Clinico-Radiological Evaluation and Correlation of CT Chest Images with Progress of Disease in COVID-19 Patients

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Abstract

Purpose: The present study was undertaken to investigate and quantify the severity of COVID-19 infection on high-resolution chest computed tomography (CT) and to determine its relationship with clinical parameters. This study also aimed to see CT changes with clinical recovery or progression of disease.

Materials and methods: In an attempt to provide extensive information pertaining to clinical and radiological characteristics of COVID-19, the present study was undertaken in 80 hospitalized patients. The patients were COVID-19 confirmed positive by genomic analysis through RT-PCR at tertiary care center in Jaipur. Initially all patients were evaluated for their clinical parameters and then correlated with HRCT chest after hospitalization. CT findings correlated with duration of disease to assess progress or recovery.

Results: A total of 80 patients of laboratory confirmed COVID-19 test by RT-PCR at SMS Hospitals, Jaipur were assessed. Among the confirmed cases, most of patients were young adults in the fifth and sixth decade of age group with mean age of 50.40 years. There was a male preponderance (59% male and 41% female). Out of total analyzed patients, 39 patients (48.75%) were symptomatic, among them fever (79.47%), cough (74.35%), shortness of breath (36%) and sore throat (17.94%) were the most common presenting clinical manifestations. A few patients (12.82%) also had other symptoms like headache, chest pain, pain abdomen, altered sensorium etc. 54% patients had some underlying co morbid disease in sample population. The most prevalent comorbidities were Diabetes mellitus (56%), Hypertension (48.83%), COPD/K-chest (12%), CAD (9.32%) and others (11.62%) like hypothyroidism, anemia, CVA etc. The lung pathological changes were evaluated by HRCT imaging and by assigning CT severity score. We found Typical COVID findings in 50% patients, Indeterminate in 11%, Atypical in 11% and 28% patients had Negative CT chest for COVID. The clinical status of patients correlated with the CT severity score, with mild cases showing score <15/25 in 45.83% patients and severe cases showing CT severity score >15/25 in 87.50% patients. The CT features varied with duration and course of disease. Proportional GGO was higher (59.37%) in early phase and it was lower (12.5%) in later stage of disease.

Conclusion: The varied spectra of COVID-19 presentation included fever, cough, shortness of breath, sore throat etc. Diabetes mellitus, hypertension, COPD/K-Chest and CAD were found as major comorbid conditions. Symptomatic presentation of COVID-19 was observed to be higher in patients with co morbid disease, especially if multiple. HRCT chest in COVID-19 patients had a major diagnostic and prognostic importance as positive CT findings were more prominent in symptomatic patients and co-morbid patients. Clinical symptoms of patients directly correlated with CT severity index. CT imaging was found to be useful in predicting clinical recovery of patients or progression of disease.

Introduction

Since November 2019, the rapid outbreak of coronavirus disease 2019 (COVID-19), which arose from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, has become a public health emergency of international concern.[1] COVID-19 has contributed to an enormous adverse impact globally. Infection by COVID-19 can result in a range of clinical outcomes, from asymptomatic to severe life-threatening course or death. Characterization of epidemiological, clinical, co morbid features with recovery and mortality of COVID-19 is crucial for development and implementation of effective control strategies and management protocol. Current estimates are that the incubation period is generally 3 to 7 days, and up to 14 days.[2] As per literature median age of patients is 47–59 years with around 41.9–45.7% of patient population being of female gender.[3] The elderly and those with underlying diseases are more seriously ill after infection.[4] Children and infants can also be infected. On admission, many patients have reported as having at least one co morbidity with diabetes, hypertension, and cardiovascular and cerebrovascular diseases being most commonly reported conditions.[5,14] The SARS-CoV-2 is highly homologous to SARS-CoV and may cause severe illness similar clinically to SARS.[6] Symptoms resulting from COVID-19 infection in the prodromal phase includes fever, dry cough, and malaise, which are nonspecific.[4,7] Some patients may not even have any obvious symptoms. Therefore, chest computed tomography (CT), in particular high-resolution computed tomography (HRCT), represents valuable tools in identifying patients with COVID-19 infections in an early stage when clinical symptoms may be unspecific or sparse.[8-10] For every suspected patient, chest CT is indispensable for definitive diagnosis and reexamination. According to the World Health Organization and the Centers for Disease Control and Prevention guidelines, chest radiography and CT were the major diagnostic components when SARS was prevalent.[11] The clinical and imaging manifestations in the early stage of COVID-19 are particularly important. They can be used to confirm the diagnosis, adjust the treatment plan, and infer the prognosis. The purpose of our study was to characterize the clinical and HRCT features in patients with COVID-19 infection retrospectively, and to facilitate early identification and early isolation. We also aimed to explore the change in HRCT on a spectrum of duration of disease and whether there was a correlation between clinical and imaging features in the course of the illness. As in with influenza, Severe Acute Respiratory Syndrome coronavirus (SARS-CoV)[12] and Middle East Respiratory Syndrome coronavirus (MERS-CoV)[13] COVID-19 more readily predisposes to respiratory failure and death in susceptible patients.[14] Recovery and mortality of patients from COVID-19 is influenced by their respiratory system involvement and other systemic comorbidities.

Method

Study Design: The present descriptive, retrospective analysis was done on eighty COVID-19 positive patients admitted in S.M.S. Medical College Hospital, Jaipur, Rajasthan from 15th April to 5th May 2020. COVID-19 was declared a public health emergency of pandemic proportions and subsequently formal screening and diagnostic investigations for SARS-CoV-2 was initiated throughout India. Our institutional review board approved this retrospective study. Informed consent was waived as the study involved no potential risk to patients. The privacy and confidentiality of patients was observed as per norms. To ensure the quality and integrity of clinical, laboratory, and imaging data, here we included 80 patients with COVID-19 who had been admitted to our institution.

Data Collection

We retrospectively collected the clinical and chest imaging data. This included epidemiological data, clinical manifestation, co-morbidities of patients, CT chest characteristics, CT severity score. After collection of all required data and careful medical chart review, the clinical data of laboratory-confirmed patients was compiled and tabulated. The diagnosis of COVID-19 was made based on the World Health Organization interim guidance, wherein confirmed cases denoted were patients whose RT-PCR assay findings for nasal and pharyngeal swab specimens were positive.[3] The epidemiological data (age, sex, residence) was recorded and clinical data, inclusive of recent exposure history, clinical symptoms and signs, co morbidities, was obtained. All 80 patients underwent initial CT scan of chest with an average 4 days of hospitalization. The admitted patients were serially followed up for their symptomatology complex, with recovery of patients being confirmed with first negative oropharyngeal or nasopharyngeal sample by RT-PCR for COVID-19. A dedicated CT scan machine was used for scanning of COVID patients and proper disinfection protocol was followed. To assess the temporal changes of CT findings date of onset of illness of each patient and date of CT acquisition for each patient was noted. Sequential imaging was done in a few patients to look for disease progression and to guide medical therapy.

Review of CT images

Thin section CT images were acquired on a 128 slice Ingenia machine. The CT images were evaluated for the presence of ground glass haziness (seen as increased attenuation with visible broncho-vascular markings), "crazy-paving" (Ground Glass Opacities with interlobular thickening), consolidation (increased attenuation of air space opacification). The distribution of lesions centrally and peripherally, and anteriorly and posteriorly was also noted. Lesions were further characterized as having vacuolations, reverse halo sign, curvilinear bands and sub-pleural sparing. Note was also made of any additional findings such as nodules, cavities, cysts, pleural effusion and mediastinal lymphadenopathy. Any other pre-existing lung diseases such as TB, bronchiectasis, and emphysema were separately noted.

CT findings were overall classified as Typical, Indeterminate, Atypical or Negative for CT features of COVID-19 pneumonia. Typical features are those that are reported in the literature to be frequently and more specifically in COVID-19 pneumonia like bilateral, peripheral GGOs with or without consolidation or crazy paving. Indeterminate features are those that are reported in COVID-19 pneumonia specifically enough to arrive at a relatively confident radiological diagnosis like multifocal, diffuse, perihilar or unilateral GGOs. Atypical features are those that are reported to be uncommon or not occurring in COVID-19 pneumonia like lobar or segmental consolidation without GGOs or small nodules or cavitation or pleural effusion. Negative for pneumonia implies that there are no parenchymal abnormalities that can be attributed to infection.[15]

The 3 lung lobes on the right and 2 lobes on the left were individually assessed and percentage involvement of the lobe was noted based on visual assessment. Visual severity scoring of CT chest was classified as Score-1 (<5% area involved), Score-2 (5-25% area involved), Score-3 (25-50% area involved), Score-4 (50-75% area involved), Score-5 (>75% area involved), making the total score 25. A CT Severity Score was assigned out of 25 based on the percentage area involved in each of the 5 lobes.

To assess the temporal changes of CT findings date of onset of illness of each patient and date of CT acquisition for each patient was noted. Sequential imaging was done for a few patients to look for disease progression specially recovery and to guide medical therapy. In early phases, areas of pure ground glass haziness were seen with visible underlying broncho-vascular markings. The density of lesions in the intermediate and late phases of disease was higher and was seen as areas of consolidation along with few areas of pure GGOs. Both rounded and linear patterns of opacification were noted with peripheral and/or central distribution of opacities. Vacuolar sign (sign of absorption of lesion and early resolution) was also described in CT images. Curvilinear bands and sub-pleural sparing, also thought to be signs of resorption and retraction also noted. Atoll sign or reverse halo sign seen as an area of GGO surrounded by consolidation, represents a stage of organizing pneumonia. Based on time of onset of illness (time of onset of symptoms in symptomatic patients or time of positive RT-PCR in asymptomatic patients) to time of scan duration, our sample population were classified as early, intermediate and late phases. Patients were considered to be in the (I) early phase of illness if this duration was <5 days, (II) intermediate phase of illness for 5-10 days duration and late if the scan was done 11 days after the date of onset of illness.

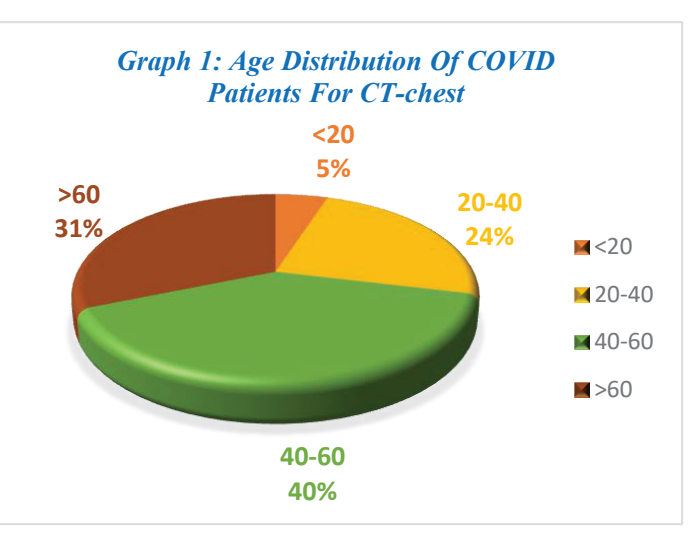
Variables: The patient characteristics were collected at baseline and confirmed cases were diagnosed based on positive viral nucleic acid test result on throat swab samples. The variables evaluated included age and gender distribution, clinical manifestations, co morbid status, CT characteristic, CT severity score, follow-up CT images and their correlation with each other and were categorized for analysis and necessary preventive and curative protocol was initiated. Age distribution graphs were constructed and sex ratio (i.e., male: female [M:F] ratio) was calculated. The clinical profile of COVID-19 positive patients was evaluated in terms of percentage prevalence. Co morbid status of patients was documented as percentage prevalence of COVID-19 in such patients and its correlation with symptomatic presentation. CT images were evaluated and assigned CT severity score, CT characteristics, pattern of opacity distribution, type of opacities characteristic, characteristics of lesion and these findings correlated with symptomatology and co-morbidity of patients. Prevalence of GGO and consolidation was correlated with total radiologically positive patients in early, intermediate and late phase of disease. Proportion of symptomatic patients with their characteristic CT findings correlated with time duration of CT imaging from date of onset of illness.

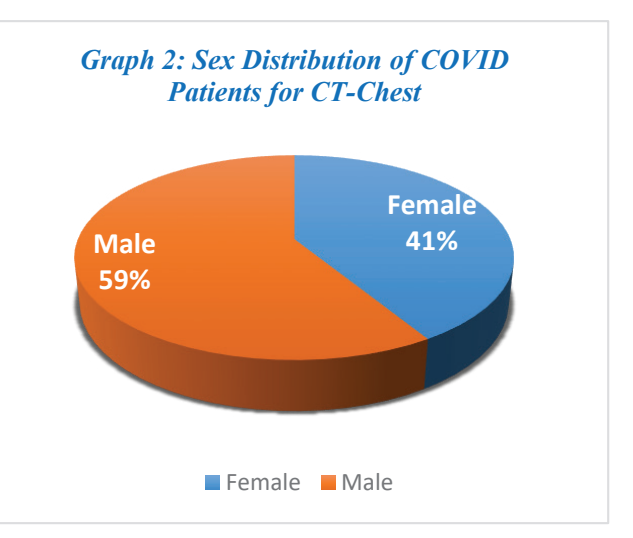
Statistical analysis

The present hospital based, observational descriptive study conducted on 80 COVID-19 patients at SMS Medical College Hospital, Jaipur to investigate epidemiological distribution, clinical manifestation, co morbid status, HRCT chest characteristics and clinic-radiological progression of disease for emerging COVID-19 infection at SMS Medical College Hospital, Jaipur, Rajasthan. The descriptive statistics for quantitative data was expressed as mean and standard deviation and qualitative data was expressed as proportions.

Results

Serial data from COVID-19 positive patients were collected, evaluated, interpreted and correlated with each other to know severity of disease by their clinical and radiological imaging in order to determine prognostic and diagnostic importance of HRCT chest. A total of 80 laboratory confirmed COVID-19 patients by RT-PCR admitted at SMS Medical College Hospital, Jaipur, Rajasthan till 5th May 2020, were assessed. In our study group most of patients in fifth and sixth decades with mean age 50.40 year. Percentage distribution of patients according to age group was found as <20 year 5%, 20-40 year 23.75%, 40-60 year 40%, >60 year 31.25% (*graph 1*). Females patients (41%) were lesser than males (59%) with an average sex ratio of female: male being 0.69 in our study (*graph 2*). Out of total analyzed patients, 39 patients (48.75%) were symptomatic while 41 patients (51.25%) were asymptomatic in our study population (*graph 3*). In symptomatic patient fever (79.47%), cough (74.35%), shortness of breath (36%) and sore throat (17.94%) were the most common presenting clinical manifestations while a few patients (12.82%) also had other symptoms like headache, chest pain, pain abdomen, altered sensorium etc. Prevalence of various clinical presentation in our study sample population distributed as fever in 39%, cough in 36.25%, SOB in 18%, sore throat in 8.75% and other manifestation in 6.25% (*graph 4*). 54% patients had some or other underlying co morbid disease in sample population (*graph 5*). The most prevalent co morbidity among sample population was noted as follow: Diabetes mellitus in 30%, Hypertension in 26.25%, Chronic obstructive pulmonary disease (COPD)/Old K-chest in 6%, Coronary artery disease (CAD) in 5% and other diseases like hypothyroidism, anemia, CVA in 6.25%. The percentage prevalence of comorbid disease among total comorbid patients were found as Diabetes mellitus in 56%, Hypertension in 48.83%, COPD/K-chest in 12%, CAD in 9.32% and other diseases in 11.62% (*graph 6*). Out of eighty patients 51 patients were found to be radiologically positive on HRCT chest imaging while 29 patients (36.25%) had normal or non-COVID CT findings. In this study, we assessed the involvement of lungs with CT chest images, in which nearly two third patients (63.75% patients) had positive CT findings while less than half of patients (48.755) were symptomatic. CT severity score of asymptomatic radiologically positive patients was found to be <5/25. The lung pathological changes were evaluated according to HRCT imaging severity score, and we found Typical COVID findings in 50% patients, Indeterminate in 11%, Atypical in 2.5% and 36.25% patients had normal CT chest findings. Among radiologically positive patients 78.43% patients had typical COVID-19 findings on HRCT chest. Symptomatic clinical presentation higher (69.23%) in patients who had Typical COVID-19 findings in CT images while it was lower in indeterminate and atypical CT findings. Percentage symptomatic presentation in COVID-19 patients with respect to CT Characteristics were found as 67.50% in Typical, 44.44% in Indeterminate, 50% in atypical and 24.13% in normal CT findings (*graph 7*). Average CT severity index had been found 8.44. Symptomatic presentation had found higher (in 87.50% patients) who had CT severity index >15/25 while symptomatic presentation lesser (only in 45.83% patients) who had CT severity index <15/25. Percentage symptomatic presentation in COVID-19 patients with respect to CT severity index were 87.50% in patients who had CT severity index 16-20, 36.36% in CT severity index of 11-15, 28.57% in CT severity index of 5-10 and 60.86% in CT severity index of 1-5 (*figure 1B*). Coincidently 38.70% symptomatic patients had zero CT severity index (*graph 8*).





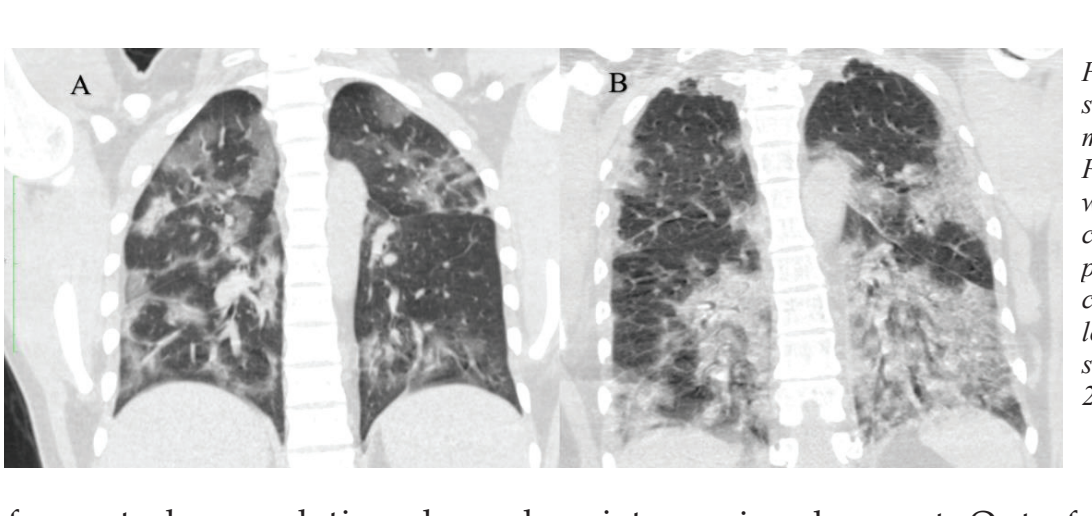
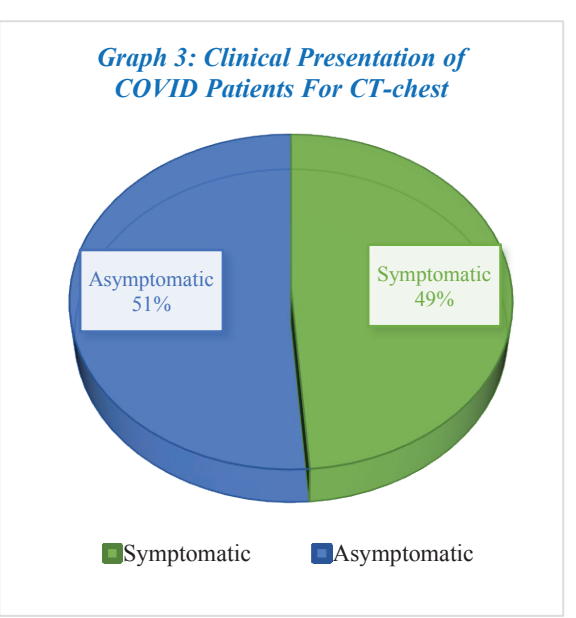
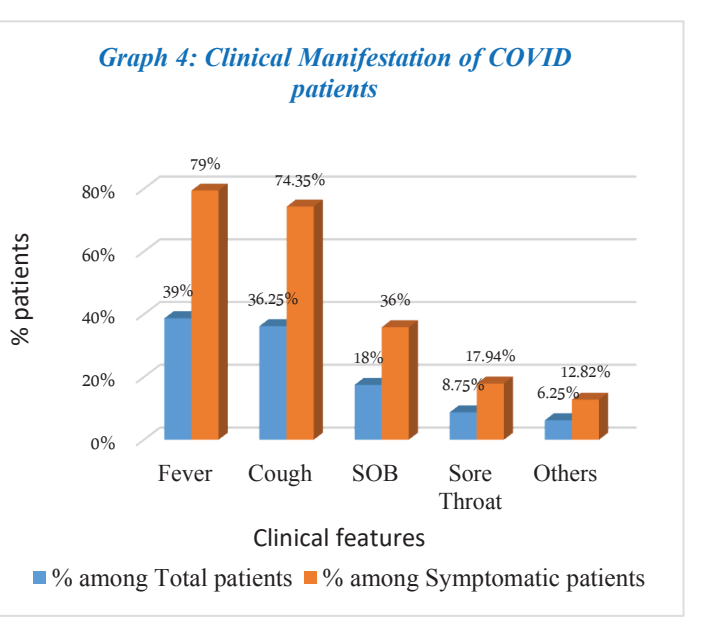
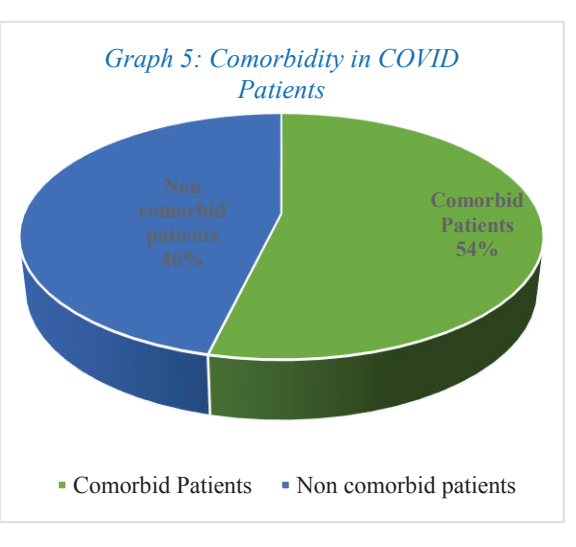


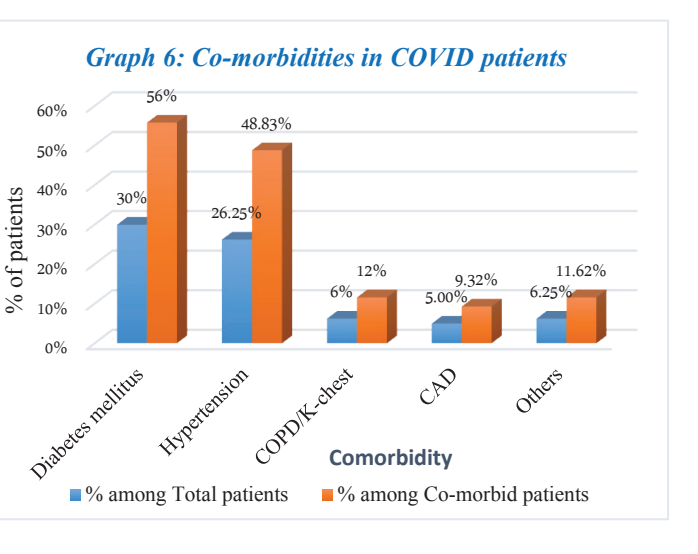
Figure 1: Coronal sections of a 56year old male patient show (A) Presence of mixed pattern with both GGO and consolidation. (B) predominance of lesions can be noted in the lower lobes in. The CT severity score in this case was 21/25

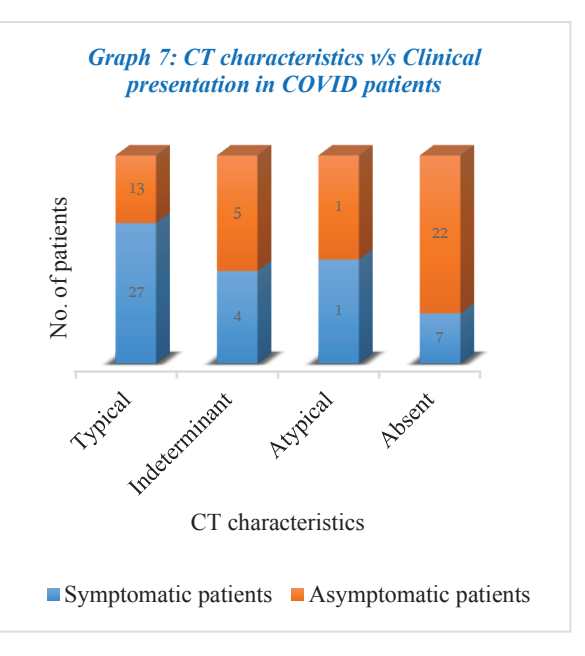
HRCT chest of our study population showed variety of opacity characteristics. Out of radiologically positive patients 25 patients (49.01%) had isolated Ground glass opacities (GGO) while another 25 patients (49.01%) had both GGO and consolidation (*figure 1A, 2*) and only one patient (1.25%) had isolated consolidation. HRCT chest had different lobe distribution of opacities in which 8 patients (10%) had only one lobe affection, 10 patients (12.50%) had two lobes affection, 4 patients (5%) had three lobes affection, 5 patients (6.25%) had four lobes affection and 24 patients (30%) had all five lobes affection while none of lobe of lungs affected in 29 patients (36.25%). In total radiologically affected 51 patients, 33 patients (64.70%) had more than two lobe affection, 39 patients (76.47%) had bilateral lung involvement. Out of study population (80 patients), 30 patients had right upper lobe involvement, 29 patients had right middle lobe involvement, 42 patients had right lower lobe involvement, 36 patients had left upper lobe involvement, 43 patients had left lower lobe involvement. Out of total radiological affected 51 patients, average 83.33% patients had predominant lower lobe involvement in COVID-19. Among study population 31 patients had predilection towards involvement of posterior surface of lung, 2 patient had anterior surface involvement while 18 patients had both anterior and posterior surface involvement (*figure 3*). Among radiologically positive patients 96.07% patients had complete or partial posterior surface affection.

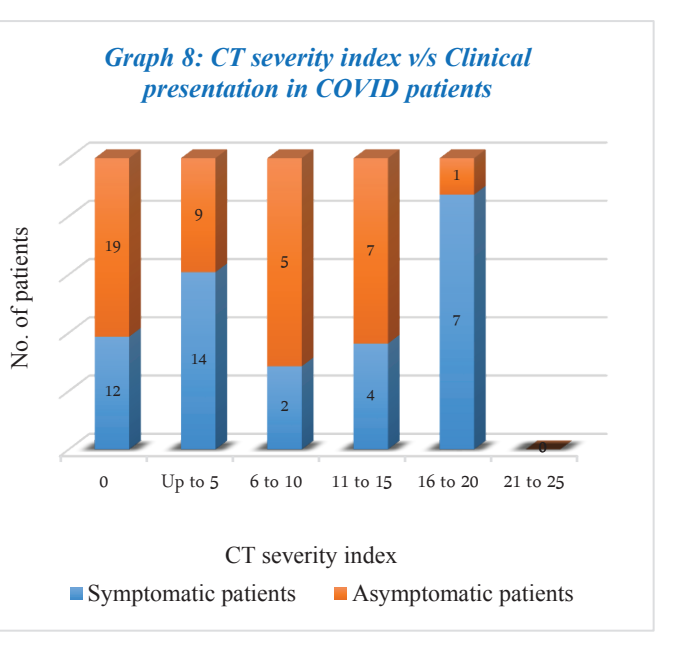












HRCT chest of study population had variable axial distribution of opacities, among them 5 patients had central distribution, 27 patients had peripheral distribution, 18 patients had both central and peripheral distribution (*figure 4*) while 1 patient had no axial distribution. Out of total radiologically affected patients, 45 patients (88.23%) had predilection towards involvement of periphery of lungs. CT chest imaging also showed some specific findings which includes pleural effusion in 6 patients (7.5%), pulmonary nodules in 6 patients (7.5%), thoracic lymphadenopathy in 19 patients (23.75%) and other nonspecific findings like granuloma, cyst, hemangioma etc. in 7 patients (8.75%) (*table 1*). In our study population CT chest done at various phase of disease with an average time duration from onset of illness to date of CT imaging was found to be 6.7 days. In this scenario 46 patients (57.5%) radiologically examined in early phase, 19 patients (23.75%) in intermediate phase, 15 patients (18.75%) in late phase of disease progression (*graph 9*). In early phase of disease (<5 days), among radiologically positive patients (32 out of 46) 59.37% patients had GGO while remaining 40.63% had both GGO and consolidation in imaging of HRCT chest. In intermediate phase of disease (6-10 days), among radiologically positive patients (11 out of 19) 45.45% patients had GGO while remaining 54.54% had both GGO and consolidation in imaging of HRCT chest. In late phase of disease (>10 days), among radiologically positive patients (8 out of 15) 12.50% patients had GGO, 75.00% patients had both GGO and consolidation (*figure 5*) while remaining 12.50% patients had only consolidation in imaging of HRCT chest (*graph 10*).

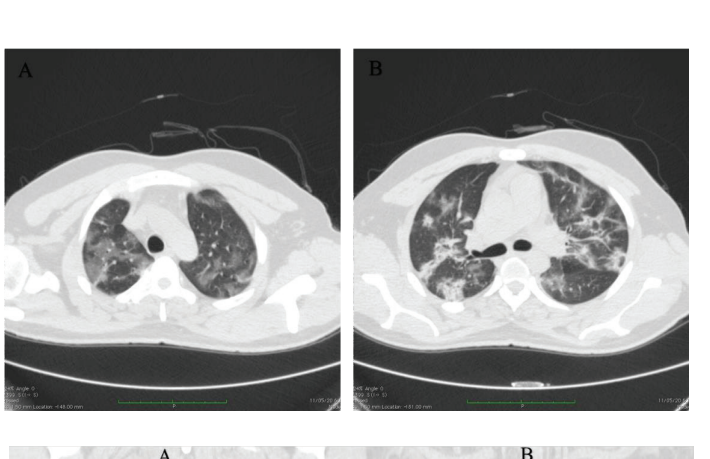


Figure 2 Axial section through the CT chest of a 42year old male patient reveals (A) ground glass opacities in bilateral upper lobes and (B) mixed consolidation and GGO pattern in the lower sections of the same patient.

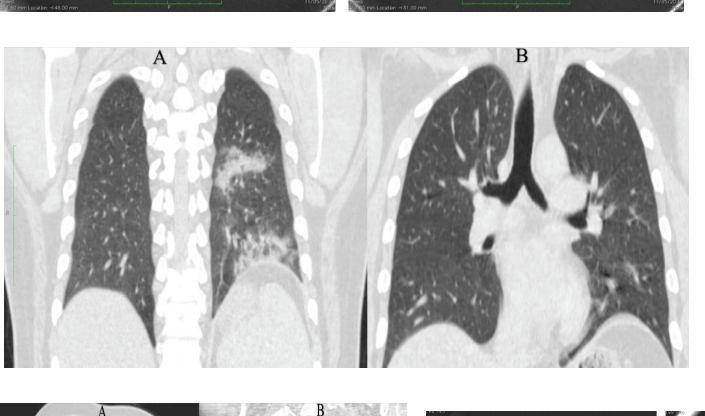


Figure 3: Coronal sections of a 52year old male patient show that (A) The lesions were mainly present in the posterior coronal section and (B) Lesion absent in the anterior coronal section.

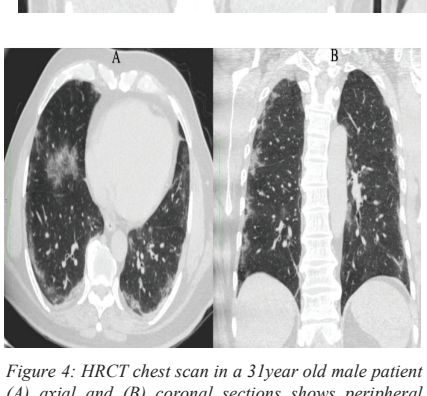


Figure 4: HRCT chest scan in a 31year old male patient (A) axial and (B) coronal sections shows peripheral areas of GGO and consolidation and sub-pleural sparing. CT severity score in this patient was 12/25.

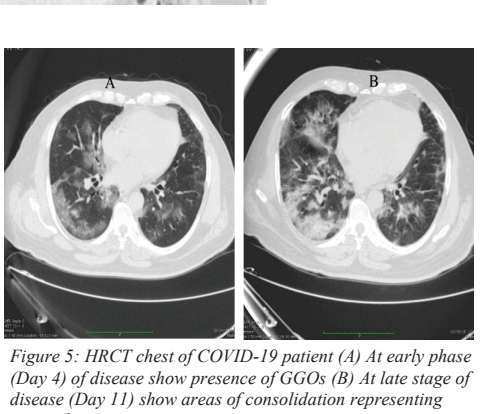
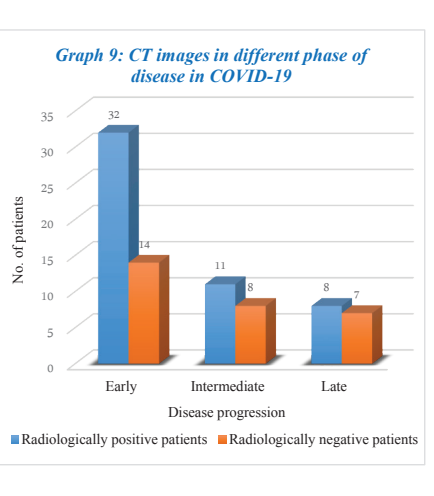


Figure 5: HRCT chest of COVID-19 patient (A) At early phase (Day 4) of disease show presence of GGOs (B) At late stage of disease (Day 11) show areas of consolidation representing signs of organizing pneumonia.



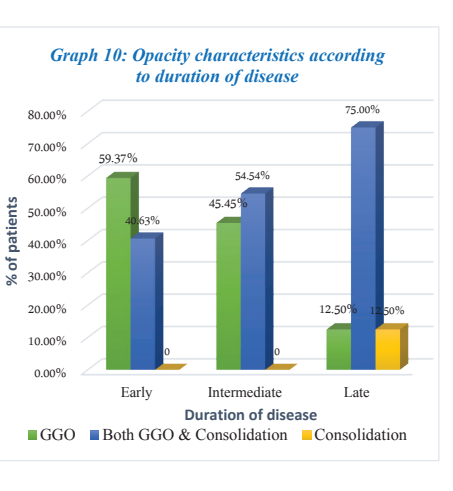


TABLE 1: IMAGING CHARACTERISTICS ON HRCT-CHEST

CT Features	Number of patients	% Among total patients (N= 80)	% Among radiologically positive patients (N=51)
Opacity distribution (Axial)			
No Axial	1	1.25%	1.96%
Central	5	6.25%	9.80%
Peripheral	27	33.75%	52.94%
Both	18	22.50%	35.29%
Underlying Lung Disease			
Pulmonary Emphysema	4	5%	7.84%
Atelectasis	4	5%	7.84%
Bronchiolitis	6	7.5%	11.76%
K-chest	4	5%	7.84%
Others	6	7.5%	11.76%
Other findings			
Pleural Effusion	6	7.5%	11.76%
Pulmonary Nodules	6	7.5%	11.76%
Thoracic lymphadenopathy	19	23.75%	37.25%
Others findings	7	8.75%	13.72%
Ground Glass Opacity & Consolidation			
Both Absent	29	36.85%	56.86%
GGO present	25	31.25%	49.01%
GGO & Consolidation both present	25	31.25%	49.01%
Consolidation present	1	1.25%	1.96%
Number of Lobe Affected			
0	29	36.25%	56.86%
1	8	10%	15.68%
2	10	12.50%	19.60%
3	4	5%	7.84%
4	5	6.25%	9.80%
5	24	30%	47.05%
>2	33	41.25%	64.70%
B/L Lung Disease	39	48.75%	76.47%
U/L	11	13.75%	21.56%
Frequency of Lobe Involvement			
Right Upper Lobe	30	37.50%	58.82%
Right Middle Lobe	29	36.25%	56.86%
Right Lower Lobe	42	52.50%	82.35%
Left Upper Lobe	36	45%	70.58%
Left Lower Lobe	43	53.75%	84.31%
Involved surface of lungs			
Anterior	2	2.50%	3.92%
Posterior	31	38.75%	60.78%
Both	18	22.50%	35.29%
CT Chest Characteristics			
• Typical	40	50%	78.4%
• Indeterminant	9	11%	17.64%
• Atypical	2	2.5%	3.92%
• Absent	29	36.25%	56.86%
CT Severity Index			
• 0	31	38.75%	
• Up to 5	23	28.75%	46.93%
• 6 to 10	7	8.75%	17.94%
• 11 to 15	11	13.75%	28.20%
• 16 to 20	8	10%	20.51%
• 21 to 25	0	0%	0%

Discussion:

The dread and specter of COVID-19 made its first appearance in Wuhan, China and it has spread like wildfire out and across precincts of China and across the globe with a pace that has taken everyone by surprise. Confirmed cases of COVID-19 is being reported from all corners of the world and subsequently World Health Organization (WHO) officially declared COVID-19 a pandemic on March 11, 2020 (16). Research is underway to understand more about transmissibility, severity, and other features associated with COVID-19.[17] The virus, SARS-CoV-2, of COVID-19 has been found to have higher levels of transmissibility with higher potential of pandemicity, as the effective reproductive number (R) of COVID-19 (2.9) is estimated to be higher than the reported effective reproduction number (R) of SARS (1.77) at this early stage.[18] The SARS-related coronaviruses are covered by spike proteins that contain a variable receptor-binding domain (RBD). This RBD binds to angiotensin-converting enzyme-2 (ACE-2) receptor found in the heart, lungs, kidneys, and gastrointestinal tract[19] thus facilitating viral entry into target cells. Based on genomic sequencing, the RBD of SARS-CoV-2 appears to be a mutated version of its most closely related virus, RaTG13, sampled from bats (Rhinolophus affinis).[20] The mutation increased the RBD affinity to ACE-2 in humans. Binding of the SARS-CoV to the angiotensin-converting enzyme 2 (ACE-2) receptors in the type II pneumocytes in the lungs triggers a cascade of inflammation in the lower respiratory tract.[21] It has been demonstrated that when the SARS spike protein binds to the ACE-2 receptor Pathogens, the complex is proteolytically processed by type 2 transmembrane protease TMPRSS2 leading to cleavage of ACE-2 and activation of the spike protein,[22] similar to the mechanism employed by influenza and human metapneumovirus, thus facilitating viral entry into the target cell. It has been suggested that cells in which ACE-2 and TMPRSS2 are simultaneously present are most susceptible to entry by SARS-CoV.[23] Early indications are that SARS-CoV-2 virus also requires ACE-2 and TMPRSS2 to enter cells.[24] Viral entry and cell infection trigger the host's immune response, and the inflammatory cascade is initiated by antigen-presenting cells (APC). The process starts with the APC performing two functions: (1) presenting the foreign antigen to CD4 +-T-helper (Th1) cells, and (2) releasing interleukin-12 to further stimulate the Th1 cell. The Th1 cells stimulate CD8 +-T-killer (Tk) cells that will target any cells containing the foreign antigen. In addition, activated Th1 cells stimulate B-cells to produce antigen-specific antibodies. It is apparent that COVID-19 infection occurs through exposure to the virus, and both immune suppressed and normal population appear to be susceptible. Some studies have reported an age distribution of adult patients between 25 and 89 years old. Most adult patients to be afflicted have been observed to be in age range of 35 and 55 years.[25] A study on early transmission dynamics of the virus has reported the median age of patients to be 59 years, ranging from 15 to 89 years, with majority (59%) patients affected being male.[26] It has been suggested that population most at risk may be people with poor immune function such as older people and those with renal and hepatic dysfunction (26).

In the present study an attempt was made to outline distribution of age, gender, clinical features at presentation, co morbidity of patients, HRCT chest findings in COVID-19 patients, severity of patients on the basis of CT imaging and their correlation with symptomatology and comorbidity of patients to put diagnostic, therapeutic and prognostic tools for COVID-19 disease. A total of 80 patients were analyzed along the course of the study. Most of COVID-19 patients of our study group in SMS Medical College Hospital, Jaipur, Rajasthan were in their fourth to sixth decades of life with mean age with a mean age of 50.40 year and male gender was affected more as compared to females, with an average sex ratio being 0.69 in our study group. In symptomatic patients, fever and cough were the most common presenting features, followed by shortness of breath, sore throat and headache while few patients also presented with chest pain and non-respiratory symptoms like pain abdomen, fatigue, joints pain, altered sensorium, etc. In our study group nearly one third of asymptomatic patients were found to be radiologically positive. This small percentage of asymptomatic COVID-19 patients, act as major carrier for transmission of virus in society, poses a real diagnostic and containment challenge for health care professionals. It was observed in the present study co morbidities have a tangible impact on clinical characteristics and course in COVID-19 positive patients. It has been observed that COVID-19 patients have circulatory and endocrine co morbidities. Patients with at least one or more co morbidity have been reported with poor clinical outcomes. In the present study population 54% patients had underlying co morbid disease with multiple co morbid diseases being was more prevalent. The most prevalent co morbidity observed in present study was Diabetes mellitus in followed by Hypertension, Chronic obstructive pulmonary disease (COPD)/Old K-chest, Coronary artery disease (CAD) and other diseases like hypothyroidism, anemia, CVA etc.

Currently the diagnosis of COVID-19 in clinic is dependent on the detection of SARS-CoV-2 nucleic acid by RT-PCR. However, it was reported that the accuracy rate is lower because it can be influenced by the viral load, the stage of the disease and the quality of specimens obtained from the upper respiratory tract.[27] The prominent radiological feature of COVID-19 is bilateral ground glass opacity in the chest CT scans.[28] In this study, we assessed the involvement of lungs with CT chest images, in which nearly two third patients (63.75% patients) had positive CT findings while less than half of patients (48.755) were symptomatic. CT severity score of asymptomatic radiologically positive patients was found to be <5/25. In present study more than three fourth of patients among radiologically positive patients had Typical CT chest images findings which includes GGO in bilateral, peripheral and lower lobe predominance distribution of opacities. Symptomatic clinical presentation higher (69.23%) in patients who had Typical COVID-19 findings in CT images while it was lower in indeterminate and atypical CT findings. Patients who had typical CT findings mostly presented symptomatically. Severity of clinical status of COVID-19 patients correlated with CT severity index, average CT severity index of our study population had been found 8.44. The clinical status of patients correlated with the CT severity score, with mild cases showing score <15/25 in 45.83% patients and severe cases showing CT severity score >15/25 in 87.50% patients. As CT severity index raised clinical status of patients deteriorated hence this show poor prognostic indicator for COVID-19 patients. At present, the judgment of the patient's condition mainly depends on symptoms and signs, blood oxygen saturation, etc., while CT images are not used as a main reference index. When the disease develops rapidly, the probability of death is greatly increased. However, we found that CT imaging changes in some patients, especially young patients, appears before the onset of signs and symptoms due to the differences in tolerability. We scored the chest CT imaging and found that clinically severe patients showed higher CT imaging score compared to that in non-severe patients. These data suggested that CT imaging score may be an informative indicator to predict the severity of the disease. In the early stages, single or multiple small ground glass infiltration, consolidation, and interstitial thickening could be seen. As the disease progressed, severe cases had more consolidation and air bronchograms in the involved lobes. The diffuse lesions, shown as "white lungs," were seen in the most severely affected patients. Fibrous bands could be seen during the remission stage. The distribution manners, together with the GGOs, are very characteristic and impressive. Cautious attention to symptoms and CT examination, are helpful for early detection of COVID-19 infection. Especially for those who were unaware of the concealed discomfort, HRCT can assist clinicians and epidemic workers with finding potentially infectious patients. However, the Fleischner Society guidelines suggested that imaging is not routinely indicated in asymptomatic or mildly symptomatic patients of COVID-19. This was corroborated by our study where 29/80 patients who were asymptomatic or who underwent CT in early phase of the disease showed no CT features of COVID-19 pneumonia.

HRCT chest of our study population showed variety of opacity characteristics, among radiologically positive patients nearly half of patients showed typical GGO while another half showed mixed pattern of GGO and consolidation. Mostly early CT on admission characterized by GGO and in late stage consolidation tends to be more dominating than GGO. The distribution of these lesions in our study was mostly peripheral and posterior involving the lower lobes more frequently. The predilection for these areas has also been reported previously. In patients who were imaged in the later stage of disease, findings such as vacuolations within opacification, linear consolidation and reverse halo sign were seen suggesting organization of the underlying disease process. Subsequently, subpleural sparing and curvilinear bands appeared likely due to retraction process suggesting resolution stage. In our experience, even if the total percentage area of lung involved remained the same, appearance of features such as vacuolation, subpleural sparing and curvilinear band formation indicated resorption stage and even corroborated with clinical features of improvement. A long-term follow-up of these patients should be done to assess if these findings completely resolve or some evidence of fibrotic changes persists.

The data collected at our hospital indicates that CT findings vary according to the time of scan from the onset of illness. This concurs with the results observed by Bernheim et al and Pan et al who suggested progression of disease in the form of GGOs in early stage to "crazy-paving" and consolidation in later stages. In addition, the CT findings also correlate with clinical status, showing a higher CT severity score in clinically worse patients. Thus, the percentage involvement of lung and CT severity score can help prognosticate and tailor the clinical management of patients. In radiologically positive patient multiple lobe affection by COVID-19 has been more popular compare to other bacterial or lobar pneumonia, among them nearly two third patients had more than two lobe involvement with bilateral lung affection in 76% patients. Most of radiologically positive COVID-19 patients (96%) had complete or some posterior surface involvement while nearly one third patients had mixed involvement of anterior and posterior surface of lung. As per view of axial distribution most of patients (nearly 88%) had peripheral distribution of opacities in COVID-19 positive patients. CT chest imaging also showed some specific findings which includes pleural effusion, pulmonary nodules, thoracic lymphadenopathy and other nonspecific findings like granuloma, cyst, hemangioma etc. In present study duration of disease correlated with CT chest characteristics and CT severity index. In these patients average CT severity index remained same in each phases of disease while opacities characteristics especially GGO and consolidation varied in different phases of disease. GGO, a characteristic feature of initial stage of disease found maximum in early phase of disease while in intermediate and late phase of disease proportional pure GGO reduced. In intermediate phase nearly half of patients had both GGO and consolidation on CT images while rest half had pure GGO pattern. In late stage nearly three fourth patients had both GGO and consolidation while remaining patients had pure GGO or consolidation in equal proportion. These characteristic changes were in favor of resolving pneumonia. No significant difference was observed in distribution of opacities and involvement of particular lobe or surface with progression of disease.

Conclusion

The varied spectra of COVID-19 presented with fever, cough, shortness of breath, sore throat etc. Diabetes mellitus, hypertension, COPD/K-Chest and CAD were found as major comorbid condition. Clinical severity of disease was higher in patients that had underlying co morbid disease, especially in patients with multiple co morbid conditions. HRCT chest in COVID-19 patients had major diagnostic and prognostic importance as positive CT findings more prominent in symptomatic patients and co-morbid patients. CT severity index also directly correlated with clinical symptoms of patients. CT imaging useful to see clinical recovery of patients. The results of this study confirmed that chest CT is important in the diagnosis and management of the COVID-19 infection. Despite meticulous treatments, most patients demonstrated progressions in the early stage from illness onset, according to the follow-up CT examinations. Our clinical findings show that radiological features positively correlate with the severity of lung abnormalities quantified on initial CT. Being familiarized with the clinical and CT features and the early changes of the COVID-19 infection is of paramount importance.

Limitations: This study has some limitations. First, this is a modest-sized case series of patients admitted to the hospital. At the time of data collection, RT-PCR tests for the diagnosis of COVID-19 had been available only for suspected patients. Besides, we only included hospitalized patients for their clinical and CT correlation with follow- up CT examinations to ensure more information on clinical and CT characteristics. Possible selection bias should be noted, and further study of a larger cohort is required to obtain a definitive answer. Second, the quantitative and semiquantitative methods for measuring the pulmonary lesions may have certain subjectivity. Third, the susceptibility of COVID-19 was considered (initially and incorrectly) to be very low among infants, children, and adolescents, so we did not retrospectively study these groups. Fourth CT imaging not be possible in severely or critically ill patients. More effort should be made to identify the clinical and imaging features in these groups in future studies.

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Author contributions: S. Bhandari, A. Singh and G. Rankawat formulated the research questions, designed the study, developed the preliminary search strategy, and drafted the manuscript; M. Bagarhatta and Aparna Singh do HRCT chest and radiological examination of patients. S. Bhandari, G. Rankawat, M. Bagarhatta refined the search strategy by conducting interative database queries and incorporating new search terms; G. Rankawat, Aparna Singh, V. Gupta collected and analysed data; S. Bhandari and A. Singh, conducted the quality assessment. All authors critically reviewed the manuscript for relevant intellectual content. All authors have read and approved the final version of the manuscript.

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References

1. WHO main website. https://www.who.int (accessed March 10th, 2020)
2. Sun K, Chen J, Viboud C. Early epidemiological analysis of the coronavirus disease 2019 outbreak based on crowdsourced data: a population-level observational study. *The Lancet Digital Health*. 2020
3. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020. https://doi.org/10.1056/NEJMoa2001316 [Epub ahead of print].
4. yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med*. 2020.
5. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020. doi: 10.1016/S0140-6736(20)30211-7
6. Gorbalenya AE. Severe acute respiratory syndrome-related coronavirus–the spe- cies and its viruses, a statement of the coronavirus study group. *BioRxiv*. 2020.
7. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020.
8. Fang Y, Zhang H, Xie J, et al. Sensitivity of chest CT for COVID-19: comparison to RT-PCR. *Radiology*. 2020;200432.
9. Xie X, Zhong Z, Zhao W, et al. Chest CT for typical 2019-nCoV pneumonia: re- lationship to negative RT-PCR testing. *Radiology*. 2020;200343.
10. Shi H, Han X, Jiang N, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet Infect Dis*. 2020.
11. WHO. Preliminary clinical description of severe acute respiratory syndrome. Available at: https://www.who.int/csr/sars/clinical/en/. Accessed March 21, 2003.
12. Booth CM, Matukas LM, Tomlinson GA, et al. Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area. JAMA. 2003;289:2801-2809
13. Alqahtani FY, Aleanizy FS, Ali Hadi Mohammed R, et al. Prevalence of comorbidities in cases of Middle East respiratory syndrome coronavirus: a retrospective study. Epidemiol Infect. 2018;5:1-5
14. Huang C, Wang Y, Li X, et al. Clinical features of patients with 2019 novel coronavirus in Wuhan, China. Lancet. 2020; doi: 10.1016/S0140-6736(20)30183-5
15. ref: simpson S, Kay FU et al. Radiological Society of North America Expert Consensus Statement on Reporting Chest CT Findings Related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology. Radiology: cardiothoracic imaging.
16. Coronavirus (COVID-19) events as they happen (n.d.). https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen(Accessed 20March2020).
17. CDC. 2019 Novel coronavirus, Wuhan, China. 2020. https://www.cdc.gov/ coronavirus/2019-nCoV/summary.html. Accessed 1 Feb 2020.
18. Liu T, Hu J, Kang M, Lin L, Zhong H, Xiao J, et al. Transmission dynamics of 2019 novel coronavirus (2019-nCoV). 2020; doi: https://doi.org/10.1101/2020. 01.25.919787.
19. Ksiazek, T.G.; Erdman, D.; Goldsmith, C.S.; Zaki, S.R.; Peret, T.; Emery, S.; Tong, S.; Urbani, C.; Comer, J.A.; Lim, W.; et al. A Novel Coronavirus Associated with Severe Acute Respiratory Syndrome. N. Engl. J. Med. 2003, 348, 1953–1966. [CrossRef] [PubMed]
20. Andersen, K.; Rambaut, A.; Lipkin, W.I.; Holmes, E.C.; Garry, R.F. The Proximal Origin of SARS-CoV-2. Available online: http://virological.org/t/the-proximal-origin-of-sars-cov-2/398 (accessed on 25 February 2020).
21. Kuba, K.; Imai, Y.; Rao, S.; Gao, H.; Guo, F.; Guan, B.; Huan, Y.; Yang, P.; Zhang, Y.; Deng, W.; et al. A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus–induced lung injury. Nat. Med. 2005, 11, 875–879. [CrossRef] [PubMed]
22. Glowacka, I.; Bertram, S.; Muller, M.A.; Allen, P.; Soilleux, E.; Pfefferle, S.; Steffen, I.; Tsegaye, T.S.; He, Y.; Gnirss, K.; et al. Evidence that TMPRSS2 Activates the Severe Acute Respiratory Syndrome Coronavirus Spike Protein for Membrane Fusion and Reduces Viral Control by the Humoral Immune Response. J. Virol. 2011, 85, 4122–4134. [CrossRef]
23. Shulla, A.; Heald-Sargent, T.; Subramanya, G.; Zhao, J.; Perlman, S.; Gallagher, T. A Transmembrane Serine Protease Is Linked to the Severe Acute Respiratory Syndrome Coronavirus Receptor and Activates Virus Entry. J. Virol. 2011, 85, 873–882. [CrossRef]
24. Zhou, P.; Yang, X.-L.; Wang, X.-G.; Hu, B.; Zhang, L.; Zhang, W.; Si, H.-R.; Zhu, Y.; Li, B.; Huang, C.-L.; et al. Discovery of a novel coronavirus associated with the recent pneumonia outbreak in humans and its potential bat origin. Microbiology 2020. [CrossRef]
25. Medical expert group of Tongji hospital. Quick guide to the diagnosis and treatment of pneumonia for novel coronavirus infections (third edition). Herald Med. 2020. http://kns.cnki.net/kcms/detail/42.1293.r.20200130.1803. 002.html. Accessed 2 Feb 2020.
26. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020. https://doi.org/10.1056/NEJMoa2001316.
27. FangY,Zhang H, Xie J, Lin M,Ying L, Pang Pand JiW.Sensitivity of Chest CT for COVID-19: ComparisontoRT-PCR. Radiology.2020:200432
28. Pan F, Ye T, Sun P, Gui S, Liang B, Li L, Zheng D, Wang J, Hesketh RL, Yang L and Zheng C. Time Course of Lung Changes On Chest CT During Recovery From 2019 Novel Coronavirus (COVID-19) Pneumonia. Radiology.2020:200370.