Original Article

The Early Days of the COVID-19 Pandemic: Clinical Features and Findings of the Chest Radiograph of the Patients in the East Coast of Malaysia

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Abstract

Background: The use of chest radiographs in managing COVID-19 is more practical than computed tomography scan in Malaysia, because of its limited resources. ***Objective***: To describe chest x-ray (CXR) characteristics and relevant parameters in COVID-19 patients. ***Methods***: This is a retrospective study of 98 COVID-19 cases admitted to general hospital in Terengganu, Malaysia. CXRs of these patients were reviewed to describe the features and distribution of the abnormalities. Clinical characteristics and laboratory parameters were extracted from the electronic medical records. ***Results***: The mean age was 42 (17). Forty-four (45%) patients had co-morbidity; the commonest were hypertension (29%) and diabetes mellitus (14%). Sixty-seven (68%) cases were symptomatic. The most common symptoms were fever (42%) and cough (45%). The mean ALC was 2.39×109/L (0.81) and mean CRP 17.51 mg/L (55.94). CXR abnormalities were detected in 37 patients (38%) which include interstitial opacity in 21 (57%) patients, consolidation in 17 (46%) patients, and ground-glass opacities 12 (32%). These changes predominantly distributed bilaterally (19 [51%] of cases), located at the lower zones (49%) and peripherally (51%). Total mean score for CXR severity was 2.43 (1.48) and the mean CXR severity score for each clinical staging was found to be increasing with the advancing clinical stage of the disease. ***Conclusion***: CXR features described here were in line with previous publications on COVID-19 CXR findings. Patients with mild to moderate staging may not have low ALC or increased CRP levels. CRP was increased in patients with advanced clinical staging.

Keywords: Corona virus disease-19, chest radiograph, lung imaging. Malaysia

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Introduction

On December 2019 there were a series of pneumonia of unknown etiology detected in the city of Wuhan (China) [1], and on the 31st of December 2019, the Chinese authorities reported the new Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) to the World Health Organization. Currently, as of 14th September 2020 the number of confirmed Coronavirus Disease 2019 (COVID-19), the disease caused by SARS-CoV-2, cases have reached 29,192,519 with 928,471 deaths worldwide (WHO Coronavirus Disease Dashboard, https://covid19.who.int/). In Malaysia, the first case of the new COVID-19 was detected on the 25th January 2020. At the time of this article completion, the number of confirmed cases in Malaysia have reached 10,031 with 128 deaths. As of 31st December 2021, the confirmed cases have reached 2,758,086 with 31,487 deaths.

A number of publications worldwide have

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described radiological changes of the lung of the COVID-19 patients but are more focused on the computed tomography (CT) scan findings as it had been shown to be more sensitive in detecting changes during the early phase of the illness [2-4]. Unfortunately, the limited availability of CT scan facility in Malaysian hospitals, coupled with the limitation of the strict infection control procedures precludes the rapid use of CT scan in managing COVID-19 patients. Hence the use of chest radiograph using portable machine was seen to be more practical and it reduces the need to mobilize COVID-19 patients around thus limiting the risk of in-hospital transmission. Two studies from Italy and Hong Kong described the most common chest radiographs findings from COVID-19 patients which includes consolidation (39-47%) and ground-glass opacity (33-91%) with bilateral involvement (50-67%) and distributed peripherally (41-55%) [5,6]. Pleural effusion was reported as an uncommon finding (3-10%). Studies from other countries have shown differing percentage of COVID-19 patients having abnormalities in their initial chest radiograph. Studies in China reported up to 60%, while in Korea only 33% have changes on the initial chest radiographs [4].

While hospitals in Malaysia rely more on the reverse transcription polymerase chain reaction (RT-PCR) for diagnosis, the use of imaging through CXR is still heavily used especially for detecting the presence and the extent of pneumonia and the monitoring of the progression of the lung abnormalities in these patients. We have found a few studies that reported the use of scoring system to score the severity of the CXR abnormalities [7-9]. However, these studies were using different scoring systems. Stevens et al applied the British Society of Thoracic Imaging (BSTI) CXR report proforma which has a coding system to classify COVID-19 findings on a CXR image into normal, classic/probable COVID-19, indeterminate for COVID-19 or non-COVID-19 [7]. Borghesi et al used their own experimental chest x-ray scoring system which scores each of the six lung zones according to the severity of the findings (from 0 to 3) and then adds up to overall CXR score that ranges from 0 to 18 [8]. In another study, Taylors et al devised a five-point CXR scoring tool to score the overall appearance of the CXR abnormalities for patients presented with severe acute respiratory illness (SARI) [9]. However, this study was published in 2015 and hence its usage is not specific to COVID-19 patients but for SARI in general. Of note, Orsi et al employed the CXR severity score similar to Wong et al which divided the lungs into eight zones and score from 0 to 8 for the CXR according to the number of zones involved with abnormalities [5,6]. This scoring system was originally adapted and simplified from the Radiographic Assessment of Lung Oedema score proposed by Warren et al [10]. Oris et al also reported that the CXR severity score was positively correlated to C-reactive protein and lactate dehydrogenase level [5].

The study aims to describe the COVID-19 patients in Terengganu based on these findings which includes 1. Demographics and clinical characteristics, 2. Laboratory parameters, 3. Clinical staging, 4. Mean CRP according to clinical staging 5. Chest radiograph features, 6. Mean CXR severity score with positive findings in their CXR. The CXR interpretations were based on recommendation by the college of radiology Malaysia in 2020.

Methods

Patient selection: The majority of COVID-19 patients who were seen in Terengganu came mainly from the person under investigation (PUI) category, of the cluster from a Tabligh gathering in Seri Petaling Mosque, Petaling Jaya, Malaysia. The Tabligh gathering was a religious congregation of Muslim free preachers which were male only group, held on the 28th of February to 1st of March of 2020. The number of attendees was stipulated between 12500 to 16000 men. By the time the first positive case among the attendees was reported, these men have travelled back to various destinations. Thus, active case detection was launched nationwide. Due to this, cases were detected in Terengganu and hence began the influx of cases into Hospital Sultanah Nur Zahirah (HSNZ) as the COVID-19 admitting hospital in Terengganu state. While waiting for the confirmatory diagnosis, the symptomatic PUIs were being admitted to hospital for quarantine while others were given the order for home quarantine. In Malaysia, all positive cases were admitted to hospital for treatment, monitoring and quarantine. The Tabligh cluster has contributed to the most cases of COVID-19 in the beginning of the second wave of cases nationwide.

Real-time reverse transcription polymerase chain

reaction (RT-PCR): As per standard protocol in Malaysia, oropharyngeal and/or nasopharyngeal swab was/were sampled from these patients and were sent to HSNZ laboratory as the authorized laboratory for Terengganu State running the COVID-19 testing. The laboratory uses Bio-Rad CFX 96 Touch Real-Time PCR Detection System and use real-time RT PCR method for diagnostic test of COVID-19.

Image acquisition and analysis: Chest radiographs were acquired for patients with RT-PCR confirmed COVID-19 positive within 24 hours of their admission, using a single CR (computed radiography) mobile x-ray machine (GE AMX-4 Plus). The average exposure for chest radiographs was 68kV and 5.0 mAs. Chest radiographs were acquired with the patients in supine position, antero-posterior (AP) projection and source-to-image distance (SID) of 100 cm. Mobile radiography was chosen to make it more feasible to comply with strict infection control procedures. The chest radiographs were then reviewed and reported by radiologists on a PACS workstation (Infinitt) with monochromatic liquid crystal display (Barco) of 2 MP (1600×1200 pixels). In our study, all included chest radiographs were reviewed again together by the three reviewers who were the senior radiologist, respiratory physician and infectious disease physician involved in this study. The consensus of the findings of the radiographs must be agreed at least by two out of the three reviewers. The chest radiographs were described based on features of clear, consolidation, ground glass opacity, interstitial opacity, nodular opacity, location (left, right or bilateral), zones (upper, middle, and lower zones) and distribution (central or peripheral) of the lung changes, based on the recommendations by College of Radiology, Academy of Medicine, Malaysia.

Data collection: All patients admitted to HSNZ with RT-PCR confirmed COVID-19 positive were included in this study. (total N=98). Paediatrics patients and patients on whom no CXR was done were excluded from this study (n=16). Demographic data and data on clinical characteristics, treatment and outcome were extracted from the electronic medical record and transcribed into the study case report forms. Demographic data include age and sex, while clinical characteristic data include presence of comorbidities, smoking status, and presenting symptoms. Laboratory parameters that were extracted include white blood cell (WBC) count, absolute lymphocyte count (ALC), C-reactive protein (CRP), lactate dehydrogenase (LDH), liver function test and renal function test. Clinical outcomes include data on clinical classification of the disease and fatality. Chest radiographs and clinical presentation data were reviewed by respiratory physician and infectious disease physician to confirm the clinical classification for each selected case. Chest radiographs were reviewed and discussed by respiratory physicians, a radiologist and an infectious disease physician to confirm the CXR findings. Data from the CRFs were entered into and analysed using IBM SPSS Statistics for Windows, version 26 (IBM Corp., NY, USA) licensed for Clinical Research Center, Hospital Sultanah Nur Zahirah. For data analysis, continuous variables were expressed as median and IQR while categorical variables were expressed by number and percentage.

Results

A total of 98 patients with positive RT-PCR for COVID-19 and chest radiographs were included. Demographics and clinical characteristics of patients infected with COVID-19 were summarized in Table 1. The patients were predominantly males, (76 [77.6%]). The mean age was 42 (17) with the youngest being 13 and the oldest being 68 years old. Twenty-six patients (26.5%) were aged 51-60 years old (Figure 1).

Of the 98 patients, 44 (44.9%) had at least one underlying medical comorbidity. The common comorbidities were hypertension (28 [28.6%]), diabetes mellitus (14 [14.3%]) and dyslipidaemia (7 [7.1%]). Smoking status was only documented for 30 patients and among them, 18 were non-smokers, eight active smokers and four ex-smokers. Regarding presenting symptoms, 31 (31.6%) cases were asymptomatic and 67 (68.4%) had at least one of the symptoms, with the most common symptoms consisting of cough (44 [44.9%] of 98 patients), fever (41 [41.8%]), runny nose (15 [15.3%]) and sore throat (10 [10.2%]).

The laboratory parameters upon admission were analysed and the mean CRP was found to be elevated at 17.51 mg/L (55.94). While the mean for ALC, WBC, platelet, LDH, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), urea, creatinine, albumin and total bilirubin were within the normal range. The

laboratory parameters findings are summarized in Table 2.

Following the clinical staging as outlined by Malaysian Ministry of Health Guidelines for COVID-19 Management [12], the patients were classified into stage 1 to 5 according to the disease severity. The description for each stage and the number of patients according to it is as in Table 3. We looked further into the mean for CRP for each category of disease severity and found that it increases with increasing severity of illness (Table 3).

On admission, 37 patients (37.8%) had abnormality detected from their chest radiographs. Of these patients with lung changes, the features that were found were interstitial opacity in 21 of 37 (56.8%) patients, consolidation in 17 of 37 (45.9%), ground-glass opacity in 12 of 37 (32.4%) and nodular opacity in five of 37 (13.5%) (Figure 2). Ten of them (27.0%) had a mixture of two types of changes, while four patients (10.8%) had three different changes in their chest radiographs. Refer to Table 5 for the details of the lung changes per patient. These changes predominantly involved bilateral sides (19 [51.4%]), 10 (27.0%) on the left side only, and 8 (21.6%) had it on right side only. The lower zone was predominant (18 [48.6%]) and involved multiple zones in 12 patients (32.4%). With regard to lesion distribution, 19 of 37 (51.4%) were peripheral lesions, 10 (27.0%) central and 8 (21.6%) had both central and peripheral lesions. We found no pleural effusion on any of the CXR included in this study.

We then further looked into the chest radiograph findings, and scored the severity of CXR changes according to number of zones involved for every patient. The zones were divided based on upper, middle and lower zones, and can be from left, right or both sides. Thus, the total number of zones gave the maximum score of 6 for severity of CXR findings. The total mean score for CXR severity was 2.43 (1.48).

Twelve patients (12.2%) were observed only and later discharged without requiring any treatment for COVID-19. Almost half of the patients, 43 (43.9%) received a combination of hydroxychloroquine and lopinavir/ritonavir (Kaletra). 30 (30.6%) patients received hydroxychloroquine only, seven (7.1%) received chloroquine only, four (4.1%) received chloroquine and lopinavir/ritonavir (Kaletra), while two (2.0%) patients received the combination of hydroxychloroquine lopinavir/ritonavir (Kaletra), and then escalated to include ribavirin and interferon beta. Oseltamivir was also given to 11 (11.2%) patients. Seventeen patients (17.3%) were also given antibiotics for superimposed bacterial infections. These antibiotics include amoxicillin/clavulanic acid, azithromycin, ceftriaxone and meropenem. For the outcome, the sole patient in Stage 5 clinical staging died on day 22 of illness (day eight of admission). While all the other patients recovered well and were discharged home.

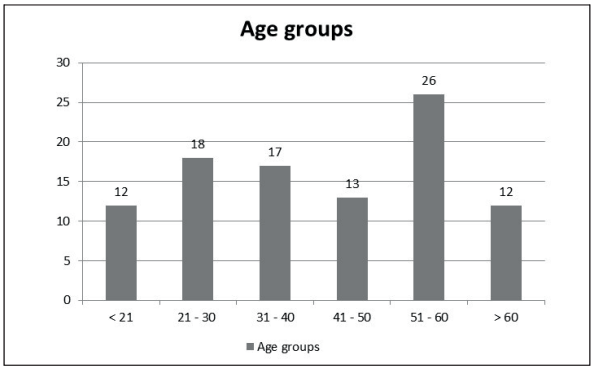

Figure 1: Age distribution of COVID-19 patients.

Table 1: Demographic and clinical characteristics of COVID-19 patients

	Mean (SD)	n (%)
Age, years	42 (17)	
Sex		
Male		76 (77.6%)
Female		22 (22.4%)
Any comorbidity		44 (44.9%)
Hypertension		28 (28.6%)
Diabetes mellitus		14 (14.3%)
Dyslipidaemia		7 (7.1%)
Ischemic heart disease		4 (4.1%)
BA/COPD		4 (4.1%)
CKD/ESRF		2 (2.0%)
Old pulmonary TB		1 (1.0%)
Stroke		1 (1.0%)
Any symptom		67 (68.4%)
Cough		44 (44.9%)
Fever		41 (41.8%)
Runny nose		15 (15.3%)
Sore throat		10 (10.2%)
Vomiting		8 (8.2%)
Dyspnoea		5 (5.1%)
Anosmia		3 (3.1%)
Lethargy		2 (2.0%)

	Mean (SD)	n (%)
Loose stool		2 (2.0%)
Loss of appetite		2 (2.0%)
Dysgeusia		2 (2.0%)
Myalgia		4 (4.1%)
Rash		1 (1.0%)

Table 2: Laboratory parameters of COVID-19 patients

	Mean (SD)
Laboratory parameters	
WBC, x 10^9/L	7.84 (2.27)
ALC, x 10^9/L	2.39 (0.81)
Platelet, x 10^9/L	284.91 (73.55)
LDH, U/L	259.99 (83.75)
CRP, mg/L	17.51 (55.94)
ALT, U/L	30.85 (28.06)
AST, U/L	28.86 (16.29)
ALP, U/L	92.35 (50.8)
Urea, mmol/L	4.23 (1.74)
Creatinine, µmol/L	74.16 (26.63)
Sodium, mmol/L	137.28 (3.08)
Potassium, mmol/L	3.88 (0.52)
Albumin, g/L	41.50 (4.96)
Total bilirubin, µmol/L	14.75 (6.25)

Table 3: Clinical staging of COVID-19 patients

Clinical stage	Description	n (%)
1	Asymptomatic	22 (22.4%)
2	Symptomatic, no pneumonia	39 (39.8%)
3	Symptomatic, with pneumonia	28 (28.6%)
4	Symptomatic, with pneumonia and requiring supplemental oxygen	8 (8.2%)
5	Critically ill, with multi organ involvement	1 (1.0%)

Discussion

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a newly emerged virus of the twenty first century which can cause symptoms from a mild cold to a fatal acute respiratory distress syndrome. This virus belongs to the Sarbecovirus subgenus of the Coronaviridae family, and it is the seventh latest known coronavirus that infects human. Global death rate of COVID -19 was 3.18% while the Malaysian COVID-19 death rate stands was 1.28% when the study was conducted in 2020.

In our study, we report a cohort of 98 patients with positive RT-PCR results during the COVID-19 outbreak in Malaysia Terengganu state. All recruited cases had chest radiograph and baseline blood investigation done upon admission. There is a predilection for male gender (77%) in this cohort, which is similar to a study in Wuhan that reported 73% males in their cohort of 41 patients [3]. However, another study reported no obvious difference in men (52%) and women (48%) getting the infection, from their cohort of 81 patients [2]. The discrepancy in these findings might not be significant due to the small cohort sizes. In the case of our study, it can be partly explained by the fact that the cluster involved had originated from the Tabligh gathering, a religious congregation which was attended by only men. Fever and cough were the predominant symptoms found in 42% and 45% of cases respectively, consistent with findings from other studies [2,3,5,6]. The presence of dyspnoea as presenting symptoms varies among studies. While some studies reported dyspnoea rate ranging from 37% to 55% [2,3,5], only 5% of the patients in our cohort had the symptom. One other study in Hong Kong similarly reported 6% of their patients as having dyspnoea. A possible explanation for the lower rate of dyspnoea in our study is that our cohort consisted of patients who were being actively screened for the infection due to their risk factor of having attended the Tabligh gathering or being in close contact with one. All these patients who tested positive were admitted to the hospital regardless of their symptoms. So, we might have captured the cases early on before more symptoms developed. For the record, another 4% of patients in our study developed dyspnoea later on during the course of admission and required supplemental oxygen.

Chest x-ray is an indispensable tool for assessment as COVID-19 is a disease of the respiratory system. In our study setting, CXR was used in the management of patients already tested positive using RT-PCR. Thus, it was to detect the presence of pneumonia in these patients, define the severity of the disease and monitor progress. In other settings where the prevalence of COVID-19 is higher and more moderate to severe patients present and are admitted, CXR also gains a more important role in the diagnosis of the disease [5].

In Orsi et al, the rate of reported commonest symptoms were high, fever (81%) and cough (54%), and 92% of their patients had abnormalities found on their CXR [5]. This is very high compared to findings from our cohort, where the commonest

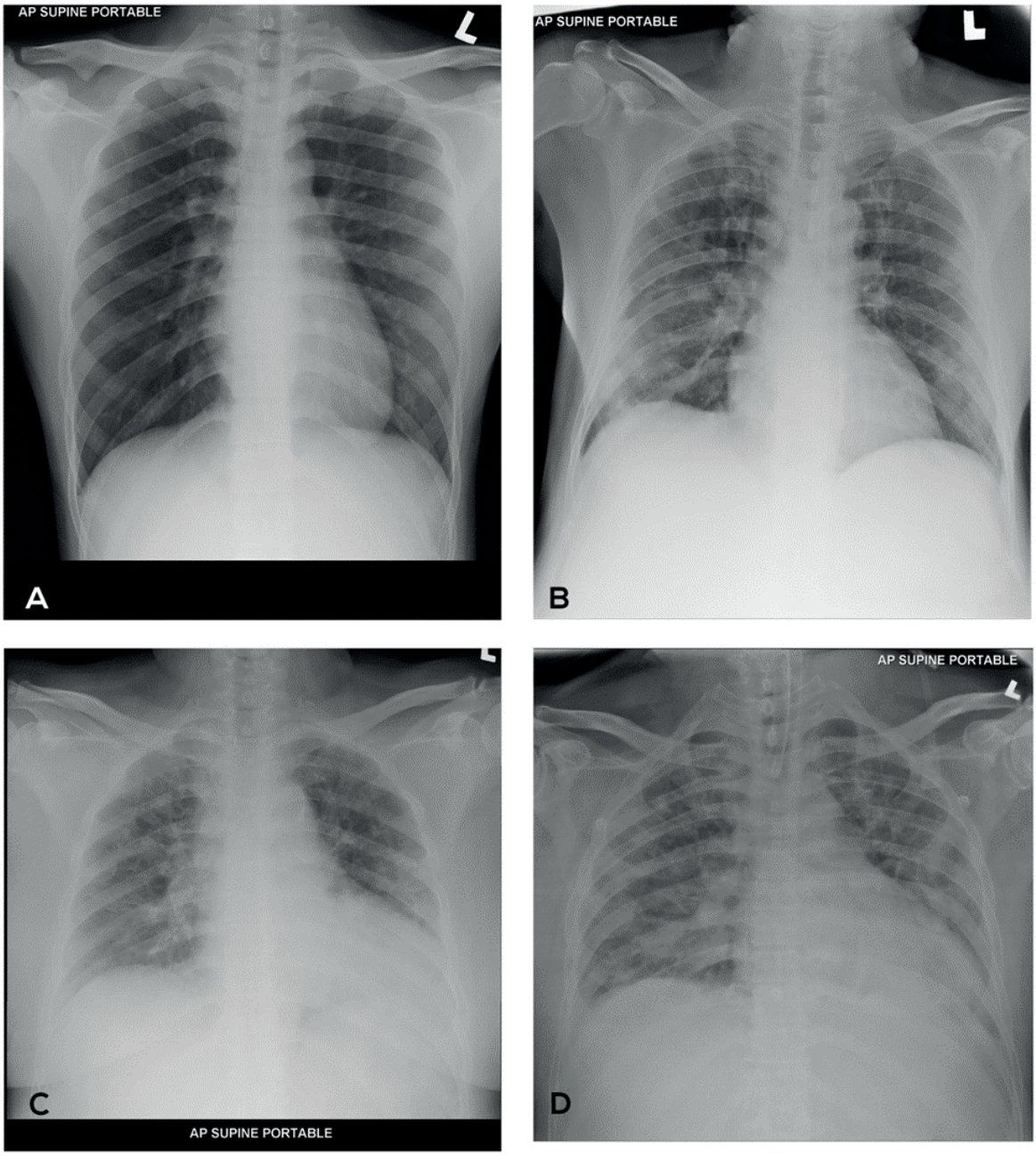

Figure 2A: Normal chest radiograph in a Stage 1 patient. **Figure 2B:** Stage 3A patient with bilateral ground glass opacities and interstitial opacities. **Figure 2C:** Stage 4 patient with bilateral ground glass opacities and interstitial opacities. Radiographic features are overlapping with those of Stage 3A. **Figure 2D:** Stage 5 patient with bilateral consolidation, ground glass opacities and interstitial opacities.

symptoms were less prevalent (fever in 42% and cough in 45%), while only 38% had positive findings detected on their CXR. Their study was done in Italy and said to have included patients who presented to their emergency department with symptoms of COVID-19 and were at a more advanced disease stage [5].

Among the patients with CXR abnormalities in our study, the most common features were interstitial opacity (57%), consolidation (46%) and ground-glass opacities, GGO (32%). Wong et al reported 47% consolidation and 33% GGO [6]. While in Orsi et al, GGO were present in 99% of positive CXR, followed by consolidation in 42% [5]. Both studies did not describe interstitial opacities in their papers, but focused on consolidation, GGO and nodules according to the Fleischner Society

glossary of terms, which was different from the Malaysian College of Radiology recommendation followed by our radiologists in Malaysia. The changes observed in our cohort were predominantly involving bilateral sides, with lower zones and peripheral distribution. This corresponds to the findings from other studies [2,5,6,16]. While we have found no pleural effusion, some studies have reported 3-10% of patients to have pleural effusion on their CXR [5,6].

Severity of the chest radiographs lesions are based on the distribution of these lung lesions according to zones- upper zone, mid zone and lower zone. There are 3 zones on each lung field, making up a total of 6 zones. Lesions involving more zones are considered to be more severe hence have a higher CXR severity score. We have found that the mean CXR severity score increases with increasing disease severity. The sole Stage 5 patient in our study showed the most severe radiographic findings at admission with a combination of consolidation, ground glass opacities and interstitial opacities with highest CXR severity score of 6. This finding cannot be easily compared to other studies due to the different scoring systems used and the way they were reported.

The limitation of this study is our small number of subjects (n=98) resulting in inability to measure some key statistics. A larger subject number would show more robust data and correlation. In addition, as this was a retrospective study utilising medical records review, it relies heavily on the quality of the data that was available from the records. Some important variables, for example, smoking history, are missing. A more standardised guideline or protocol would be helpful in determining when to repeat chest radiograph and blood investigation.

Conclusion

We described the CXR features of our cohort of COVID-19 patients, which were in line with the findings from other publications in 2020. Patients with mild presentation and disease severity may not have changes in their CXR, low white blood cell, absolute lymphocyte counts or increased C-reactive protein level. However, we noted that C-reactive protein showed an increased trend in a more advanced clinical staging especially in those with fever, requiring supplementary oxygen and advanced age.

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Ethical clearance: This study was conducted in accordance with the amended Declaration of Helsinki. The local independent ethics committee of Malaysia, the Medical Research and Ethics Committee of the Ministry of Health has approved the protocol on 16th April, 2020. The approval reference number is KKM/NIHSEC/P20-901(6).

Authors' contribution: All authors were equally involved in conception and design of the study.

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