Findings	No. of Patients with Abnormal Findings (n=33)
Ground Glass Opacity	12 (24%)
Centrilobular nodules	10 (20%)
Consolidation	6 (12%)
Traction Bronchiectasis	2 (24%)
Reticular pattern	3 (6%)

Table 4. Abnormal Findings Seen in HRCT Chest

Spirometry Findings	No. of Patients (Total No. of Patients=50)
Normal	24 (48%)
Abnormal	26 (52%) Restrictive pattern – 16 (62%), obstructive pattern – 6 (23%) and mixed pattern – 4 (15%)

Table 5. Spirometry Findings

All our subjects underwent radiological assessment by doing HRCT scan for any persistent lesion after recovery from swine flu. Among 50 patients, 33 (66%) had abnormal HRCT findings. Ground glass opacity was the commonest finding observed during the follow up, seen in 12 (24%) patients, followed by centrilobular nodules 10 (20%), consolidation in 6 (12%) patients, traction bronchiectasis seen in 2 (4%) patients and reticular pattern in 3 (6%) patients.

Pulmonary function test (spirometry and DLCO) performed by all 50 patients to assess the functional impairment when they presented to our clinic with symptoms after recovery from swine flu. Out 50 patients, 26 (52%) patients had abnormal spirometry findings. Among these 26 patients, 16 (62%) had restrictive pattern i.e, FVC <80% and FEV1/FVC ratio >70%, 6 (23%) patients had obstructive pattern i.e., FEV1/FVC <70% and 4 (15%) had mixed pattern. Diffusion study was done in patients with abnormal spirometry findings. Out of 26, 12 (46%) patients had reduced diffusion capacity.

DISCUSSION

Swine flu influenza generally causes mild self-limiting illness, but a small percentage of patients developed severe pneumonia and respiratory failure. Long-term sequelae including pulmonary fibrosis may occur in treated swine flu patients after recovery. A study from China reported high levels of transforming growth factor-beta 1 (TGF-β1) in patients of swine flu pneumonia even after recovery.[3] This may be responsible for the development of pulmonary fibrosis in swine flu pneumonia survivors which lead to some pulmonary function impairment. There are very few studies that describes the long-term sequelae of swine flu pneumonia. We correlated the findings of our study with the available literatures and studies from the past.

Quispe-Laime et al presented a study of 11 swine flu patients who were followed up for 6 months. The mean age of the study population was 37 +/-9.5 years and males (73%) were predominantly affected.[4] Soraia Koppe et al conducted a study on 84 swine flu patients followed up for 3 months showed similar findings, males (63.63%) were predominantly affected and the mean age of study population was 44.27 years (+/-9.6).[5] Similar findings observed in our study also, the mean age of the study group was 40 years and males (64%) were predominantly affected.

In a study conducted by Luyt et al included 25 swine flu patients in which 45.94% were smokers.[6] Soraia Koppe et al reported 27.7% were smokers out of 84 swine flu patients.[5] We also observed similar findings in our study, 25% males were smokers.

In our study 33 (66%) patients had abnormal CT findings during 6 to 12 months follow up. Ground glass opacity (GGO) was the most common CT finding, seen in 12 (24%) patients followed by centrilobular nodules in 10 (20%), consolidation in 6 (12%), traction bronchiectasis in 2 (4%) and reticulation in 3 (6%) patients. A follow-up case study of 65 subjects of swine flu conducted by Bai L et al showed the evidence of ground glass opacity after 3 months of infection.[7] Like our study, similar findings were observed in a study conducted by Zhi – Hang Xing.[8] Out of 24 patients of swine flu followed up for 3 years, 17 (70.8%) patients had abnormal CT findings and ground glass opacity (GGO) was the predominant finding. In contrast to our study there were some findings observed in the same study like architectural distortion seen in 10 (41.7%) patients and few new findings like parenchymal bands and air trapping were observed. There was no consolidation observed in that study. The reason for additional findings may be due to long term follow up design of study (3 years).

In our study 26 (52%) patients had abnormal spirometry findings. Among these 26, the most common abnormality was restrictive pattern. Zarogoulidis[9] and Toufen et al[10] observed in their study that most of the patients had

restrictive pattern which was similar to our study. In our present study 12 (24%) patients had abnormal diffusion capacity (reduced). In a study done by Liu et al[11] in which 48 patients were followed up for 1 year, showed 26 (54%) patients had abnormal diffusion capacity. In contrast to our study, Quispe - Laime et al[4] observed that spirometry and DLCO both were normal in patients of treated H1N1 with ARDS who were followed up for 6 months. The reason may be study population was small (11 patients) and they were followed up for a short period (6 months).

The reason for this functional abnormality seen in our study may be due to underlying pulmonary parenchymal abnormality (fibrosis). Mineo G et al[12] done 4 months follow up of post ARDS patients of swine flu showed pulmonary fibrosis in 10% of cases.

CONCLUSIONS

Usually swine flu infection resolves without any residual abnormality; but some patients have respiratory symptoms and abnormal pulmonary function test even after recovery from the illness. Such patients need a proper work up and follow up which will help the patients in getting proper pulmonary rehabilitation. By doing this, it will help in improving the patients' quality of life and may prevent further worsening of lung function. Our study, emphasises the need and significance of workup and follow up of all symptomatic swine flu patients who recovered from the illness.

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