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Spectrum of chest Computed Tomographic (CT) findings in the coronavirus disease (Covid-19) patients in Barak valley, India.

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ABSTRACT

Introduction: COVID-19 is a serious global pandemic causing widespread social disruption and increased intensive care admissions and deaths. Infections by coronavirus disease 2019(COVID-19) continue to increase in India and worldwide. The coronavirus was first reported in December 2019 in Wuhan China. Assam reported its first case of covid 19 at Silchar Medical College and Hospital on 31st March 2020, with a 52-year-old man testing positive. More than 100 COVID tests are being performed on a daily basis at Silchar Medical College.

There is varying information on human infection with coronavirus and the World Health Organization continues to monitor its developments while revising recommendations for testing and control. Basically, testing is based on clinical and epidemiological factors and linked to the assessment of the likelihood of an infection. This is a systematic meta-analysis study to evaluate the spectrum of Chest Computed Tomography (CT) findings in COVID-19 positive cases in Barak Valley, India.

Aims and Objectives: To find out the spectrum of Chest CT findings in COVID positive case series, to evaluate the advantage of chest CT in diagnosis and management of patients, and to compare the findings among patients with co-morbid conditions

Materials and Methods: In this study, we derive data from observation while addressing diagnostic accuracy and effectiveness questions. Data were collected from patients with confirmed RTPCR COVID-19 positive cases who were more than 18 years

Results: The study involved 135 adult patients with RTPCR confirmed COVID 19. The study compares severe cases that were hospitalized and non-severe cases. 12 cases progressed to severe

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disease and were older (p<0.001). Cough was the most predominant feature (p=0.011) and still the older were more likely to have higher levels of lactate dehydrogenase (LDH) (p=0.011). Chest tomography images were evident of multilobar (p=0.016), peripherally (p=0.001) distributed mixed ground-glass opacities and consolidation (p<0.001), crazy-paving pattern (p=0.007), and higher total CT severity score (p<0.001) were significantly associated with severe disease.

Conclusions: Bilateral peripheral GGOs and pulmonary consolidations are the most common features in COVID 19 pneumonia but imaging findings differ depending on stage and patient. Nevertheless, Chest CT provides an essential tool for COVID-19 pneumonia diagnosis

Keywords: COVID 19, CT, Chest CT, GGO, Coronavirus, Covid 19 pneumonia

INTRODUCTION

According to the World Health Organization (WHO) [1] coronavirus involves a group of viruses belonging to the family of Coronaviridae and can affect humans and animals. Signs and symptoms in mild cases include respiratory symptoms such as fever, cough, and shortness of breath while in severe cases pneumonia, severe acute respiratory syndrome, and sometimes death. There are two types of tests done to detect coronavirus, the diagnostic test, and the antibody tests. The diagnostic test shows whether a patient has active coronavirus infection and includes two types, the molecular (Real-time reverse transcription-polymerase chain reaction [RT-PCR]) test that detects the virus genetic material and the antigen test that detects specific proteins on the surface of the virus. The antibody test looks for antibodies that are released by the immune system in response to a pathogen such as a specific virus to fight infections. However,

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antibodies can take several days or weeks to be released after infection and may remain in the body after recovery. Therefore, antibody tests cannot be used to diagnose an active coronavirus infection (U.S Food and Drug Administration [FDA] [2]

In case a patient meets the suspect case, COVID-19 testing should be carried out. Also, patients should be tested for other respiratory pathogens using routine laboratory procedures. PCR testing of either asymptomatic or mildly symptomatic contacts may be considered during the assessment of individuals who have had contact with a COVID-19 case. On the other hand, Computed Tomography (CT) of the chest plays a critical role in the diagnosis and management of COVID-19 but should not be used indiscriminately [3]. Chest CT findings can precede positivity on RTPCR and together with patient history and laboratory values, it can help to predict critical illness in hospitalized patients. However, Chest CT is not indicated as a routine screening modality due to its poor sensitivity and specificity although it is useful in a small subset of COVID-19 suspects who test negative on RTPCR or those with pneumonia. The hallmark CT manifestations of Covid19 include bilateral and peripheral ground glass and consolidative pulmonary opacities, sometimes with a rounded morphology and peripheral lung distribution. As the time between the onset of symptoms and initial chest CT increases, some CT findings are observed with increasing frequency, including consolidation, bilateral and peripheral lung disease, greater total lung involvement, linear opacities, and the appearance of the crazy-paving pattern. Certain chest CT findings including pleural effusions, lymphadenopathy, pulmonary nodules, and lung cavitation are characteristically absent, and many patients imaged quickly after the onset of symptoms has a normal CT scan.

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Pneumonia is the main clinical manifestation in COVID-19 patients. RT-PCR is an important test in diagnosis, however, due to its limited sensitivity, further radiological examinations should be carried out. RT-PCR is performed by nasopharyngeal swab but it has high rate of false-negative results, therefore chest computed tomography is preferred in case of COVID-19 pneumonia suspicion. Comorbidities such as COPD, hypertension and diabetes complicate COVID-19. Older adults and patients with underlying comorbidities show poor prognoses. The majority have increased morbidity and mortality rates associated with more hospitalization and admission into the intensive care unit (ICU). Furthermore, patients with chronic obstructive pulmonary disease (COPD) or any respiratory illness are at a higher risk for severe COVID-19 illness and the risk for contracting COVID-19 is also higher [5]. Such comorbidities may affect lung inflammation and a chest CT scan can quickly and effectively diagnose pneumonia

Materials and Methods

The study was carried out in the Department of Radiology, Silchar Medical College & Hospital, Silchar. The hospital is situated in the Cachar district of Barak Valley in the state of Assam, India. A tertiary and referral centre for the patients of different districts of Barak Valley of Assam and nearby north-eastern states.

Study Design: A systematic review study

Period of Study: The study began on 31-03-2020 until enough data was gathered for a valid conclusion

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Source of Data: Data was collected from RTPCR COVID 19 confirmed positive patients referred from COVID-19 screening and COVD-19 positive wards of Silchar Medical College with respiratory symptoms. In all cases, history taking and physical examination were done.

Inclusion criteria: Patients with RTPCR confirmed COVID-19 positive cases and patients of age more than 18 years

Exclusion criteria: Patients with previous lung pathologies, patients in whom CT scan is a contraindication (for instance pregnant patients and patients not giving consent for the examination.

TECHNIQUE:

HRCT scans were acquired using Philips 128 Slice Ingenuity Elite CT scanner at the Radiology Department of Silchar Medical College & Hospital. HRCT scans will be acquired in volumetric mode scanning extending from the thoracic inlet to caudally including the upper abdomen. Patients are imaged in a supine position in suspended deep inspiration with arms extended overhead to reduce artefact. The scans are acquired in axial view and reformatted to obtain sagittal and coronal views. Modifications like expiratory films and prone scans were used as whenever needed.

RESULTS

The study involved a total of 135 cases of confirmed COVID-19 patients with a mean age of 39+/- years ranging from 18-64 years. 66 were female representing 48.9% and 69 males representing 51.1% of the total number of patients. 30 patients had a history of contact with a case of COVID 19 patient. The most common symptoms were fatigue at 46.7%, sore throat at

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33.3%, cough at 31.1%, and fever at 26.7%, and headache at 26.7%. There was one patient who presented with diarrhoea without fever. 75 patients representing 55.6% had abnormal laboratory results with the most common abnormalities being lymphopenia at 33.3%, elevated C-reactive protein (CRP) level at 48.9%, and lactate dehydrogenase (LDH) at 33.3%

Table 1 : Laboratory blood test results

Laboratory results	All patients ($n = 135$)	Non-severe group ($n = 123$)	Progress-to-severe group ($n = 12$)	*P* value*
Hemoglobin (g/dL) Decreased-n (%)	13.8+/-1.8 69(53.3)	– 66 (59.1)	– 3(25)	– 0.116
White blood cell count (×10^9/L) Increased- n(%) Decreased-n(%)	5.4+/-1.7 3(2.2) 24(17.8)	- 3(2.4) 21(17.1)	- 0 3(25)	- 0.230 0.805
Neutrophil count (×10^9/L) Increased- n (%) Decreased-n (%)	2.94 (1.34-7.71) 9(6.7) 18(13.3)	- 9(7.3) 15(12.2)	- 0 3(25)	- 0.232 0.470
Lymphocyte	1.6+/-0.6	-	-	-

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count (×*10*^{9}/*L)*				
Decreased-n (%)	45 (33.3)	39 (31.7)	6 (50)	0.403
Monocyte count (×*10*^{9}/*L)*	0.4 (0.11-2.33)	-	-	-
Increased- n (%)	6 (4.4)	6 (4.9)	0	0.210
Decreased –n (%)	30 (22.2)	27 (22)	3 (25)	0.813
Platelet count (×*10*^{9}/*L)*	198.5 +/- 61.6	-	-	-
Decreased- n (%)	24 (17.8)	24 (19.4)	0	0.193
C-reactive protein (mg/L)	4.40 (0.33-34.30	-	-	-
Increased- n (%)	66 (48.9)	57 (46.3)	9 (75)	0.058
Alanine aminotransferase (U/L)	24 (10-66)	-	-	-
Increased-n (%)	24 (17.8)	24 (19.5)	0	0.085
Aspartate aminotransferase (U/L)	19 (8-141)	-	-	-
Increased –n (%)	15 (11.1)	15 (12.2)	0	0.228

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Bilirubin (µmol/L) Increased –n (%)	0.36 (0.16-1.45) 3 (2.2)	- 3 (2.4)	- 0	- 0.222
Urea (mmol/L) Increased-n (%)	26.6+/- 3 (2.2)	- 3 (2.4)	- 0	- 0.241
Lactate dehydrogenase (U/L) Increased-n (%)	217.9+/-63.7 45 (33.3)	- 36 (29.3)	- 9 (75)	- 0.011

*p-value≤0.05[18]

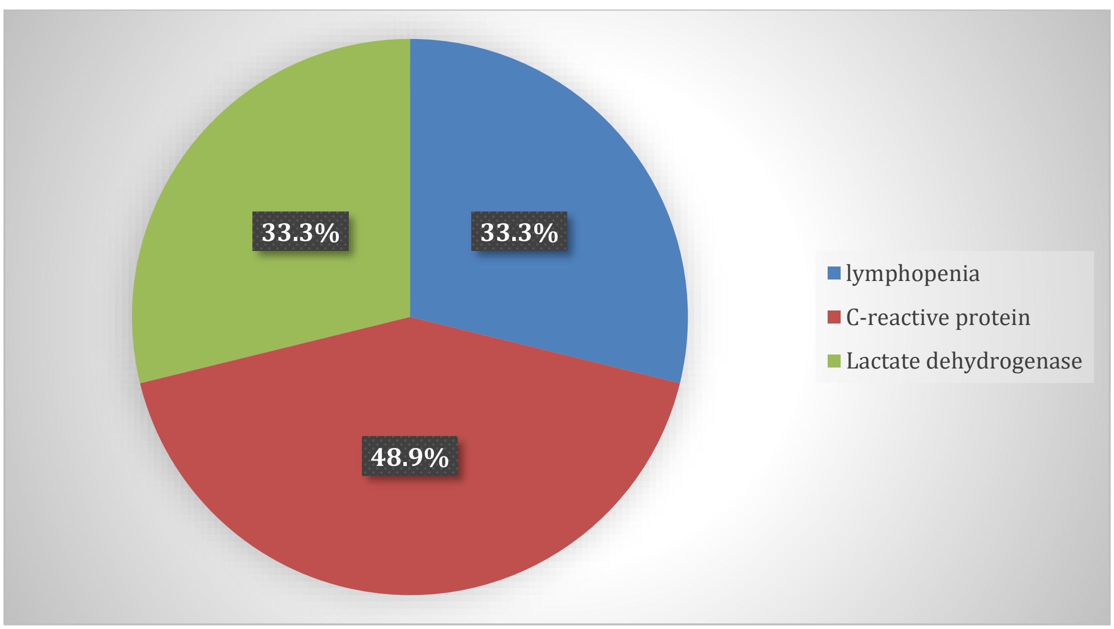

Fig 1 : Abnormal laboratory results

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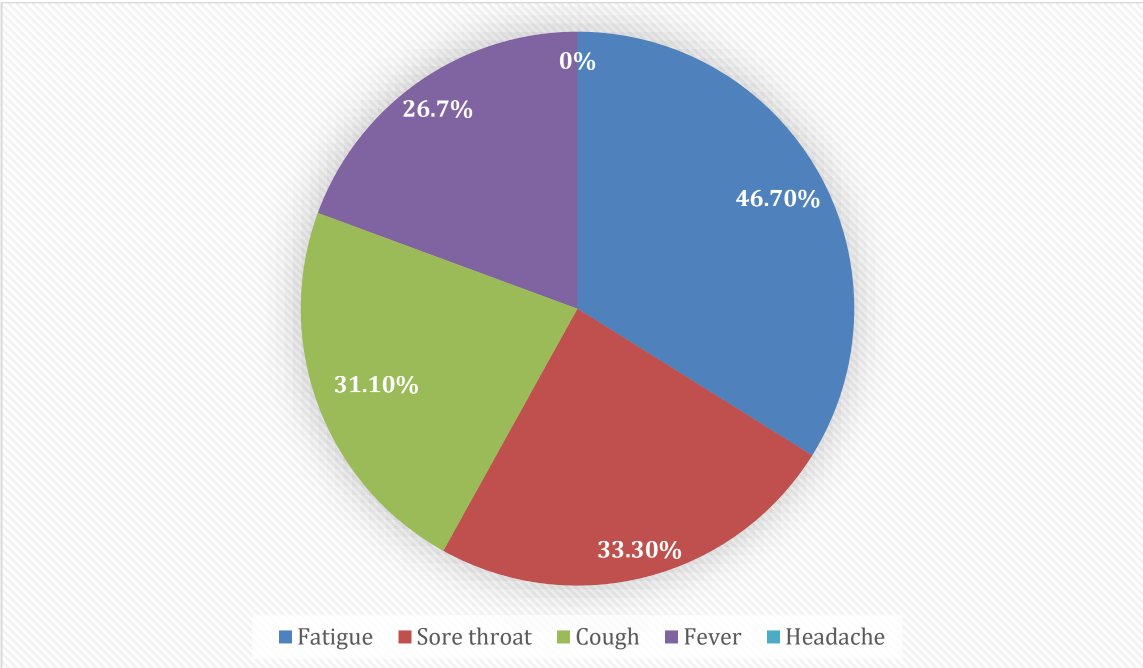

Fig 2 : Common presenting symptoms

A total of 30 patients were hospitalized and placed under isolation while others were recommended to undertake home-based care but were followed as an outpatient. Treatment was commenced following the guidelines provided by the Ministry of health. However, during hospitalization, 12 (8.9%) of the patients developed respiratory distress and progressed to severe illness. The remaining 123 (91.1%) were included in the non-severe patient group. Patients who progressed to severe disease were older than 59+/-5 years ranging between 56-67 years, p<0.001, and more likely to have a cough (p=0.011). LDH levels were found to be higher in people who progress to the severe group. However, no significant difference was found in other clinical and laboratory findings between severe and non-severe groups.

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Furthermore, pulmonary parenchymal abnormalities were visualized on 75 (55.6%) CT scans although 60 cases were negative for pneumonia. The typical appearance was detected in 57 cases, intermediate appearance in 9 cases, and atypical appearance in 9 cases. Ground-glass opacities were the first to be detected, 53.3%, followed by consolidations with ground-glass opacities, 33.3%. Parenchymal lesions showed typical multilobar peripheral involvement with the affection of lower zones of the bilateral lungs. There were no pleural effusion, cavitary lesions, or pathologic mediastinal lymph nodes detected. Nevertheless, as atypical appearances, isolated lobar consolidation was detected in 1 case, and solitary ground-glass nodules in 8 patients. The mean CT-SS of the study in all patients was found to be 1.98+/-2.2 (0.8). Patients who progressed to severe disease were more likely to have CT abnormalities including peripheral distribution (p=0.001), multilobar involvement (p=0.016), and GGO with consolidation (p<0.001). It was also evident that the CT severity score was higher in the progressive group than in the non-severe group (p<0.001).

Table 2: A Summary of CT findings between non-severe and the progress to severe group

Parenchymal lesions at baseline chest CT	All patients $n = 135$ *n (%)*	Non-severe $n = 123$ *n (%)*	Progress-to-severe $n = 12$ *n (%)*	*P* value*
COVID 19 Pneumonia	75 (5.6)	63 (51.2)	12 (100)	-

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positive				
Imaging-based classification system				
Negative for pneumonia	60 (44.4)	-	-	-
Typical appearance	57 (42.2)	48 (39)	9 (75)	
Intermediate appearance	9 (6.7)	6 (4.9)	3 (25)	
Atypical appearance	9 (6.7)	9 (7.3)	9 (75)	

Table 3: Morphology of parenchymal lesions

Ground-glass opacities	72 (53.3)	60 (48.8)	12	0.001
With consolidation (mixed)	45 (33.3)	33 (26.8)	12 (100)	<0.001
Pure ground-glass opacities	27 (20)	27 (22)	0	0.060

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Crazy-paving pattern	2 (1.5)	0	2 (16.7)	0.007
Isolated lobar consolidation	1 (0.7)	1 (0.8)	0	0.911
Solitary ground-glass nodule	8 (5.9)	2 (1.6)	0	0.830
Location of parenchymal lesions				
Unilobar	18 (13.3)	15 (12.2)	3 (25)	0.201
Multilobar	57 (42.2)	48 (39)	9 (75)	0.016
Right lung involvement	15 (11.1)	12 (9.8)	3 (25)	0.084
Left lung involvement	6 (4.4)	3 (2.4)	3 (250	0.566
Bilateral involvement	54 (40)	48 (39)	6 (50)	0.328
Distribution of parenchymal lesions				
Peripheral predominant	60 (44.4)	48 (39)	12 (100)	0.001

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Peripheral and perihilar	15 (11.1)	15 (12.2)	0	0.199
Lower zone predominant	60 (44.4)	54 (43.9)	6 (50)	0.685
No zonal predominance	12 (8.9)	9 (7.3)	3 (25)	0.075
CT Severity score	1.98+/- 2.2 (0-8)	1.68+/- 1.92 (0-6)	5+/- 2.66 (1-8)	<0.001

*p-value≤0.05

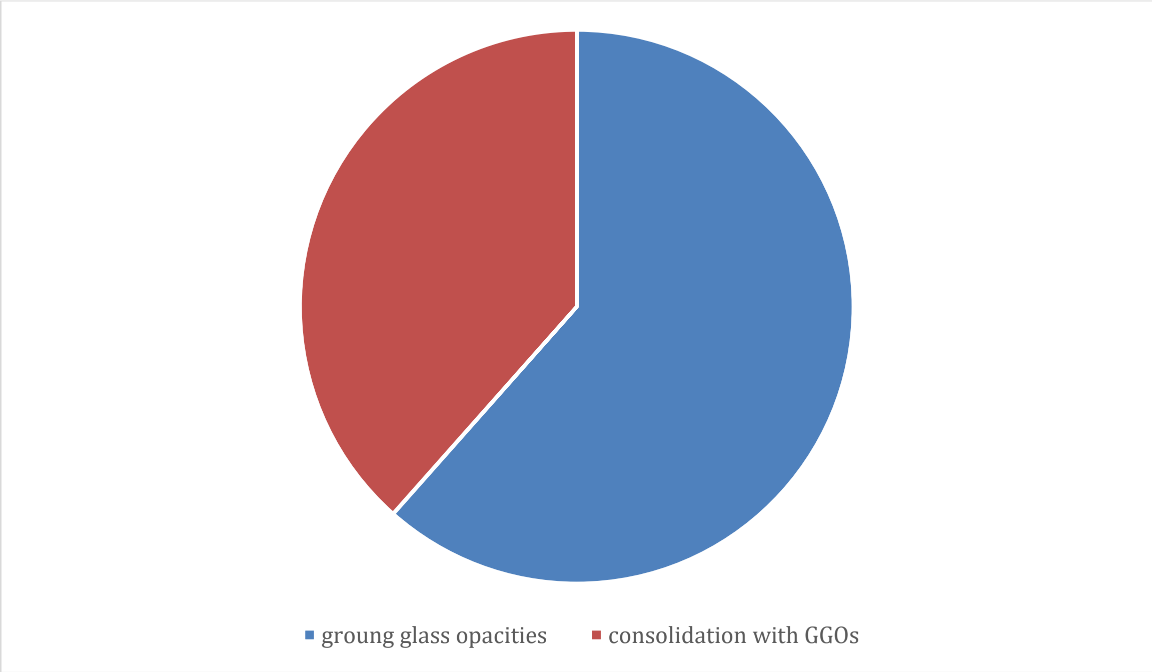

Fig 3: Most common CT findings

OBSERVATIONS

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According to the WHO [8], coronavirus disease, also referred to as COVID 19, is an infectious disease caused by the SARS-CoV-2 virus. The most common symptoms are mild-moderate respiratory illness and people recover even without specialized treatment. However, older people and those with underlying medical conditions such as hypertension, cardiovascular disease, diabetes, chronic respiratory disease, or cancer are likely to develop serious illnesses. COVID 19 is highly contagious and people need to be well-informed about the disease and its management. People should protect themselves and those that suspect to have contracted COVID 19 should get tested. The World Health Organization continues to monitor the development and revise recommendations and the decision to test should be based on clinical and epidemiological factors and linked to an assessment of the likelihood of an infection. The incubation period for COVID 19 is between 1 and 14 days and the most common manifestation is pneumonia. Pneumonia may be complicated by acute respiratory distress syndrome (ARDS) which can cause acute respiratory failure and exitus [4]. RT-PCR was the main test done but given the high rate of false-negative results, chest computed tomography has been suggested as an alternative as well as a reliable tool for detecting COVID 19.

CT is a computerized x-ray imaging procedure where a beam of x-rays is aimed at the patient and quickly rotated around the body to produce signals that are then processed by the machine's computer to generate cross-sectional images referred to as slices. The slices are termed tomographic images that provide more detailed information than conventional x-rays. The clinicians collect a number of successive slices that can be stacked together to form a three-dimensional (3D) image of the patient to allow for easier identification of basic structures including tumors or abnormalities. The technique does not use a fixed x-ray tube but rather a

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motorized x-ray source that rotates around the circular opening of a donut-shaped structure referred to as a gantry. The patient lies on the bed that slowly moves through the gantry while the x-ray tube rotates around the patient while shooting narrow beams of x-rays through the body. The scanners have special digital x-ray detectors located directly opposite the x-ray source. X-rays leaving the patient are picked up by the detectors and transmitted to the computer [9]

Chest CT can detect abnormalities in the lung segment and can establish disease severity. The most common distribution pattern is bilateral lung involvement at 79% followed by peripheral and diffuse distributions at 54 and 44 % respectively. A typical CT pattern is usually characterized by a bilateral distribution of ground-glass opacities (GGO) that can be accompanied by consolidations in the posterior and peripheral lung fields. GGO is the areas of misty pulmonary opacity that have a conservation of parenchymal architecture caused by the thickening of the alveolar septa due to the inflammatory process. A patient who has COVID 19 pneumonia presents with unilateral and bilateral GGO as the common CT findings [4].

The imaging findings in COVID 19 patients resemble other viral pneumonia with the main feature being ground-glass opacities with a peripheral and basal predominance as the key manifestation. The GGOs gradually transform into consolidations during the intermediate stage as the peak finding peaks at around 9-13 days after the onset of the symptoms. Consolidations occur with the development of interlobular septal thickening leading to characteristic crazy paving patterns. In most cases, clinical recovery is linked to the gradual resorption of pulmonary opacities with the development of subpleural lines, reticulations, fibrous stripes, and perilobular opacities clearly visible after the second week. However, in some patients, the condition deteriorates to develop extensive lung opacities that cause acute respiratory distress syndrome

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(ARDS) that can cause of death. Apart from ARDS, patients with COVID 19 pneumonia can also be complicated by pulmonary embolism which is the main cause of death in addition to pleural effusion, pericardial effusion, and mediastinal lymphadenopathy in severe disease [6].

The main observation from the study is that bilateral, peripheral, and basal *ground-glass opacities* with multilobar involvement are the initial CT manifestations of COVID 19 pneumonia. In GGO, the lungs are highly attenuated making it possible to see vascular and bronchial structures. It results from the partial filling of alveoli with fluid, blood, or cells or as a result of pulmonary interstitium thickening and GGO can be patchy or confluent, rounded or elongated. On the other hand, *the crazy-paving pattern* involves GGO that has superimposed interlobular thickening on a GGO area due to alveolar proteinosis resulting in a crazy pavement-like pattern. This is indicative of a transition to a progressive stage of COVID-19 pneumonia.

Consolidation refers to the increased pulmonary attenuation with obscuration of underlying vascular and bronchial structures and the air is replaced by fluids or cells while vascular structures and bronchial walls are not recognizable. Pathologically represents flooding of air-filled alveolar spaces with fluid, blood, or inflammatory cells. The area has increased density with the elimination of normal lung parenchymal architecture. Consolidations are mainly found in GGO areas while pure consolidations are not common. Consolidation in COVID 19 patients is an indication of disease progression.

Reticular pattern refers to the collection of innumerable interweaving linear or wavy shadows with a mesh-like pattern or the presence of several linear opacities with an appearance of a network due to the varying combination of interlobular and intralobular septal thickening. These CT findings are common during the resorptive phase of the COVID 19 disease after GGO.

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Fibrosis refers to the replacement of normal tissue into scar tissue. While some may identify it as a sign of recovery, some describe it as a sign of poor prognosis

Air bronchogram or airway abnormalities refer to a situation where air-filled bronchus are seen in the context of an opacity. The air is replaced by highly viscous mucus.

Subpeural curvilinear lines also referred to as the pleural lines refer to thin curvilinear opacities of about 1-3 mm in thickness and less than 1 cm from and parallel to the pleural surface

Air bubble refers to the small air-containing spaces between pulmonary infiltrates. In COVID-19, it is also referred to as round cystic changes or air bubble signs, or vacuolar signs that can be a pseudocavity signs of pre-existing changes [10]

Pulmonary nodules are abnormal growths in the lungs that are small and rounded opacities associated with a surrounding halo. It is a sign of a progressive course [11]

Halo sign is a non-specific and histopathologically representing alveolar edema and haemorrhage

The Reverse halo sign refer to the area of ground-glass haze surrounded by a complete or incomplete ring of consolidation. This is apparent in the progressive or resorptive stages of COVID-19 [7]

Pleural changes are common in patients with COVID 19 although the occurrence of pleural effusions is low [12]

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Pericardial effusions refer to a condition where extra fluid collects between the heart and the pericardium although the scope in COVID 19 is unknown. Pericardial effusion is common in hospitalized COVID 19 patients and it is rarely attributed to pericarditis [13]

Mediastinal lymphadenopathy refers to the enlargement of the mediastinal nodes a manifestation of severe COVID 19 disease.

Perilobular opacities or organizing pneumonia refers to the interstitial lung disease where the small airways also called the bronchioles and the alveoli also called the tiny air sacs become inflamed leading to difficulties in breathing and flu-like illness. It is a common manifestation in COVID 19 pneumonia patients seen through the Chest CT imaging that evolves from focal unilateral to diffuse bilateral ground-glass opacities that progress to consolidations within 1 to 3 weeks [14].

Advantages of Chest CT in diagnosis and Management of COVID-19 patients

A Chest CT scan is the most sensitive especially in the initial diagnosis of COVID 19 pneumonia. The scans have greater sensitivity and are used in disease staging. Chest CT provides a specific diagnostic test and is stratified based on the severity of the disease. It has the potential to detect COVID 19 pneumonia even in the early stage and good indicator of the infection in patients with negative viral testing but is suspected to have COVID 19 [17].

Comparing Findings among patients with co-morbid conditions

Older people and people with underlying medical conditions such as diabetes and hypertension show poor prognosis in COVID 19 disease. The patients have increased morbidity and mortality rates and are more likely to be hospitalized and admitted into the intensive care unit. COVID 19

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is also complicated by chronic obstructive pulmonary disease (COPD) or respiratory illnesses. Patients with COPD are at a higher risk for contracting COVID 19. 4 folds higher than people without COPD [16].

GGO is the most common CT manifestation in COVID 19 pneumonia patients with comorbidities. Chest CT has patchy or punctate GGO in addition to large or multiple GGO. Also, consolidation, fibrous stripes, irregular solid nodules, and irregular solid nodules and reticulation or interlobular septal thickening were seen although with less incidence. The majority of patients had 4-5 lobes involved being bilaterally distributed an indication that the lungs of these patients with comorbidities are more susceptible to viral infections [15]

Conclusion

Chest CT plays a critical role in the diagnosis, staging, and management of COVID-19 pneumonia patients and CT findings can vary depending on stages and patients. During the early phase, there is a visualization of multiple small patchy shadows and interstitial changes that show a distribution from the pleura or bronchi rather than pulmonary parenchyma. In the progressive phase, the lesions increase and enlarge forming multiple GGOs leading to consolidations in both lungs. During the severe phase, there is a visualization of massive pulmonary consolidations and lungs covered in mucus or white lungs but rare apparent pleural effusion. Finally, in the dissipative phase, the GGOs and the consolidations are not visible but the lesions begin to change into fibrosis.

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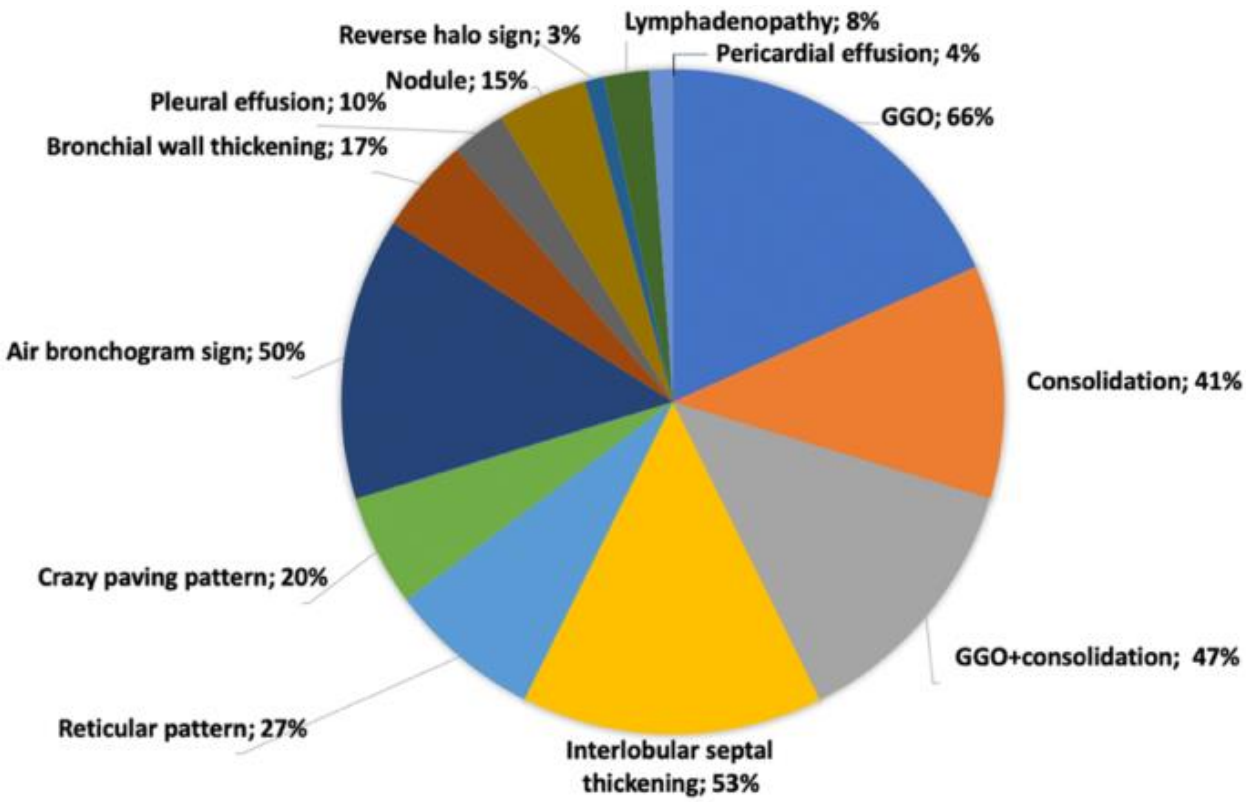

Fig 4: A figure showing the percentage of each chest CT findings of COVID 19 obtained and based on different studies [19]

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