Review Article

SARS, MERS and CoVID-19: An overview and comparison of clinical, laboratory and radiological features

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Abstract

In the 21st century, we have seen a total of three outbreaks by members of the coronavirus family. Although the first two outbreaks did not result in a pandemic, the third and the latest outbreak of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) culminated in a pandemic. This pandemic has been extremely significant on a social and international level. As these viruses belong to the same family, they are closely related. Despite their numerous similarities, they have slight distinctions that render them distinct from one another. The Severe Acute Respiratory Distress Syndrome and Middle East Respiratory Syndrome (MERS) cases were reported to have a very high case fatality rate of 9.5 and 34.4% respectively. In contrast, the CoVID-19 has a case fatality rate of 2.13%. Also, there are no clear medical countermeasures for these coronaviruses yet. We can cross information gaps, including cultural weapons for fighting and controlling the spread of MERS-CoV and SARS-CoV-2, and plan efficient and comprehensive defensive lines against coronaviruses that might arise or reemerge in the future by gaining a deeper understanding of these coronaviruses and the illnesses caused by them. The review thoroughly summarises the state-of-the-art information and compares the biochemical properties of these deadly coronaviruses with the clinical characteristics, laboratory features and radiological manifestations of illnesses induced by them, with an emphasis on comparing and contrasting their similarities and differences.

Keywords: CoVID-19, MERS, MERS-CoV, SARS, SARS-CoV, SARS-CoV-2

Introduction

More than 178 million people worldwide have contracted the COVID-19, after the novel virus emerged from Wuhan City in November 2019. Around 4 million people have lost their lives to this virus.[1] The novel coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is the causative agent for this pandemic. This is not the first time that a coronavirus has caused an outbreak. SARS-CoV and MERS-CoV, members of the coronavirus family, also have caused outbreaks of Severe Acute Respiratory Distress Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) in 2002 and 2012 respectively.[2,3] While these viruses belong to the same family, there are many similarities and dissimilarities between the pathogenesis and clinical features of their respective diseases.[4] SARS-CoV-2 is much less pathogenic as compared to MERS-CoV and SARS-CoV.[5] The case fatality rate with MERS and SARS is very high as compared to the novel coronavirus disease 2019, but the novel virus has somehow managed to spread rampantly throughout the world and to cause a pandemic.[6-8] SARS, which first emerged in 2002, spread around the world until being contained in 2003.[9] MERS, on the other side, has been causing sporadic cases in hospital settings without spreading worldwide.[10]

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With unsuccessful drug trials, uncertain efficacy of current vaccinations, and a strain on specialist care for CoVID-19 patients during the pandemic, it is expected that primary care physicians would identify and effectively manage cases of these emerging diseases like COVID-19.[11] In developing countries such as India, where the health-care system is already overburdened and where specialist care has yet to arrive in its many remote areas, family physicians and primary care physicians were tasked with handling COVID-19 patients. In the standard operating procedure released by Union Ministry of Health and Family Welfare, it is stated that 80–85% of COVID-19 patients usually do not require specialized care and may be isolated at home or in a COVID care centre with supportive care.[12] This underlines the need of primary care physicians being familiar with the symptoms of COVID-19 or any other viral infection. If a similar outbreak occurs in the near future, our surveillance and notification system should be prepared. Because primary care physicians are the initial point of contact between the population and the health-care system, this information will assist them in early detection, notification and quick warning of impending epidemics, therefore strengthening the national surveillance system.

All three coronavirus diseases vary in some manner from one another in terms of presentation. Albeit, there are many common features between the clinical presentation of these diseases. Since these disorders have a similar presentation, it is often difficult to contrast between these diseases from their symptoms. There are still many things to be known about the novel virus, as with other coronaviruses. In this review, we intend to compare and contrast the clinical and laboratory features, along with radiological manifestations of the three coronavirus diseases.

Clinical Features

COVID-19

The pathogenesis of human coronaviruses is mostly determined by viral particle binding to specific receptors rather than viremia. Human Angiotensin 1 converting enzyme 2 receptor is the cellular target of SARS-CoV and SARS-CoV-2.[13] MERS-CoV, however, targets the DPP-4 receptor in the cell.[14] The pathogenesis of these diseases is shown in Figure 1.

The clinical features of coronavirus diseases are nonspecific and most of the time they mimic influenza or atypical pneumonia. CoVID-19 patients show a variety of clinical symptoms, from mild to severe, increasingly progressing and fulminant illness. Asymptomatic CoVID-19 occurrences may be around 15.6%, and some patients do not have any usual physical symptoms or presentations at all.[15-21] Besides, certain people develop anosmia or hypogeusia. Most of the adult patients present with the symptoms listed in Table 1, as reported in various studies.

Recovered patients with recurrent symptoms often months after the original infection have been referred to as "longhaulers" or "long COVID patients". The prevalence rate of these longhaulers vary and has yet to be completely identified owing to insufficient studies.[38] Rales or rhonchi have been detected on auscultation of the lungs in the majority of patients in several studies. In addition to this, a phenomenon called "happy hypoxia" has also been seen with CoVID-19 patients, a condition in which patients report no dyspnea or visible symptoms of respiratory distress.[39,40]

Table 1: Frequency of clinical features in coronavirus diseases reported in several case series

Feature	SARS[22-26]	MERS[27-31]	CoVID-19[32-37]
Incubation Period	2-10 Days	2-12 days	2-14 days
Fever[$]	~100%	81-98%	34-80%
Cough (Nonproductive)	75-80%	57-83%	19-57%
Chills or Rigor	15-90%	87%	25%
Myalgia	45-50%	43%	6.5-34%
Headache	20-70%	20.4%	2.5-38%
Dyspnea	35-60%	22-72%	6-36%
Tachypnea	40-75%	-	30-35%
Tachycardia	40-75%	-	20-27%
Hypoxemia	40-75%	-	40-50%
Cachexia	-	-	37%
Malaise	45-70%	38%	56%
Nausea/Vomiting	35%	14-21%	2-13%
Diarrhoea	6-25%	19.4-26%	5-21%
Sore throat	25%	9.1-14%	2.5-10%
Rhinorhea	15%	1.6%	5-10%
Hemoptysis	-	4.3%	22.4%
Asymptomatic	-	-	6.5%

[$]>38°C for more than 24 h

Apart from the respiratory symptoms, the virus is found to cause various gastrointestinal, cardiovascular and neurological symptoms as well. As far as neurological symptoms are concerned, headache, malaise, languidness, and even cerebral infarction and cerebral hemorrhage have been reported.[41] Anosmia and ageusia were also some of the frequently reported symptoms of CoVID-19.[32,42] In gastrointestinal symptoms, diarrhoea, vomiting, belching, anorexia were frequent symptoms.[43] In terms of cardiac complications, heart failure and arrhythmia were the most common. For the most part, hematological abnormalities, including clotting disorders, lymphopenia and thrombocytopenia, are prevalent.[44]

CoVID-19 may also trigger coagulopathy, which is a serious complication. Organ failure is its most common form of it, with hemorrhages being less common. Increases in D-dimer and fibrin–fibrinogen degradation products in hemostatic biomarkers mean that the core of coagulopathy is fibrin production. In CoVID-19, prolongation of prothrombin duration and activated partial thromboplastin time, as well as a decline in antithrombin production, are less common than in other coagulopathies, like bacterial sepsis-associated coagulopathy or disseminated intravascular coagulation (DIC). Thrombocytopenia was rarely observed in this CoVID-19-related coagulopathy. Coagulopathy's mechanism, in contrast, is not fully known.[45]

SARS

When it comes to SARS, apart from the family's common features, watery diarrhoea has been identified in 73% of patients

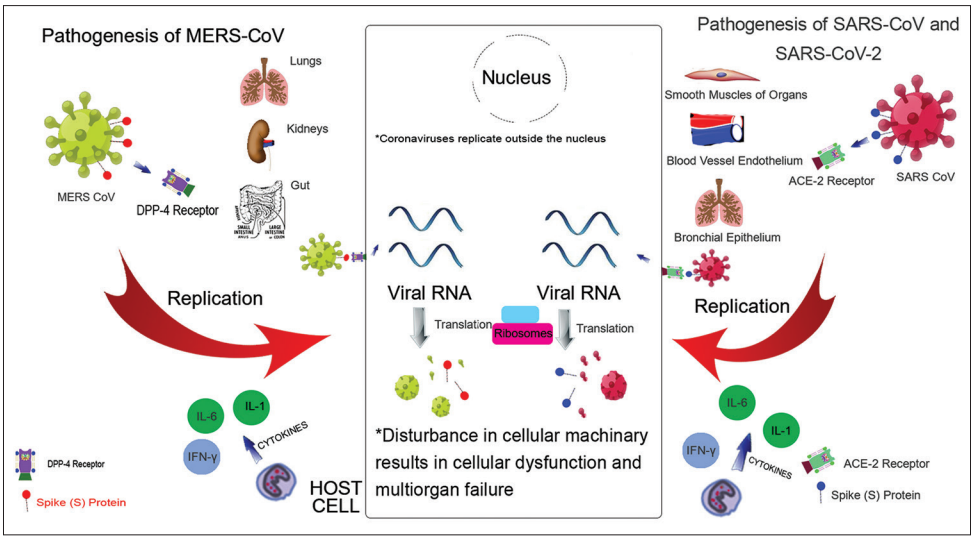

Figure 1: Pathogenesis of coronaviruses

1 week after an outbreak related to a flawed sewage system, possibly attributed to gastrointestinal tract infection through the fecal-oral route. Elderly SARS patients can also exhibit anorexia or falls complicated by fracture. Delirium is also possible.[46,47] The signs of SARS in adolescents are close to those found in adults.[48] Rales or rhonchi have been detected on auscultation of the lungs in the majority of patients in several studies. In a case series done in Hong Kong by JSM Peiris *et al.*, the majority of the patients had recurrent symptoms. The study outlined a 3-week course that began with fever and myalgia in week 1 and progressed to intermittent fever, hypoxemia, diarrhoea and fleeting chest infiltrates in week 2. ARDS developed in 20% of patients during the third week of their disease.[49]

MERS

Patients with MERS infections often had headaches, myalgia and diarrhoea.[50] In a case series of 70 patients of MERS, 30 (42.9%) patients developed acute renal failure.[27] The figures are much higher for chronically ill MERS patients. In one report, 58% (7/12 patients) needed renal replacement therapy. Furthermore, since MERS can be extracted from the urine of infected patients, the researchers speculated on the risk of possible renal intervention by the viral infection.[51] In contrast to this, a research conducted by Chu KH *et al.* in patients with SARS, 6.3% of patients experienced acute renal failure and 91.7% of patients with renal failure died.[52]

Laboratory Features

The laboratory and radiological characteristics of coronavirus diseases have varied. Elevated alanine transaminases and lactate dehydrogenase consistently linked to active SARS infection.[22-25] In a study done by Wong RS *et al.*, low T lymphocyte count was associated with poorer outcomes in SARS patients.[53] Hypocalcemia was observed in 60% of patients with SARS infection.[24] Features indicative of low-grade DIC, like elevated d-dimers and thrombocytopenia, were also found in these patients. In patients with MERS, neutrophilia along with lymphocytopenia and monocytosis was reported in a case series from Korea.[50] MERS patients have also shown laboratory evidence of DIC.[54-56] One the other hand, patients with CoVID-19 showed lymphocytopenia along with eosinophilia. In severe cases of CoVID-19, serum albumin tends to be decreased.[57]

Table 2 compares the laboratory parameters of coronavirus diseases. The frequency of abnormal laboratory findings is given in Table 3.

Radiological Features

Concerning the radiological properties of SARS, around 20–25% of patients presented with normal chest X-ray (CXR). Although the most frequent abnormalities in SARS patients were airspace opacification.[73-75] X-Ray radiograph findings are often not as useful in differentiating viral causes.[76] However, high-resolution computed tomography (HRCT) can be used to detect the opacities early in coronavirus diseases.[77]

In a study by *Assiri A et al.* on patients with MERS,[28] all patients had an abnormal radiological picture. CXR findings in their study showed abnormalities in all (n = 47) patients. Increased bronchovascular markings, patchy infiltrates, interstitial changes, consolidation, nodular and reticular opacities, pleural effusions, total and airspace opacities were seen. CT scan of the chest showed infiltrates and lobar consolidation in a few patients.[63,64]

Surprisingly, the radiological presentation of CoVID-19 has been variable. For instance, Egyptian scientists performed chest computed tomography (CCT) on all patients with positive COVID-19 RT-PCR tests. They found the most conspicuous radiographic finding was nonuniform (patchy) peripheral subpleural ground-glass opacity, followed by consolidation, and ground-glass opacity and induration together.[78] Other authors described different radiology findings, such as thickening of

Table 2: Mean laboratory values of patients with confirmed coronavirus disease

Parameter	SARS[25,58-62]	MERS[50,63-65]	CoVID-19[33,34,57,66-69]	Lab. Normal Value
Hemoglobin (g/dL)	12.9±1.7	12.27±1.46	13.3 (12.2-14.7)	12-17
Hemocrit (%)	37±3.21	42.74±3.94	39.21±2.45	40-50
RBC Count ($\times 10^9$/dL)	4.4±0.5	4.70±0.45	4.24±0.619	4.2-6.1
WBC Count ($\times 10^6$/dL)	8.3±4.9	3.7-11.7	1.725 (2.18-11.14)	4.5-11
Platelet counts ($\times 10^9$/L)	206.3±89.9	64-309	158 (131-230)	150-450
Neutrophil (%)	78.8±21.56	52.27±23.36	64.92±17.14	40-60
Eosinophil (%)	-	2.71±4.33	2.32±2.53	1-4
Basophil (%)	-	0.19±0.17	0.25±0.53	0.5-1
Monocyte (%)	5.6	10.40±5.94	6.86±3.77	2-8
Lymphocyte (%)	9.7	24.13±13.97	24.96±14.22	20-40
CRP (mg/L)	3.9±3.6	9±2.31	10.5 (2.7-51.2)	<10
LDH (U/L)	532.2±260	>300 U/L in 62.8% patients*	320.5 (248.5-385.3)	140-280
ALP (U/L)	75.6±27.9	72.43±18.69	61 (50.5-74.5)	44-147
ALT (U/L)	89.8±104.5	58.61±27.56	26 (12.9-33.15)	<45
AST (U/L)	36.7±20.0	86.38±52.59	33.4 (27.8-43.7)	<40
Creatinine (µmol/L)	82.7±27.2	907.19±11.49	66 (57.8-74.5)	74.3-107
Creatine kinase (U/L)	228.6±572.05	181.25±195.04	66 (42-126)	25-200

*Data not available, CRP - C-Reactive protein, LDH - Lactate dehydrogenase, ALT - Alanine aminotransferase, AST - Aspartate aminotransferase, and ALP - Alkaline phosphate. Data reported in either Mean±Standard deviation, Mean (95% Confidence interval) or Range

Table 3: Frequency of abnormal laboratory findings in coronavirus diseases reported in several case series

Finding	SARS[22,31,59]	MERS[28,31,70]	CoVID-19[33,57,71,72]
Leukopenia (<4·0 $\times 10^9$ cells per L)	25-35%	14%	20%
Thrombocytopenia (<140 $\times 10^9$ platelets per L)	40-45%	36%	17%
High lactate dehydrogenase	50-71%	48%	43%
High alanine aminotransferase	20-30%	11%	22.7%
High aspartate aminotransferase	20-30%	14%	25.3%

the interlobular septum, bronchiectasis, pleural thickening, crazy-paving pattern, bilateral lower lobe lesions and predominance of peripheral and posterior localization, with varying frequency in their studies.[79-81] Radiologic signs like pleural effusion, cavitation, pulmonary nodules, lymphadenopathy, and lung fibrosis have not been reported in patients with coronavirus diseases.[82] When it comes to CXRs, almost 40% of the CoVID-19 patients showed a normal CXR picture.[83] Moreover, at the primary diagnosis of this viral infection, the CXR had shown a lower sensitivity for detection of CoVID-pneumonia compared to CCT.[84] Therefore, the CoVID-19 lung infection can go unnoticed, reducing the value of CXR in diagnosing the CoVID-19. The highly sensitive CCT radiologic imaging signs of COVID-19 pneumonia were found. Although the radiologic features of SARS, MERS and COVID-19 lung infection overlap, the differences are still existing notably early in the course of the illness.[82]

The most common radiological (CCT) findings are shown in Table 4.[82,33]

Discussion

In this article, we performed a comparative analysis of three coronavirus diseases, which may sometimes cause severe consequences and even death. Very few studies have actually compared the fundamental characteristics of these diseases. We described the individual features of these diseases above.

In terms of clinical features, no coronavirus disease has been documented to have a "asymptomatic" or carrier condition to yet.[85] This was seen in the case of the novel virus, where 6.5% of the lab-confirmed cases were actually asymptomatic.[32,34-36] Like any other viral infection, almost all patients with coronavirus disease present with fever. But from what has been seen before, the new virus seems to be distinct in the way that only three out of every five patients with CoVID-19 presented with fever. Nonproductive cough was most frequently observed in SARS, followed by MERS and CoVID-19. Fever and cough as such were the most common presenting features of coronavirus diseases. Chills with rigors were commonly seen in MERS and SARS infections, whereas not many of the COVID-19 patients presented with these symptoms. Myalgia and headache, which are more often found in influenza illnesses, have also been seen in a number of patients with coronaviral diseases, particularly in the MERS. Nausea and vomiting were more consistent with SARS and MERS than CoVID-19.[22,24,32,34-36]

When it comes to laboratory features, hematological parameters were most reported in the literature concerning coronavirus diseases. Almost all these patients were shown to have their hemoglobin near the lower end of the normal range. Total leukocyte count of most of the SARS patients showed upper normal range or leucocytosis, while MERS and CoVID-19 cases ranged from profound leucopenia to leucocytosis, a few patients even being to the normal range. Thrombocytopenia was common

Table 4: Comparison of main radiologic (CCT) finding in COVID-19, SARS and MERS

	CoVID-19	SARS	MERS
CCT findings			
Prevalent	multifocal peripheral lungs opacities (ground-glass opacity, consolidation or both)		
Presence	bilateral, multifocal, basal lobes	unilateral, focal/multifocal; diffuse	bilateral, multifocal, basal lobes; isolated unilateral
Follow-up imaging presentation	permanent or progressing lungs opacities	unilateral, focal; progressing (most common) may be unilateral and multifocal or bilateral with multifocal consolidation	extension into upper lobes or perihilar spaces, pleural effusion, interlobular septal thickening
Indicators of poor prognosis	consolidation	bilateral, 4 or more lung areas, progressing involvement post 12 days	larger lungs involvement, pleural effusion, pneumothorax
Normal findings	15-20% of patients		17% of patients

CCT - Chest computer tomography

in patients with MERS, whereas SARS and CoVID-19 patients had platelet counts in slightly lower than normal to normal ranges. To our surprise, SARS patients had their CRP within normal ranges, while in MERS and CoVID-19 infections it tends to increase. MERS Patients have been reported to experience renal failure.[25,27-32,34-36,58,59,63] Consistent to this, creatinine is shown to be raised in MERS patients, while that of almost all SARS and CoVID-19 patients ranged in normal limits.[50] MERS and CoVID-19 have also been shown to trigger coagulopathy, with laboratory evidence to back that up. However, DIC has not been identified in any SARS cases to date.

Since a few retrospective studies have demonstrated that systemic inflammation and "cytokine storm" are correlated with adverse outcomes, hyperinflammation in COVID-19 may be a driver of severity that could be targeted therapeutically.[86] However, association does not imply causation, and it is equally possible that elevated viral burden (as a result of the immune system's inability to suppress infection) drives inflammation and severity (as has been seen with other viruses), rather than enhanced inflammation being an unwanted host reaction that needs to be corrected.

Coming to the radiological features, all these viruses showed the same peripheral opacities as in any pneumonia. In total, 15–20% of the patients tend to depict normal radiological findings in HRCT of the thorax. CoVID-19 and MERS are primarily reported to have bilateral involvement, whereas SARS patients are more likely to have unilateral involvement. Pleural effusion, septal thickening and pneumothorax observed in MERS patients are strong signs of a bad prognosis in these patients. With CoVID-19, as with every other pneumonia, consolidation was shown to be a prognostic factor. Although this emphasizes the significance of HRCT imaging in understanding these diseases, it is restricted to reality because these changes appear late in the disease.

Recently, many cases of fungal and bacterial (e.g., mucormycosis, Klebsiella, etc.) coinfections or postinfections have been reported. In the case of SARS or MERS, this has not been documented.[87,88]

Implications for primary care physicians

Despite being from the same genus, the three viruses presented differently, so identifying the causative agent during the first encounter is critical for primary care physicians in order to detect, manage and report future outbreaks early. It also emphasises how even small mutations might alter the spectrum of symptoms as well as the range of mortality and morbidity. Because results vary, early diagnosis and treatment should be emphasised and made available to primary care physicians so that they can successfully manage the case.

Radiological investigations are not of much importance, as they arrive late in SARS and COVID-19. Overall, the evidence suggests that it is not needed to wait for radiological abnormalities to emerge, particularly when we are getting things like "happy hypoxia" in COVID-19 patients, and where indicators like SPO2 decrease should be more trustworthy. When it comes to laboratory findings, they are all abnormal in all of these diseases.

Key points

- With COVID-19, it was the first time in the coronavirus family that a coronavirus disease presented asymptomatically.
- Myalgia and headache, which are more often associated with influenza infections, have been reported in a number of patients with coronavirus disorders, especially MERS.
- Clinically, diarrhoea is a distinct feature of SARS, while acute kidney injury is a frequent feature of MERS.
- SARS may show normal CXRs, but the most common pathology is airspace opacification. In MERS, all patients have abnormal X-ray results, while COVID-19 has a varied and nonspecific radiological picture.
- The COVID-19 may be associated with fungal or bacterial (e.g., mucormycosis, Klebsiella) coinfections or infections in post COVID state. These are not reported in case of SARS or MERS.

Conclusions

Each of these diseases, SARS, MERS and CoVID-19, and their respective causative agents have subtle differences in their clinical, laboratory and radiological features. Understanding these differences was an important aspect in a primary care physician's perspective. The most frequent signs of COVID19, SARS and MERS infected patients are fever and cough. COVID19 reported victims to have a lower mortality rate than SARS and MERS-affected patients. The CoVID-19 was the only disease that showed an "asymptomatic"

phase. However, merely reporting confirmed cases can distort clinical results and conclusions, which should be acknowledged while analyzing the data. As the planet struggles to cope with the CoVID-19 pandemic, it is important to concentrate on different methods for eradicating (rather controlling) the contagious agent and managing the symptomatic cases properly. The purpose of this review was to concentrate on the similarities or just about any aspect of the differences in these viruses and their respective diseases in order to manage case effectively.

Ethical considerations

No human or animal participants were involved in the study. Ethics approval was not required for this study.

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Conflicts of interest

There are no conflicts of interest.

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