COVID-19, SARS and MERS: are they closely related?

Nicola Petrosillo, Giulio Viceconte, Onder Ergonul, Giuseppe Ippolito, Eskild Petersen

PII: S1198-743X(20)30171-3
DOI: https://doi.org/10.1016/j.cmi.2020.03.026
Reference: CMI 1988

To appear in: Clinical Microbiology and Infection

Received Date: 16 February 2020
Revised Date: 9 March 2020
Accepted Date: 21 March 2020

Please cite this article as: Petrosillo N, Viceconte G, Ergonul O, Ippolito G, Petersen E, COVID-19, SARS and MERS: are they closely related?, Clinical Microbiology and Infection, https://doi.org/10.1016/j.cmi.2020.03.026.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2020 Published by Elsevier Ltd on behalf of European Society of Clinical Microbiology and Infectious Diseases.
COVID-19, SARS and MERS: are they closely related?

Nicola Petrosillo¹, Giulio Viceconte², Onder Ergonul³,⁴, Giuseppe Ippolito¹,

Eskild Petersen⁵,⁶,⁷

¹National Institute for Infectious Diseases “L. Spallanzani”, IRCCS, Rome, Italy
²University “Federico II”, Department of Clinical Medicine and Surgery, Naples, Italy
³Koc University, School of Medicine, Istanbul, Turkey
⁴ESCMID Executive Committee
⁵Directorate General for Disease Surveillance and Control, Min of Health, Muscat, Oman
⁶ESCMID Emerging Infections Task Force, ESCMID, Basel
⁷Institute for Clinical Medicine, Faculty of Health Sciences, University of Aarhus, Denmark
ABSTRACT

Background: The 2019 novel coronavirus (SARS-CoV-2) is a new human coronavirus which is spreading with epidemic features in China and other Asian countries with cases reported worldwide. This novel Coronavirus Disease (COVID-19) is associated with a respiratory illness that may cause severe pneumonia and acute respiratory distress syndrome (ARDS). Although related to the Severe Acute Respiratory Syndrome (SARS) and the Middle East Respiratory Syndrome (MERS), COVID-19 shows some peculiar pathogenetic, epidemiological and clinical features which have not been completely understood to date.

Objectives: We provide a review of the differences in terms of pathogenesis, epidemiology and clinical features between COVID-19, SARS and MERS.

Sources: The most recent literature in English language regarding COVID-19 has been reviewed and extracted data have been compared with the current scientific evidence about SARS and MERS epidemics.

Content: COVID-19 seems not to be very different from SARS regarding its clinical features. However, it has a fatality rate of 2.3%, lower than SARS (9.5%) and much lower than MERS (34.4%). It cannot be excluded that because of the COVID-19 less severe clinical picture it can spread in the community more easily than MERS and SARS. The actual basic reproductive number ($R_0$) of COVID-19 (2-2.5) is still controversial. It is probably slightly higher than the $R_0$ of SARS (1.7-1.9) and higher than MERS (<1). The gastrointestinal route of transmission of SARS-CoV-2, which has been also assumed for SARS-CoV and MERS-CoV, cannot be ruled out and needs to be further investigated.
Implications: There is still much more to know about COVID-19, especially as concerns mortality and capacity of spreading on a pandemic level. Nonetheless, all of the lessons we learned in the past from SARS and MERS epidemics are the best cultural weapons to face this new global threat.
INTRODUCTION

The 2019 novel coronavirus (SARS-CoV-2) is a new human coronavirus which emerged at the end of December 2019 in Wuhan, China. It is currently spreading with epidemic features in China and other Asian countries, with cases reported in Europe, Australia and North America. Currently, at the date of 8th of March 2020, 105 586 confirmed cases have been reported in 101 countries with a total number of 3584 deaths.¹

COVID-19 (Coronavirus Disease) is the clinical syndrome associated with SARS-CoV-2 infection, which is characterized by a respiratory syndrome with a variable degree of severity, ranging from a mild upper respiratory illness to severe interstitial pneumonia and acute respiratory distress syndrome (ARDS).²⁻⁴

Although SARS-CoV-2 belongs to the same betacoronavirus genus of the coronaviruses responsible for the severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS) (i.e SARS-CoV and MERS-CoV, respectively), this novel virus seems to be related to milder infections. Moreover, SARS and MERS were mainly associated with nosocomial spread, whereas SARS-CoV-2 is much widely transmitted in the community.⁵

In this review we aim to analyze the differences in terms of pathogenesis, epidemiology and clinical features between COVID-19, SARS and MERS.

PHYLOGENY

Genome sequence analysis has shown that SARS-CoV-2 belongs to betacoronavirus genus, that includes Bat SARS-like coronavirus, SARS-CoV, and MERS-CoV.⁶ SARS-CoV-2 possesses a genomic structure which is typical of other betacoronaviruses. Similarly to other coronaviruses, its genome contains 14 open reading frames (ORFs), encoding for 27 proteins: the ORF1 and ORF2 at the 5’-terminal region of the genome encode for 15 non-structural proteins important for virus replication.⁷,⁸ The 3’-terminal region of the genome encodes for
structural proteins, namely spike (S), envelope protein (E), membrane protein (M) and nucleocapsid (N), plus 8 accessory proteins.\textsuperscript{7,8} Phylogenetic tree analysis of the novel coronavirus showed that SARS-CoV-2 belongs, together with SARS-CoV and Bat SARS-like coronavirus, to a different clade from MERS-CoV and it is more phylogenetically related to Bat SARS-like coronaviruses isolated in China from horseshoe bats between 2015 and 2018 than to the SARS-CoV (Table 1). This suggests a different viral evolution from SARS and MERS, involving bats as wild reservoir.\textsuperscript{9–14} Genomic comparison between SARS and SARS-CoV2 has shown that there are only 380 amino acid substitutions between SARS-CoV-2 and SARS-like coronaviruses, mostly concentrated in the nonstructural protein genes, while 27 mutations have been found on genes encoding for viral spike protein S responsible of receptor binding and cell entry.\textsuperscript{8} This mutations might explain the apparent lower pathogenicity of SARS-CoV-2 than SARS-CoV, but further studies are required.\textsuperscript{9}

**PATHOGENICITY**

Accumulating evidence based on genomic analysis suggest that SARS-CoV-2 shares the same human cell receptor with SARS-CoV, the angiotensin-converting enzyme 2 (ACE2), while MERS-CoV uses dipeptidyl peptidase 4 (DPP4) to enter in host’s cells (Table 1).\textsuperscript{15} It is well established that SARS-CoV emerged as human pathogen thanks to favorable mutations on the receptor binding domain (RBD) of the S protein, that increased its pathogenicity by strengthening its affinity to the receptor; it is therefore assumed that SARS-CoV-2 has behaved in a similar way.\textsuperscript{15} However, in SARS-CoV-2 no amino acid substitutions were present in the RBD that directly interact with human receptor ACE2 compared with SARS-CoV, but six mutations occurred in the other regions of the RBD.\textsuperscript{8} The role of such substitutions on the pathogenicity of SARS-CoV-2 must be further investigated. Analysis of receptor affinity shows that SARS-CoV-2 binds ACE2 more efficiently than the 2003 strain of SARS-CoV, although less efficiently than the 2002 strain.\textsuperscript{15} Moreover, it has
been predicted that a single nucleotide mutation on RBD of SARS-CoV-2, if occurs, could further increase its pathogenicity.\textsuperscript{15}

ACE2 is an ectoenzyme anchored to the plasma membrane of the cells of several tissues, especially lower respiratory tract, heart, kidney and gastrointestinal tract.\textsuperscript{16} Inoculation of the 2019-nCoV onto surface layers of human airway epithelial cells in vitro causes cytopathic effects and cessation of the cilia movements.\textsuperscript{17} SARS-CoV highly replicates in the type I and II pneumocytes and in enterocytes, and the SARS-induced down-regulation of ACE2 receptors in lung epithelium contributes to the pathogenesis of acute lung injury and subsequent ARDS.\textsuperscript{16,18} It must be further investigated if the higher receptor affinity of SARS-CoV-2 than SARS-CoV for ACE2 could lead to a more severe lung involvement in COVID-19 than in SARS.

**TRANSMISSIBILITY**

The reproductive number (\(R_0\)) of the novel infection is estimated by World Health Organization (WHO) to range between 2 and 2.5, which is higher than SARS (1.7-1.9) and MERS (<1), suggesting that SARS-CoV-2 has a higher pandemic potential.\textsuperscript{19–23} However, it must be noted that some published studies have estimated a \(R_0\) for SARS reaching the value of 4.\textsuperscript{24} Interestingly, a recent review by Liu and colleagues has shown that the average reproductive number of SARS-CoV-2 is estimated to be 3.28, with a median value of 2.79, thus exceeding the WHO estimates.\textsuperscript{25}

Nonetheless, in Table 1 we only report the WHO data, since the estimation of \(R_0\) depends on the estimation method used and the current estimate can be biased by insufficient data and short onset time of the diseases, as Liu and colleagues also state.

According to a recent large descriptive study carried out by the Chinese Center for Disease Control and Prevention (CCDC) on 44 672 individuals diagnosed with COVID-19 in China, the fatality rate of novel coronavirus infection is estimated to be 2.3\textsuperscript{26}, lower than SARS (9.5\%) and much lower than MERS (34.4\%).\textsuperscript{5,27} Interestingly, according to CCDC, the case fatality rate in the Hubei province,
where the epidemic has started, is 7-fold higher than other provinces. This could be related to the fact that, among the 44,672 cases reported by CCDC, 10,567 (14.6%) cases were diagnosed only clinically and exclusively in the Hubei province. Therefore, it cannot be excluded that clinically diagnosed cases presented with a more severe clinical picture, thus increasing the case fatality rate. After the change of case definition, the number of cases increased due to the inclusion of cases cumulated over the past weeks. The question is: were mild cases registered at all? It is not a minor matter, because including mild cases will reduce the mortality rate. Indeed, the number of infected outside of China is currently 24,727 with 484 fatal outcomes, and a mortality rate of 1.9%. Of interest, the fatality rate of the novel coronavirus infection increases to an estimated 14% when considering only the hospitalized cases, reaching the overall SARS case-fatality rate that was estimated to be around 15%.

**CLINICAL FEATURES**

Up to date, complete clinical data concerning COVID-19 have been reported for 458 cases in the English-language literature, of which 415 from Hubei province in China, 17 in other Chinese provinces, 25 in Korea and 1 in USA. In Table 2 the main clinical characteristics from the three most significant case series of COVID-19 cases are listed and compared with the most recently available data about SARS and MERS. The median age of the COVID-19 cases ranges from 49 to 57 years, similar to SARS and MERS, higher in those admitted to ICU; up to 50% of patients reported a chronic comorbid illness in a slightly lower percentage compared to patients diagnosed with MERS. The most common presenting symptoms is fever, followed by cough, sore throat and dyspnea; all of the infected patients had at least one symptom. However, according to the CCDC report, 81% of the cases had mild symptoms and 1.2% were asymptomatic. Laboratory findings in patients diagnosed with COVID-19 are not remarkably different from those diagnosed with the other coronavirus infections, with lymphopenia as the most common finding,
together with low platelet count, decreased albumin levels and increased aminotransferases, lactic dehydrogenase, creatine kinase and C-reactive protein levels. No data are available on lymphocyte subpopulations levels, but it can be interesting to know if the virus associated lymphopenia affects in a different way CD4+ and CD8+ subpopulations, to predict the possible development of superimposed bacterial or opportunistic infections, which have currently been reported in a small amount of cases to date.²

Radiological presentation of COVID-19 is not much different from the other two coronavirus-associated pneumonia, even though the proportion of cases with bilateral findings seems to be higher in COVID-19 cases. The most common CT findings in COVID-19 is bilateral pulmonary parenchymal ground-glass, consolidative or “crazy paving” pulmonary lesions, often with a rounded shape and a peripheral distribution.³⁶ Interestingly, in a recent study on 167 patients from Hubei province with suspected COVID-19 who underwent chest CT scan and respiratory swab for detection of SARS-CoV-2, five subject (3%) had a CT scan that was strongly suggestive of COVID-19, but an initially negative real-time polymerase reaction (RT-PCR). These patients were isolated for presumed COVID-19 pneumonia and the respiratory swab repeated between 2 and 8 days later turned positive.³⁷

Patient diagnosed with COVID-19 may have an unfavorable clinical course with the onset of dyspnea within 5 days, ARDS within 8 days in 30% of cases and need for invasive mechanical ventilation and extracorporeal membrane oxygenation (ECMO) in 17% and 4% of cases, respectively.³ These findings are in line with SARS percentages, while clinical course of MERS seems to be characterized by a more frequent development of ARDS and needing of invasive life support, especially in elderlies and smokers.³⁸ In particular, acute kidney injury (AKI), which rarely occurs in SARS and COVID-19, seems to be a peculiar complication of MERS. Although this could be explained by a direct renal cytopathic effect induced by the virus, since DDP4 receptors are largely
represented in tubules and glomeruli, it seems more probable that the high percentage of AKI reported is due to multi-organ failure, which occurs more frequently in MERS than in the other coronavirus infections.\(^{39}\)

**CONCLUSIONS**

COVID-19 seems no to be very different from SARS regarding the clinical features; it seems to be less lethal than MERS, which is less related with the other two coronavirus both in terms of phylogenetic and pathogenesis features.

COVID-19 generally has a less severe clinical pictures, and thus it can spread in the community more easily than MERS and SARS, which have been frequently reported in the nosocomial setting. The previous knowledge learned from SARS and MERS lessons might have contributed to the institution of more efficient preventive measures in the healthcare settings.

Which are the causes of such different ability to spread among these three viruses? A first hypothesis is a different viral tropism for the respiratory tract, resulting in a milder but highly transmittable disease when the virus replicates in the upper respiratory tract and a severe pneumonia with lower spreading potential when the viral tropism is higher for the lower respiratory tract. This hypothesis derives from the example of the influenza viruses, namely seasonal influenza viruses H1N1 and H3N2. They preferably bind alpha 2,6-linked sialic acid receptors of the upper respiratory tract, usually causing a less severe but more transmissible disease than avian influenza H5N1 or H7N9, which preferably bind alpha 2,3-linked sialic acid in the lung alveoli, causing severe pneumonia.\(^{40}\) On the other hand, SARS-CoV-2, SARS-CoV and MERS-CoV use receptors that have been found both in the upper and in the lower respiratory tract. Moreover, other human coronaviruses, such as NL63-CoV, cause a mild illness even if they bind to the same receptor of SARS-CoV-2 and SARS-CoV\(^5\). So, in our opinion, it is likely that the different inoculum dose at the time of infection makes the difference in terms of severity of the
disease; heavy inoculum exposures seem to be linked to an higher penetration in the lower respiratory tract, giving severe pneumonia, whereas lower inoculum exposures allow viruses to only reach the upper airway, causing a milder infection.

Viral loads are higher at the time of symptoms onset and higher in nose than in throat specimens.\textsuperscript{41,42} Furthermore, in patients affected by COVID-19, viral load progressively decreases within days, following a different pattern than SARS, in which the highest shedding is recorded after 10 days from the symptoms’ onset.\textsuperscript{41–43} These findings suggest that SARS-CoV-2 may spread more easily in the community than SARS even when initial mild symptoms or no symptoms are present.

The differences in the intrinsic virulence of the viruses themselves can explain the different capacity of spreading. MERS-CoV has a higher mortality but a lower transmissibility probably because it causes a more severe clinical picture than COVID-19 and SARS, requiring hospitalization more frequently, thus reducing the community spreading of the infection and increasing the nosocomial transmission.\textsuperscript{5,21} On the other hand, the higher mortality of MERS could be biased by the fact that the largest data available on MERS were derived from hospitalized patients, thus implicating a more severe clinical picture than community acquired cases.\textsuperscript{44} This hypothesis is strengthened by the observation that, when the cohort of patients with MERS was derived from the community and not from hospital outbreaks, the mortality rate decreased to 10%, as it has been observed in a cohort study carried out in 2015 in Saudi Arabia.\textsuperscript{44}

Interestingly, despite the high virological similarity between the SARS-CoV-2 and SARS-CoV, gastrointestinal (GI) symptoms and diarrhea seem to be much more common in SARS, although the proportion of SARS patients with GI symptoms varies among different studies, from 23% to 70% in the Toronto outbreak and in the Hong Kong community outbreak, respectively.\textsuperscript{43,45} Such difference could be related to the fact that the Hong Kong outbreak seemed to originate from a
fecal contamination of a residence complex due to a faulty sewage system, while the Toronto outbreak was mainly caused by nosocomial hospital droplet transmission. The GI route of transmission has been also hypothesized for MERS-CoV, through the consumption of infected camel milk; moreover, GI transmission has been demonstrated in the animal model through intestinal DPP4 receptors. According to this findings, the reported detection of SARS-CoV-2 RNA in the loose stools of the first US patient with COVID-19 is not surprising. SARS-CoV replicates in the enteric epithelium by binding to the ACE2 receptor and it cannot be excluded that SARS-CoV-2 would behave in the same way. This may contribute to the hypothesis that SARS-CoV-2 could also be transmitted via this route, together with the evidence that SARS-CoV and MERS-CoV remain viable in environmental conditions that could facilitate faecal–oral transmission. In Table 3 we provide a synthesis of what is certain to date about COVID-19 and what needs to be further addressed.

In conclusion, there is still much more to know about COVID-19, especially its epidemiological features, such as mortality and capacity of spreading on a pandemic level. The lessons we have learned in the past from the SARS and MERS epidemics are the best cultural weapons to face this new global threat.
<table>
<thead>
<tr>
<th>Phylogenetic origin</th>
<th>Animal reservoir</th>
<th>Intermediate host</th>
<th>Receptor</th>
<th>Case fatality rate</th>
<th>$R_0$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SARS-CoV-2</strong></td>
<td>Clade I, cluster IIa</td>
<td>Bats</td>
<td>Unknown</td>
<td>angiotensin-converting enzyme 2 (ACE2)</td>
<td>2.3%$^{26}$</td>
</tr>
<tr>
<td><strong>SARS-CoV</strong></td>
<td>Clade I, cluster IIb</td>
<td>Bats</td>
<td>Palm civets</td>
<td>angiotensin-converting enzyme 2 (ACE2)</td>
<td>9.5%</td>
</tr>
<tr>
<td><strong>MERS-CoV</strong></td>
<td>Clade II</td>
<td>Bats</td>
<td>Camels</td>
<td>dipeptidyl peptidase 4 (DPP4)</td>
<td>34.4%</td>
</tr>
</tbody>
</table>

*Table 1 - Phylogenetic, pathogenetic and epidemiologic characteristics*
<table>
<thead>
<tr>
<th></th>
<th>COVID-19</th>
<th>SARS</th>
<th>MERS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Date of emergence in human population</strong></td>
<td>2019</td>
<td>2002</td>
<td>2012</td>
</tr>
<tr>
<td><strong>Absolute number of cases</strong></td>
<td>80</td>
<td>239</td>
<td>8096</td>
</tr>
<tr>
<td><strong>Demographic and general characteristics, % of cases</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>40-60</td>
<td>38-42</td>
<td>59.5-64</td>
</tr>
<tr>
<td>Female</td>
<td>40-55</td>
<td>64-68</td>
<td>35-40</td>
</tr>
<tr>
<td>Cardiovascular diseases</td>
<td>10-46</td>
<td>8</td>
<td>9.1</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>1-2</td>
<td>1-2</td>
<td>10.2</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10</td>
<td>16</td>
<td>18.8</td>
</tr>
<tr>
<td>Malignancy</td>
<td>2-4</td>
<td>6</td>
<td>15.5</td>
</tr>
<tr>
<td><strong>Signs and symptoms, % of cases</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>81-91</td>
<td>99-100</td>
<td>81.7-98</td>
</tr>
<tr>
<td>Cough</td>
<td>48-68</td>
<td>57-75</td>
<td>56.9-83</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>19-31</td>
<td>40-42</td>
<td>22-72</td>
</tr>
<tr>
<td>Sore throat</td>
<td>29</td>
<td>13-25</td>
<td>9.1-14</td>
</tr>
<tr>
<td>Dizziness and confusion</td>
<td>22</td>
<td>4-43</td>
<td>5.4</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>16</td>
<td>23-70</td>
<td>19.4-26</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>6</td>
<td>20-35</td>
<td>14-21</td>
</tr>
<tr>
<td><strong>Laboratory findings on admission, % of cases</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukopenia</td>
<td>35</td>
<td>33.9</td>
<td>14</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>35-72</td>
<td>54-70</td>
<td>32</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>12</td>
<td>44.8</td>
<td>36</td>
</tr>
<tr>
<td>Elevated aminotransferases</td>
<td>28-35</td>
<td>23</td>
<td>11-40</td>
</tr>
<tr>
<td><strong>Radiological chest findings on admission, % of cases</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral infiltrate</td>
<td>10</td>
<td>46-54</td>
<td>14.3-62.6</td>
</tr>
<tr>
<td>Bilateral infiltrate</td>
<td>84-90</td>
<td>29-45</td>
<td>37.4-75</td>
</tr>
<tr>
<td>No findings</td>
<td>14</td>
<td>13-25</td>
<td>4.3-30</td>
</tr>
<tr>
<td><strong>Complications, % of cases</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensive Care Unit admission</td>
<td>24</td>
<td>23-34</td>
<td>53-89</td>
</tr>
<tr>
<td>Acute Respiratory Distress Syndrome</td>
<td>18-30</td>
<td>20</td>
<td>20-30</td>
</tr>
<tr>
<td>Acute Kidney Injury</td>
<td>3</td>
<td>6.7</td>
<td>41-50</td>
</tr>
<tr>
<td>Deaths in hospitalized</td>
<td>10-11</td>
<td>3.6-15.7</td>
<td>30-40</td>
</tr>
</tbody>
</table>

**Table 2 - Clinical characteristics**
### Facts about COVID-19

- SARS-CoV-2 is more phylogenetically related to SARS-CoV than to MERS-CoV.
- Only minor differences have been found in the genome sequences of SARS-CoV-2 comparing with SARS-CoV.
- SARS-CoV-2 affinity for angiotensin-converting enzyme 2 (ACE2) receptor is higher than in SARS-CoV.
- COVID-19 fatality rate is lower than that found in SARS and MERS.
- SARS-CoV-2 RNA has been detected in the stools of infected patients, similarly to SARS-CoV and MERS-CoV.
- 1.2% of COVID-19 cases are asymptomatic.
- COVID-19 is not very different from SARS and MERS regarding demographic characteristics, laboratory and radiological findings.
- Clinical complications in COVID-19 are as frequent as in SARS, but less frequent than in MERS.
- Viral loads in COVID-19 patients are higher at the time of symptoms onset and progressively decrease during the clinical course of the disease.

### Questions needing to be further assessed

- Which is the role of aminoacid substitutions on the SARS-CoV-2 receptor binding domain in terms of pathogenesis?
- Does the higher affinity of SARS-CoV-2 than SARS-CoV for angiotensin-converting enzyme 2 (ACE2) receptor have an implication in respiratory complications?
- Is the fecal-oral route of transmission possible for COVID-19?
- Which is the role of asymptomatic COVID-19 cases in the epidemiology of the disease?
- Which is the actual COVID-19 basic reproductive number ($R_0$)?
- Are differences in viral kinetics in respiratory tract responsible of the different spreading potential of COVID-19, SARS and MERS?

---

**Table 3 - Facts and open issues about COVID-19**
TRANSPARENCY DECLARATION

- Conflict of interest disclosure: authors have no conflict of interest to disclose.

- Funding: no external funding was received.

- Acknowledgments: work supported by Ricerca Corrente, IRCCS.

- Contribution: NP and GV contributed to literature search and writing the paper. EP, OE and GI revised the manuscript and gave their final opinion for its intellectual content.
REFERENCES


24. Bauch CT, Lloyd-Smith JO, Coffee MP, Galvani AP. Dynamically Modeling SARS and Other


32. Chang D, Lin M, Wei L, et al. Epidemiologic and Clinical Characteristics of Novel Coronavirus...


1755.2005.67130.x

doi:10.3947/ic.2016.48.2.118

52. Saad M, Omrani AS, Baig K, et al. Clinical aspects and outcomes of 70 patients with Middle