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Letter to the Editor

Pharmacotherapy for COVID-19 infection in the countries of the Cooperation Council for the Arab States

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To the Editor

The relative performance levels of various COVID-19 therapeutic options in countries with similarly developed health systems have been examined, and various therapies have been found to correspond to different fatality rates. An examination of therapeutic approaches can contribute to explaining why fatality rates can vary by up to ten times despite the presence of similar rates of infection in various countries. On December 15, 2020, before the start of the vaccination campaign, the fatality rates of such cases in the United Kingdom and Belgium were 3.43% and 2.97%, respectively, while the United Arab Emirates and Qatar had rates of 0.33% and 0.17%. On August 7, 2021 (latest data-collection point at the time of this letter's writing) the United Kingdom and Belgium had rates of 2.15% and 2.22%, while the United Arab Emirates and Qatar had rates of 0.28% and 0.26%.

The other members of The Cooperation Council for the Arab States have also noted fatality rates among COVID-19 patients that are well below those of most other countries with similarly developed health care systems, such as Italy, Australia, Belgium, the United Kingdom (UK), Canada, and France. Data from ourworldindata.org,¹ based on the COVID-19 Data Repository by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University, are presented in [Figure 1](#).

The latest (August 7, 2021) ratios between confirmed deaths and cases are 1.56% in the KSA (KSA), 1.32% in

Oman, 0.59% in Kuwait, 0.51% in Bahrain, 0.28% in the United Arab Emirates (UAE), and 0.26% in Qatar. In Australia, the rates are 2.56% (4% in the state of Victoria), 2.92% in Italy, 2.15% in the UK, 2.22% in Belgium, 1.84% in Canada, and 1.76% in France.

The cumulative numbers of cases per million demonstrate that there are similarities in the percentages of infected persons across countries so far. The percentages are 15.86% in Bahrain, 9.80% in Belgium, 9.40% in France, 7.90% in Qatar, 7.27% in Italy, 9.44% in Kuwait, 8.98% in the UK, 7.00% in the UAE, 5.85% in Oman, 3.83% in Canada, 1.53% in KSA, and 0.14% in Australia.

While there are undoubtedly many other explanations for the marked variations in the cumulative fatality rates in various countries, the issue that we wish to highlight here is that the adoption of therapeutic approaches differs considerably between countries. Specifically, almost all of the antiviral agents used in KSA, the UAE, and the other Gulf states are unavailable in the other countries mentioned, where the local health authorities recommend against their use in accordance with the advice of the World Health Organization (WHO).²

According to the WHO, 'all 4 treatments evaluated (remdesivir, hydroxychloroquine, lopinavir/ritonavir and interferon) had little or no effect on overall mortality, initiation of ventilation and duration of hospital stay in hospitalized patients.' The positive chemotherapeutic advances made so far in the UAE and the other Gulf states (as well as countries in other regions, such as Singapore) are ignored in many other countries, which do not allow the administration of chemotherapeutics for COVID-19 infection.

The Saudi protocol for treating patients with COVID-19 infection as of January 22, 2021³ proposes some alternatives. For mild cases in outpatient settings,³ in early treatment, it is suggested that hydroxychloroquine (HCQ) be administered if no contraindications apply. If HCQ is unavailable, then chloroquine (CQ) may be used. Favipiravir may also be used. For severe cases,³ physicians are urged to administer favipiravir or remdesivir. As an adjunctive therapy,

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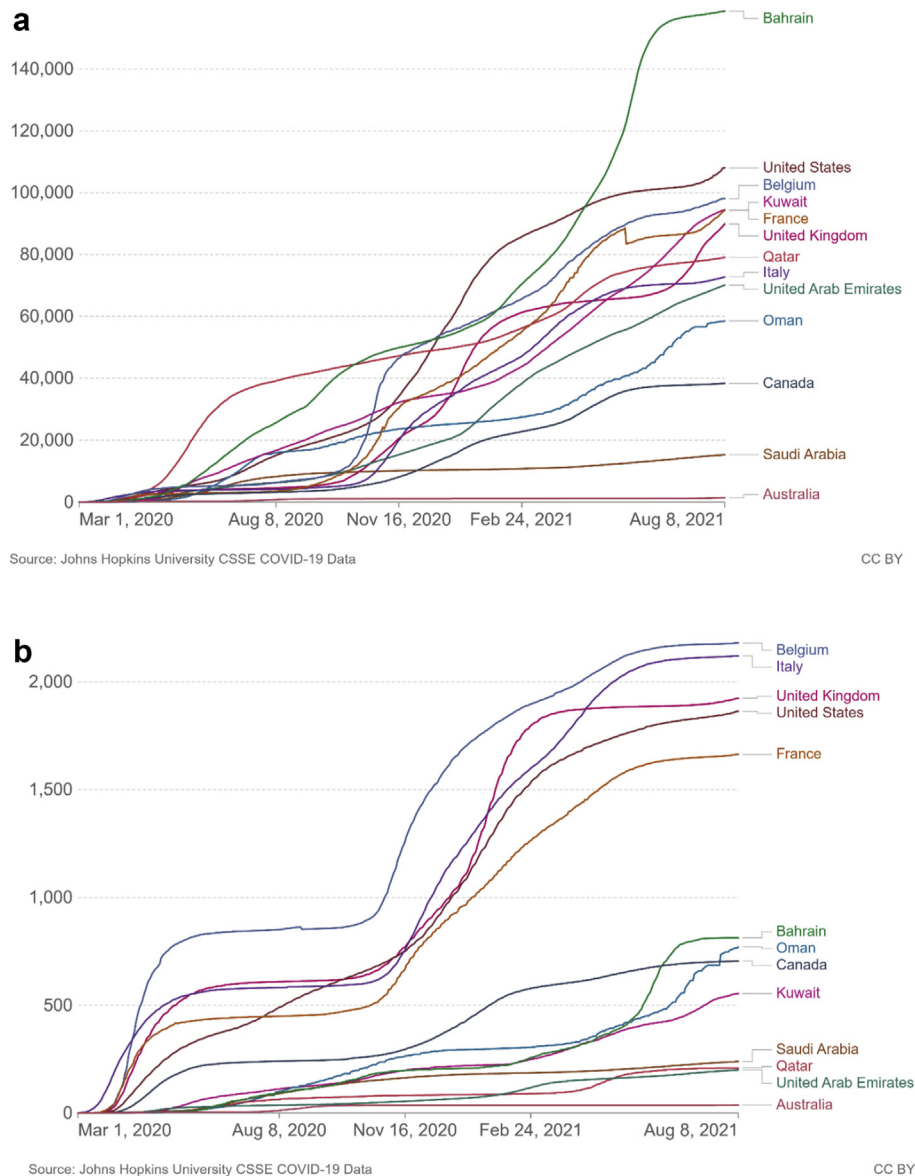


Figure 1: Cumulative confirmed COVID-19 cases (a) and fatalities (b) per million people, related fatality rates (c), and percentage of fully vaccinated (d) people in selected countries. Images from ourworldindata.org (CC BY).

dexamethasone is the preferred corticosteroid. For critical cases,³ physicians are urged to administer favipiravir or remdesivir. Remdesivir and baricitinib are suggested for patients with severe acute respiratory distress syndrome (ARDS), on invasive mechanical ventilation with high settings, or extracorporeal membrane oxygenation (ECMO). Even more pharmacotherapy options are available in the UAE.^{4,5}

Since December 20, 2020,⁵ for asymptomatic COVID-19 cases that are high-risk, HCQ (CQ) has been recommended. For COVID-19-related pneumonia lasting five days, the suggested therapies include HCQ, CQ, favipiravir, and lopinavir-ritonavir, all \pm camostat. For COVID-19-related pneumonia lasting seven days, the suggested therapies include favipiravir + HCQ \pm camostat,

favipiravir + CQ phosphate \pm camostat, and lopinavir-ritonavir + HCQ (CQ) \pm camostat or remdesivir. Nebulised interferon is an optional adjunctive therapy in less severe cases. For severe pneumonia resulting from COVID-19/patients who have been critically ill for ten days, favipiravir + camostat \pm nebulised interferon α or interferon β , lopinavir-ritonavir + ribavirin + interferon, and remdesivir are recommended. Tocilizumab may be considered in the event of a cytokine storm.

The use of combination therapies⁵ in complex cases, rather than a single therapeutic agent, is also worth noting. Immune-based therapies are mostly being used as adjunctive therapies, supplementing antiviral therapies.⁵ Surprisingly, the local health authorities in most countries recommend against the use of the antiviral treatments

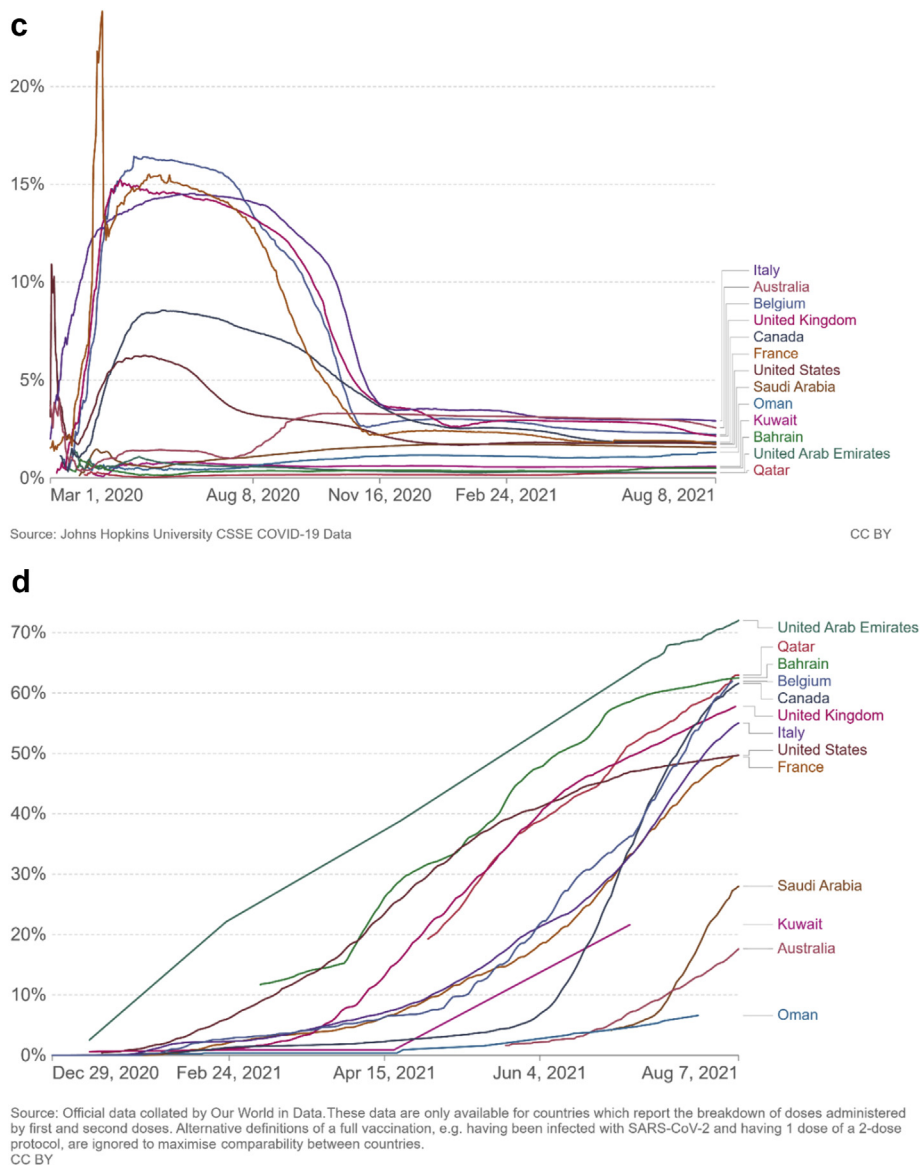


Figure 1: (continued).

mentioned above. This recommendation, is, however, not supported by the scientific literature.

From a purely statistical standpoint, among the papers published so far on the use of CQ/HCQ for COVID-19 infection,⁶ almost all are favourable toward their use in the early stages of the infection, while, in the later stages, the results are predominantly positive while showing some contradictory findings. Based on 326 CQ/HCQ studies, 240 of which were peer reviewed, and 273 of which compared treatment and control groups in the literature, it can be observed that all the early-treatment, and most of the late-treatment, studies' results were positive. CQ/HCQ is not recommended in very late stages of infection, nor are high dosages recommended over a long period. Nevertheless, the WHO and health organisations of many countries strongly advise against any use of CQ/HCQ for treating COVID-19 infection. Disregarding this recommendation does not seem to affect fatalities negatively. Similar conclusions could be

drawn regarding remdesivir, lopinavir-ritonavir, and nebulised interferon.

The success story of the UAE is also discussed in 7.

Reference 8 finally notes that the success of the therapeutic approach of the UAE and the other countries of the Cooperation Council for the Arab States is also due to case finding, contact tracing, and disease management. In the UAE, implementing mass testing and setting up large field hospitals and a large-capacity quarantine facility has permitted physicians to find cases and treat them while easing the pressure on city-based hospitals and permitting fast responses. This has prevented the viral load build-up that occurs with lack of care, lack of therapies, sharing of overcrowded spaces, and masking of infected individuals, which then becomes a driver of higher fatality rates.

We conclude that the use of antivirals, especially in the early stages of COVID-19 infection, is a determining factor in preventing the incremental growth of the viral load in late

stages, which then becomes much more difficult to manage. CQ/HCQ, remdesivir, favipiravir, lopinavir-ritonavir, and nebulised interferon are important components of the Gulf states' pharmacotherapy regimen. Based on an assessment of the efficacy of the therapies based on the percentages of fatalities, it appears that most of the Gulf states have performed well during the first year of the pandemic and have fared better than the other countries referenced and herein considered.

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Conflict of interest

The author has no conflict of interest to declare.

Ethical approval

The authors confirm that this letter has been prepared in accordance with COPE roles and regulations. Given the nature of the letter, no IRB review was required.

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