Review Article

COVID-19 and MERS: Are their Chest X-ray and Computed Tomography Scanning Signs Related?

Abstract

Background: COVID-19 is a respiratory infection brought about by SARS-COV-2. Most of the patients contaminated by this pathogen are afflicted by respiratory syndrome with multiple stages ranging from mild upper respiratory involvement to severe dyspnea and acute respiratory distress syndrome cases. Keeping in mind the high sensitivity of computed tomography (CT) scan in detecting abnormalities, it became the number one modality in COVID-19 diagnosis. A wide diversity of CT features can be found in COVID-19 cases, which can be observed before the onset of clinical signs. The review article is aimed to highlight recent discrepancies in CT-scan and chest X-ray (CXR) characteristics between COVID-19 and Middle East Respiratory Syndrome (MERS). **Method:** This review study was performed in the literature from the beginning of COVID-19 until the middle of April 2021. For this reason, all relevant works through scientific citation websites such as Google Scholar, PubMed, and Web of Science have been investigated in the mentioned period. **Results:** COVID-19 was more reproductive than MERS, while MERS was significantly higher in terms of mortality rate (COVID-19: 2.3% and MERS: 34.4%). Signs of ground-glass opacity (GGO), peripheral consolidation, and GGO accompanying with consolidation are the same signs CXR in both MERS and COVID-19. Indeed, fever, cough, headache, and sore throat are the most symptoms in all studied patients. **Conclusion:** Both COVID-19 and MERS have the same imaging signs. The most similar chest CT findings are GGO, peripheral consolidation, and GGO superimposed by consolidation in both studied diseases, and no statistical differences were seen among the mean number of chest CT-scans in MERS and COVID-19 cases.

Keywords: *Chest X-ray, computed tomography scan, COVID-19, Middle East Respiratory Syndrome-CoV, SARS-coronavirus-2*

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Introduction

COVID-19 is a viral infection caused by SARS-CoV-2.[1] Its origin is yet to be found, but it was first seen in Wuhan city of China.[2,3] The basic reproductive number of this virus is relatively high due to its human-human transmission.[4,5] Emerging the novel coronavirus causes a pandemic throughout the world.[6] The number of infected cases ramping up staggeringly, and by the time of authoring this essay, more than 220 countries and 150 million people have been contaminated by COVID-19, and a rising number of more than 3 million cases have been died so far due to this virus.[7] MERS-CoV is other type of coronavirus, which was originated in Saudi Arabia, and as of July 2019, 2458 cases of MERS were tested positive in 28 countries and 848 patients were died.[8]

COVID-19 is a clinical manifestation of SARS-COVID-2 infection. In the majority of cases, it will lead to respiratory syndrome with several stages from mild upper respiratory tract illness to severe cases of acute respiratory distress syndrome (ARDS) and pneumonia.[9,10] SARS-COVID-2 and MERS both belong to the β-coronavirus genus, but SARS-COVID-2 seems to have milder symptoms.[11] The most significant clinical sign after 1 week of COVID-19 onset is fever and cough, followed by a sore throat. Other symptoms are expectoration headache, nausea, diarrhea, and vomiting which in severe cases will lead to dyspnea, hypoxia, and ARDS.

Considering the initial involvement of the respiratory tract in COVID-19 and MERS,

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the first line in diagnosis is a computed tomography (CT scan) followed by a chest X-ray (CXR) with less diagnostic value.[12] Especially with Reverse Transcription Polymerase Chain Reaction (RT-PCR) being less sensitive in terms of confirming COVID-19, CT scan is of great importance in COVID-19 and MERS diagnosis.[13] A vast diversity of CT scan and CXR features is found in COVID-19 and MERS cases that can even be found before clinical symptoms onset.[14,15] Many studies describe the CT scan manifestation of COVID-19 and MERS in different stages of the disease.[15] The main primary characteristics for both COVID-19 and MERS include bilateral ground-glass opacity (GGO) both in the lateral and posterior segments of lung lobes with diffuse distribution, consolidative opacity, and interstitial septal thickening in the initial phases of the disease. Some less frequent presentations are pleural effusion, pericardial effusion, cavitation, lymphadenopathy, and pneumothorax.[13] In advanced stages of the disease, a progressive sign of ARDS may be presented, which would be an indication for the use of mechanical ventilation for the patient.[15-17] These radiologic signs are the same in both disease cases but with a little difference in distribution.[11,18]

A better understanding of the similarities and differences of the clinical and chest CT presentation of these two viral diseases will help the clinicians to better diagnosis. Thus, more efficient patient management and a higher chance of treatment and recovery. The aim of this review article is to investigate recent discrepancies in clinical and CT characteristics between COVID-19 and MERS.

Materials and Methods

This review study was performed in the literature from the beginning of COVID-19 until the mid of April 2021. A shorter review article regarding to this topic was published in the Persian language previously.[19] For this reason, all related works through citation scientific websites such as Google Scholar, PubMed, and Web of Science have been investigated in the mentioned period, and more than 40 studies have been found using the keywords including COVID-19, MERS-CoV, CT-Scan, and CXR. Non-English language published papers as well as studies relevant to SARS were excluded from this study. Then, radiological and CT-scan findings were extracted and categorized in Tables 1-4.

Statistical analysis

Meta-analyses were performed by using SPSS version 26.0 (Chicago, IL, USA) software. Due to the limited number of MERS cases and the abnormality of pertained data, Mann–Whitney test and Kolmogorov–Smirnov test were used to analyze the data. According to a 95% confidence interval, statistical significance was set at $P < 0.05$.

Results

A preview of data collected from studies reviewed in this literature is provided in Tables 1-4. CT scan was the primary diagnostic modality in all published papers, and a CXR was used occasionally. The sample size was varied and was notably small in MERS studies due to its restricted affected region.

Clinical features

According to acquired collected data, both MERS and COVID-19 had the same quarantine period of 1–14 days.[19,38] Both spread through respiratory tracts and contaminated surfaces.[38,39] COVID-19 had more transition rate compared to MERS. Considering the World Health Organization report, the infection transmission rate (reproduction number) for COVID-19 roughly around 2–2.5 patients, which was less than MERS (>1).[27] Lui *et al.* had remarked that the reproduction number of COVID-19

	Number of cases	GGO (%)	Consolidation (%)	Mixed GGO and consolidation (%)	CPP (%)	Fibrous lesion (%)	Patchy (GGO/consolidation) (%)	Oval
Diao *et al.*[20]	6	100	16.7			33.3		
Pan *et al.*[21]	24	75						
Lu *et al.*[22]	91 patients (991 lesions)	76.9	19.8	40.7	61.5			
Liu *et al.*[23]	55 patients (614 lesion)	78	15	60		36		
		57	19	24		8		
Pan *et al.*[24]	63	22	19			17.5	58.7	
Salehi *et al.*[15]	Variable	88	31.8					
Xie *et al.*[25]	5	100	40					
Yang *et al.*[26]	2375 segments	12.08	7.15	26.1		48	39.35	6.6
Yoon *et al.*[27]	3 patients (77 lesion)	35	peripheral 5	50	10		39	
Yuan *et al.*[28]	27	67	19	30				
Zhu *et al.*[29]	12	83	67		33	25		67
Ng *et al.*[30]	21	86	62	19				
Xu *et al.*[31]	50ª	60	30	50				
		73.17	36.58	60.97				

Table 1: A radiological presentation in coronavirus disease 2019 cases

ªOf which 41 patients are in severe NCP. CPP: Crazy-Paving Pattern, GGO: Ground-Glass Opacity, NCP: Novel coronavirus pneumonia

Table 2: Radiological presentations in coronavirus disease-2019 cases

	Number of cases	Lymphadenopathy (%)	Pleural effusion (%)	Pericardial effusion (%)	Septal thickening (%)	Vascular thickening (%)	Air bronchogram (%)	Pulmonary infiltration (%)	Nodular opacities (%)	Chronic lesions
Lu *et al.*[22]	91 patients (991 lesion)				1 (64.8)	38.5	46.2		16.5	
Liu *et al.*[23]	55 patients (614 lesion)		13/55 (23)							
Yang *et al.*[26]	144	48	6.9				56			
Yoon *et al.*[27]	3 (77 lesions)						20		100	
Yuan *et al.*[28]	27		4				30		7	
Zhu *et al.*[29]	12				75	33				
Xu *et al.*[17]	50		8		73.17			22/41 (53.66)		
			9.76		60					
Diao *et al.*[20]	6								33.3	
Pan *et al.*[21]	63								12.7	
Ng *et al.*[30]	21								4.7	

Table 3: Radiological presentations in Middle East respiratory syndrome-coronavirus cases

	Number of cases	GGO (%)	Consolidation (%)	Mixed (%)	Air bronchogram (%)	Fibrous (%)	Multicentric cavitation (%)	Interlobular thickening (%)	Pleural effusion (%)	Pneumo thorax (%)	Irregular linear (%)
Das *et al.*[31]											
Chest radiographic findings		66	18	16	11		25	26			9
CT findings within the first week		53	20	33					33		
Cha *et al.*[32]	25					56			56	4	
Das *et al.*[33]	55	66	18	18.2	10.9		1.8		30.9	16.4	9.1
Das *et al.*[34]	15	86.6	33	60		6.6	6.6	40	60		
Hamimi[35]	12	91	160			41	16		66		
Ajlan *et al.*[37]	7	100	85		28			42	42		14
Das *et al.*[36]	36	5.5				33		5.5			

GGO: Ground-glass opacity

was averagely considered to be 3.28 patients.[4] Mutations are one of the critical parameters which contribute to more reproduction value.[40] However, low doses of X-ray radiation can stimulate anti-infection immune factors that will disrupt the cycle of virus dispersing.[41] COVID-19 had several prevalent clinical symptoms such as cough, fever followed by dyspnea and myalgia, which were also common in MERS in most cases.[8] There were less common clinical presentations such as chest pain, headache, nausea, and vertigo.[42] The severity of symptoms varied, but overall, MERS cases had gone through more severe symptoms due to its high mortality rate.[11] The average time between being exposed to SARS-COVID-2 and the onset of symptoms was approximately 10 days.[43] This interval shrunk a bit in MERS cases, and the average time was about 4-10 days.[44] Based on the recent study on a large population of 44672 cases diagnosed with COVID-19 conducted by the Chinese Center for Disease Control and Prevention, MERS had a such higher mortality

rate (around 30%), largely exceeding the COVID-19 with a 3.1% mortality rate. These numbers increased to a 14% death toll when it came to only hospitalized patients with diagnosed COVID-19.[11]

Some risk factors such as underlying comorbidities are related to short-term mortality rate of both MERS and COVID-19.[26,38] Cases with diagnosed MERS had a wide range of clinical features from asymptomatic to diffuse alveolar damages, which in severe cases will cause ARDS making patients to need of a ventilator.[32] Multiorgan failure was another symptom of MERS that led to acute kidney injury (AKI), which was seldom seen in COVID-19 cases. Another explanation for AKI was related to direct cytopathic effects of the virus on glomeruli and tubule cells in the kidney. On the other hand, both MERS and COVID-19 had neurological defect like cerebra vascular disease and cerebral hemorrhage like interparenchymal hemorrhage, intercranial hemorrhage, epidural hemorrhage,

Table 4: Lung lobes involvement

	Number of Cases	Nuumber of affected lobes	Central lobe involvement (%)	Peripheral involvement (%)	Bilateral involvement (%)	Posterior involvement (%)	Multilobar involvement (%)
COVID-19							
Liu *et al.*[23]	55 patients (614 lesion)	174	1/55 (1.8)	54/59 (98)	37/59 (67)		
Salehi *et al.*[15]	Variable			92/121 patients (76)	435/497 patients (87.5)	41/51 patients (80.4)	108/137 patients (78.8)
Yang *et al.*[26]	2376 segments		2.15	35.9	8.12		
Yoon *et al.*[27]	9 (77 lesion)		23	78	88.8	(67)	
Yuan *et al.*[28]	27		74	74	86	(96)	
Zhu *et al.*[29]	12		17	92	50		
MERS							
Das *et al.*[31]							30
Cha *et al.*[32]	25		4	60	64		
Das *et al.*[33]	33						
Das *et al.*[34]	281 lesions		24	54	22		
Hamimi *et al.*[35]	12						66
Ajlan *et al.*[37]	7			57	85		
Das *et al.*[36]	36						5.5

COVID-19: Coronavirus disease 2019, MERS: Middle East Respiratory Syndrome

subdural hemorrhage, and subarachnoid hemorrhage that would lead to ischemic or hemorrhagic strokes.[17]

Computed tomography-scan features

In terms of CT presentations, 485 COVID-19 patients and 150 MERS cases were participated in the included papers. Lack of MERS cases was predictable because of the limited region affected by the virus and the studies surveying before mentioned disease. After manual screening and extracting abnormal chest CT-Scans and CXR, the CT scan and radiological patterns and manifestations were extracted from the entry articles. In COVID-19, CT symptoms initiation is 7 ± 4 days after disease onset, and its peak signs were in the 10th day, while in the MERS population, the initiation time was lower. Primary lung lobal involvement in the COVID-19 population has peripheral multi-lesion distribution and relatively localized inflammation in subpleural and parabronchus in the dorsal segment of the right lower lobe, basal segment, and the lateral segment of the same lobe. In contrast, MERS affected the upper airway tract followed by lower respiratory tract involvement in advanced stages.[45] Based on accumulated data, GGO with mean = 67.92 and standard deviation (SD) = 28.32 accompanied by mixed GGO and consolidation (mean = 39.4, SD = 14.9) and peripheral consolidations (mean = 27.7, SD = 19.84), which is known as hyperdense patterns in bronchial tracks and blood vessel borders. These were orderly the most common radiological manifestations in COVID-19 cases [Table 1]. Other reported patterns were fibrous lesions (mean = 31.96, SD = 15.61), lymphadenopathy, pleural effusion (mean = 10.47, SD = 8.52), pericardial effusion, septal thickening, vascular thickening, and air bronchogram sign (mean = 41.17,

SD = 11.5). In a study conducted by Lu *et al.*,[22] a total of 91 patients diagnosed with COVID-19 were examined, and GGO was observed in 76 of them that calculated as 76.9% of the studied population. They reported GGO co-exist with consolidation applied to 37 patients forming 40.7% of the community. Indeed, they conducted crazy paving pattern is seen in 56 patients, which is 6.5% of all patients. Septal thickening was also notable by appearing in 59 patients (64.8%), same as air bronchogram sign (46.2%) and vascular thickening (38.5%).[22] Another peculiar study conducted by Yang *et al.*[26] was performed on 144 cases and 2375 lobes. According to this study, 26% of lung lobes were affected by GGO mixed with consolidation, which occurs in severe stages of the disease. The formation of opacities was mostly in the shape of patchy GGO (39.35%). They conducted 6.6% of opacities were formed in an oval shape. Furthermore, 74 individuals had a fibrous lesion in the follow-up chest scans, which consist of 48% of the population[26] [Tables 1 and 2].

Moreover, in chest CT scan of MERS cases, GGO is the most prevalent findings with mean = 67.92, SD = 28.3 followed by peripheral consolidation (mean = 38, SD = 32.24). Other symptoms including mixed GGO and consolidation (mean = 39.1, SD = 29.56), air bronchogram (mean = 19.45, SD = 12.1), fibrous (mean = 34.15, SD = 20.69), multicentric cavitation, interlobular thickening, pleural effusion (mean = 50.98, SD = 14.28), pneumothorax, and irregular lines. Das *et al.*[34] had performed a study on 15 patients and a total of 281 lesions. They argued that 86.6% of cases had GGO and 40% had a mixture of GGO and consolidation. Interlobular thickening, which

mainly involved bilateral and peripheral lobes was seen in six patients (40%). Pleural effusion, which is a late-stage symptom was presented in nine individuals (60%) [35] [Table 3]. Fully described details of all studies are provided in the presented tables.

Lung involvement distribution

Based on the studies included in this review in confirmed patients of COVID-19, peripheral involvement was the most prominent presentation by 75.65%.(posterior involvement had higher percentage but due to the lack of studies cannot be referred to). Only one review study reported multilobar involvement in 108 severe cases out of 137 population.[15] This may suggest that multilobar involvement is less common in mild stages of the disease and frequent in critical patients.[15] Among six articles determining lung lobar involvement, 75.65% of patients had peripheral involvement and 64.57% had bilateral involvement and 23.58% had central lobe involvement. These numbers indicated that in the majority of cases, peripheral and bilateral involvement was a symptom of early stages of the disease.

In MERS cases, lung involvement is somewhat the same as COVID-19. Numbers associated with the lobar involvement are not as accurate as COVID-19 because of the limited number of cases and studies. Bilateral involvement was the most findings in confirmed cases with 86.5% following by peripheral involvement and multifocal involvement with 50% and 55.7%, respectively. Other lobar involvement was unifocal involvement (42%) and central involvement (14%).

Discussion

COVID-19 and MERS-COV are both from the same type of β-coronavirus with the same clinical and radiologic symptoms and disease stages in both adults and children.[11,46,47] The fatality rate for COVID-19 is less than MERS. Some scholars argue the answer to this issue is within the number of studies and its populations. The studies were limited and performed on hospitalized MERS cases, so the high mortality rate was somehow predictable.[11] While COVID-19 has much more reproductive value and cause a pandemic, MERS remained localized with less transmission rate.[4] Thus, early diagnosis of both diseases is of great importance to stop the transmission chain and maintain the epidemic. RT-PCR is a known gold standard for COVID-19 and MERS diagnosis. However, with its low sensitivity and other limitations like not evaluating the severity of the disease, chest CT scan is suggested as a substitution with its high sensitivity, availability, timely, and rapid scans.[48,49]

In terms of CT scan findings in this review, it is concluded in Table 1.

Ground-glass opacity

There are no meaningful statistical differences among mean number of GGOs in diagnosed cases of MERS and COVID-19, according to Mann–Whitney test ($P > 0.05$, $U = 37.00$).

Consolidation

There are no significant statistical differences among the mean number of consolidations in diagnosed cases of MERS and COVID-19 according Mann–Whitney test ($P > 0.05$, $U = 28.00$).

Mixed ground-glass opacity and consolidation

There are no significant statistical differences among the average cases with mixed GGO and consolidation in diagnosed cases of MERS and COVID-19, according to Mann–Whitney test ($U = 6.50$, $P > 0.05$).

Fibrous lesion

There are no significant statistical differences among the average cases with fibrous lesions in diagnosed cases of MERS and COVID-19, according to the Mann–Whitney test ($U = 11.00$, $P > 0.05$).

Air bronchogram

There are no significant statistical differences among the average cases with air bronchograms in diagnosed cases of MERS and COVID-19, according to the Mann–Whitney test ($U = 1.00$, $P > 0.05$).

Pleural effusion

T-test results demonstrated that average cases with pleural effusions in COVID-19 cases are statistically and significantly lower than MERS cases ($U = 20.00$, $P < 0.05$).

Central involvement

There are no significant statistical differences among the average cases with central involvements in diagnosed cases of MERS and COVID-19, according to Mann–Whitney test ($U = 6.00$, $P > 0.05$).

Peripheral involvement

There are no significant statistical differences among the average cases with peripheral involvements in diagnosed cases of MERS and COVID-19, according to the Mann–Whitney test ($U = 3.00$, $P > 0.05$).

Bilateral involvement

There are no significant statistical differences among the average cases with bilateral involvements in diagnosed cases of MERS and COVID-19, according to the Mann–Whitney test ($U = 6.00$, $P > 0.05$).

Multifocal involvement

There are no significant statistical differences among the average cases with multifocal involvements in diagnosed

cases of MERS and COVID-19, according to Mann–Whitney tests (U = 0.00, $P > 0.05$).

All other CT scan symptoms provided beforehand in the text are the same and had no significant statistical differences among the average cases with their respective groups.

This study had some limitations that is worth mentioning. First, most of the articles had inclusion and exclusion bias in single centers. Second, the severity and stages of the diseases were unclarified. Studies about MERS were limited in numbers and population and the statistical results should be taken with a grain of salt.

Conclusion

This review included the similarities and differences of MERS-COV and COVID-19 in terms of CXR results and clinical symptoms. The most similar Chest CT-Scan findings are GGO, peripheral consolidation, and GGO superimposed by consolidation in both studied diseases. The most similarities and common clinical signs in MERS and COVID-19 are cough, fever, and sore throat. This review brings forth insight on the differential diagnosis of both diseases and monitoring their progression with a focus on current findings and their challenges.

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Conflicts of interest

There are no conflicts of interest.

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