

A response letter to a prior Eye Reports publication, with original data:

COVID-19 cases are less prevalent in countries where malaria is endemic, suggesting a role for anti-malarial drugs as prophylaxis

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Abstract

Almost every country across the world has felt the repercussions of the pandemic of disease termed coronavirus disease 2019 (COVID-19) caused by the novel coronavirus identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). A recently published article points to a method of prevention and prophylaxis of COVID-19 through the use of anti-malarial drugs such as the 4-aminoquinolones: chloroquine and hydroxychloroquine, based on their mechanisms of action against SARS-CoV-2. This report aims to explore the correlation between COVID-19 cases and countries where malaria is prevalent using statistical means. It is hypothesized that countries where malaria is endemic will have few cases of COVID-19 since these countries use the 4-aminoquinolone anti-malarial drugs for prophylaxis.

Statistical analysis demonstrates that the numbers and incidence of COVID-19 cases and COVID-19 related deaths are substantially lower (multiple-fold lower) in countries with the highest prevalence of

malaria. The difference between both the COVID-19 incidence rate and the COVID-19 mortality rate in malaria prevalent countries compared to COVID-19 prevalent countries is statistically significant ($p = 0.02$ and $p = 0.04$ respectively).

This study provides further evidence that anti-malaria drugs may prove essential to breaking the spread of SARS-CoV-2 and preventing COVID-19 and COVID-19 related mortality. As the pandemic continues to evolve and doctors and researchers across the globe try to attenuate or stop the spread of SARS-CoV-2, the medical community should not overlook the potential role of the 4-aminoquinolones anti-malarial drugs, chloroquine and hydroxychloroquine, and 8-aminoquinolone anti-malaria drugs, tafenoquine and primaquine, as a prophylaxis.

Introduction

Almost every country across the world has felt the repercussions of the pandemic of disease termed coronavirus disease 2019 (COVID-19) caused by the

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Conflict of Interest: The author reports no conflicts of interest.

Submitted for Publication: March 26, 2020

Accepted for Publication: March 28, 2020

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novel coronavirus identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).¹ This pandemic is spreading across different populations rapidly, overwhelming countries around the world.² Amidst this public health crisis, researchers have been tracking which countries around the world are most affected by the pandemic in search of a possible pattern.³ A recently published article points to a method of prevention and prophylaxis of COVID-19 through the use of anti-malarial drugs such as the 4-aminoquinolones: chloroquine and hydroxychloroquine, based on their mechanisms of action against SARS-CoV-2.⁴ The use of these drugs as a prophylaxis for malaria is effective; however, malaria resistance of some of these drugs including chloroquine has made this form of prophylaxis less effective.⁵

This report aims to explore the correlation between COVID-19 cases and countries where malaria is prevalent using statistical means. It is hypothesized that countries where malaria is endemic will have few cases of COVID-19 since these countries use the 4-aminoquinolone anti-malarial drugs for prophylaxis.^{5,6}

Methods

As reported by the World Health Organization (WHO), the five countries with the highest prevalence of malaria cases in 2017, which accounted for about 50% of all malaria cases worldwide, are Nigeria, Democratic Republic of Congo, Mozambique, India, and Uganda.⁷ Since these countries have a high prevalence of malaria, they will be of focus in this report. These countries take anti-malarial drugs as a prophylaxis.⁶ Also examined in this report are the 4 countries (China, United States, Italy, and Spain) with the highest prevalence of COVID-19.¹

Data, as of March 26, 2020, regarding the number of COVID-19 cases,¹ the number of COVID-19 related deaths,¹ the country population size,⁸ and the country average age⁹ are examined. Using these

statistics, the mortality rate, case fatality rate, and incidence rate are calculated.

A one-tailed t-test was performed to determine whether there was statistical significance (defined as $p \leq 0.05$) between coronavirus statistics of malaria prevalent countries compared to coronavirus prevalent countries. The coefficient of determination was also examined to determine correlation between two variables.

Results

The numbers of COVID-19 cases and COVID-19 related deaths are substantially lower (multiple-fold lower) in countries with the highest prevalence of malaria (Table 1). Similarly, the COVID-19 incidence rate and COVID-19 related mortality rate are substantially lower (multiple-fold lower) in countries with the highest prevalence of malaria (Table 2). The difference between the COVID-19 incidence rate in malaria prevalent countries compared to COVID-19 prevalent countries is statistically significant ($p = 0.02$) (Figure 1). The difference between the COVID-19 related mortality rate in malaria prevalent countries compared to COVID-19 prevalent countries is also statistically significant ($p = 0.04$) (Figure 2). A slight correlation was found between the average age in a country and the COVID-19 related deaths ($R^2 = 0.71$) (Figure 3).

Discussion

These results demonstrate a negative correlation between countries with high malaria prevalence and COVID-19 incidence and COVID-19 mortality. In comparison to countries where COVID-19 is prevalent, the incidence rate of COVID-19 in malaria prevalent countries is statistically negligible (Figure 1). The malaria-stricken country that has the most deaths is India with 16 deaths, which is a mortality rate of 1.2×10^{-8} (0.0000012%) while the rest of these countries have less than very few deaths (3 deaths in one country, 1 death in another country, and no deaths in the two other countries). Conversely, countries affected most

Country	COVID-19 Cases ³	COVID-19 Related Deaths ³	Country Population Size ⁴	Country Average Age ⁵
Italy	80,589	8,215	60,480,000	45.4
Spain	56,197	4,145	46,660,000	43.1
China	81,285	3,287	1,386,000,000	37.4
United States	80,854	1,163	327,200,000	38.2
India	722	16	1,339,000,000	26.8
Democratic Republic of the Congo	51	3	81,340,000	18.8
Nigeria	65	1	190,900,000	18.1
Mozambique	7	0	29,670,000	17.6
Uganda	14	0	42,860,000	16.7

Table 1

In the countries of with the highest prevalence of COVID-19 cases as of March 26, 2020 (red) and the highest prevalence of malaria cases in 2017 (green), the number of COVID-19 cases and COVID-19 related deaths as of March 26, 2020 are identified and compared with the country population size and country average age.

Country	COVID-19 Incidence Rate (%)	COVID-19 Related Mortality Rate (%)	COVID-19 Related Case Fatality Rate (%)
Italy	0.1332	0.0135	10.19
Spain	0.1204	0.0088	7.376
China	0.0059	0.0002	4.044
United States	0.0247	0.0004	1.438
India	0.0000	0.0000	2.216
Democratic Republic of the Congo	0.0001	0.0000	5.882
Nigeria	0.0000	0.0000	1.538
Mozambique	0.0000	0.0000	0.000
Uganda	0.0000	0.0000	0.000

Table 2

The COVID-19 incidence rate, COVID-19 related mortality rate, and COVID-19 related case fatality rate are calculated in the countries of with the highest prevalence of COVID-19 cases as of March 26, 2020 (red) and the highest prevalence of malaria cases in 2017 (green).

by COVID-19 have between 1,000 to 8,000 deaths and have a country-wide mortality rate upwards of 0.01%.

Furthermore, since death from COVID-19 is of higher likelihood with older age groups,¹⁰ population age was compared to determine whether there is a

correlation. A correlation does appear to present, but the correlation is not extremely strong with a coefficient of determination 0.71. Age appears to be a confounding variable; however, it is unlikely that age alone is the reason for very little COVID-19 related

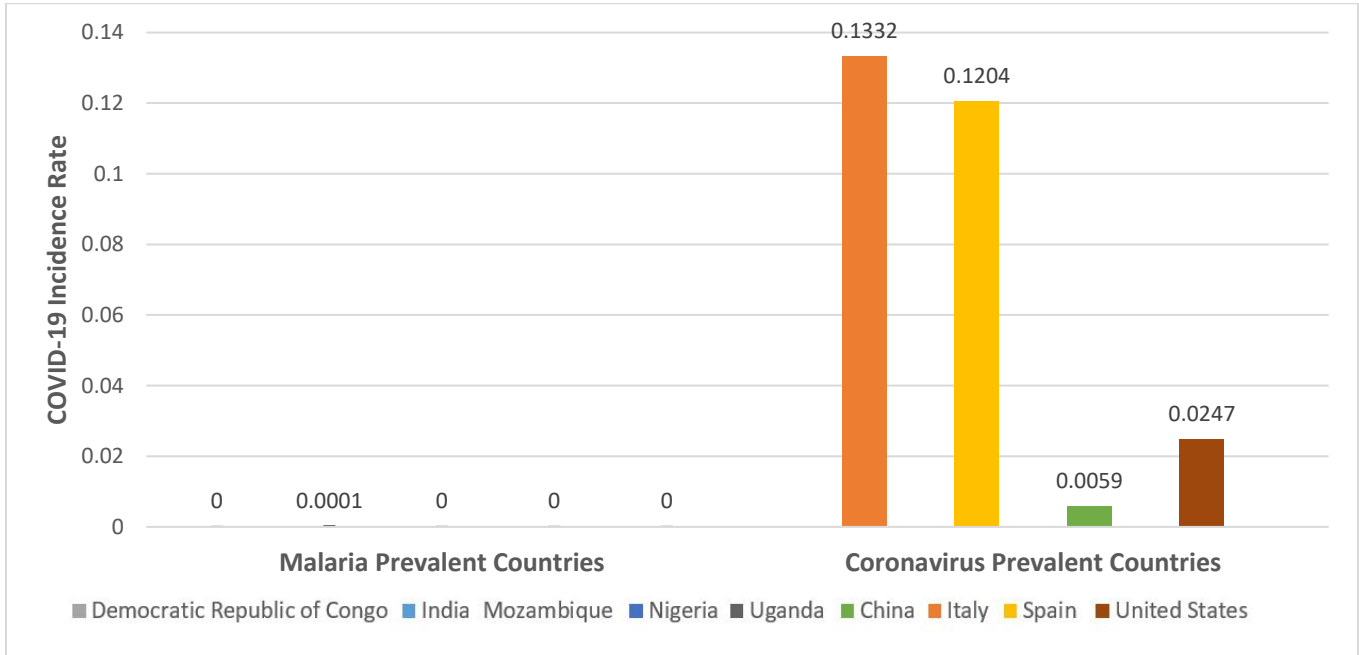


Figure 1

The difference between the COVID-19 incidence rate in malaria prevalent countries compared to COVID-19 prevalent countries is statistically significant ($p = 0.02$).

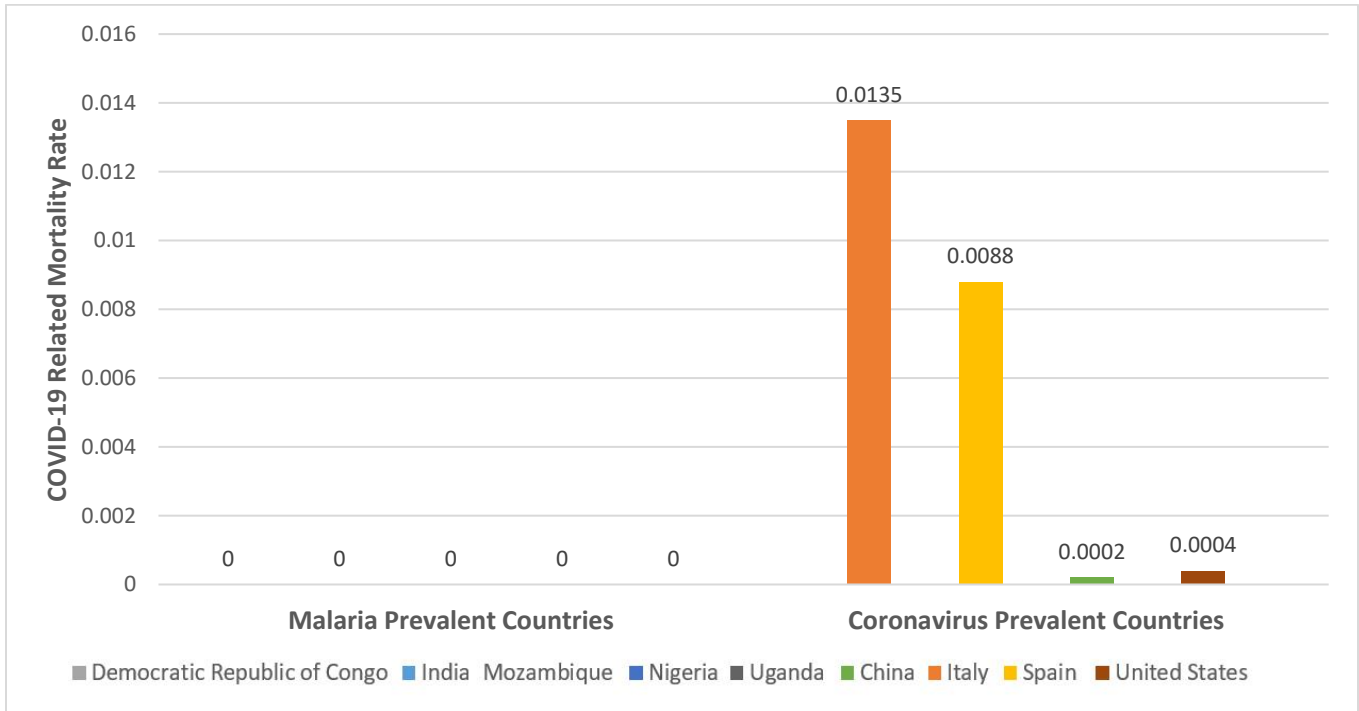


Figure 2

The difference between COVID-19 related mortality rate in malaria prevalent countries compared to COVID-19 prevalent countries is statistically significant ($p = 0.04$).

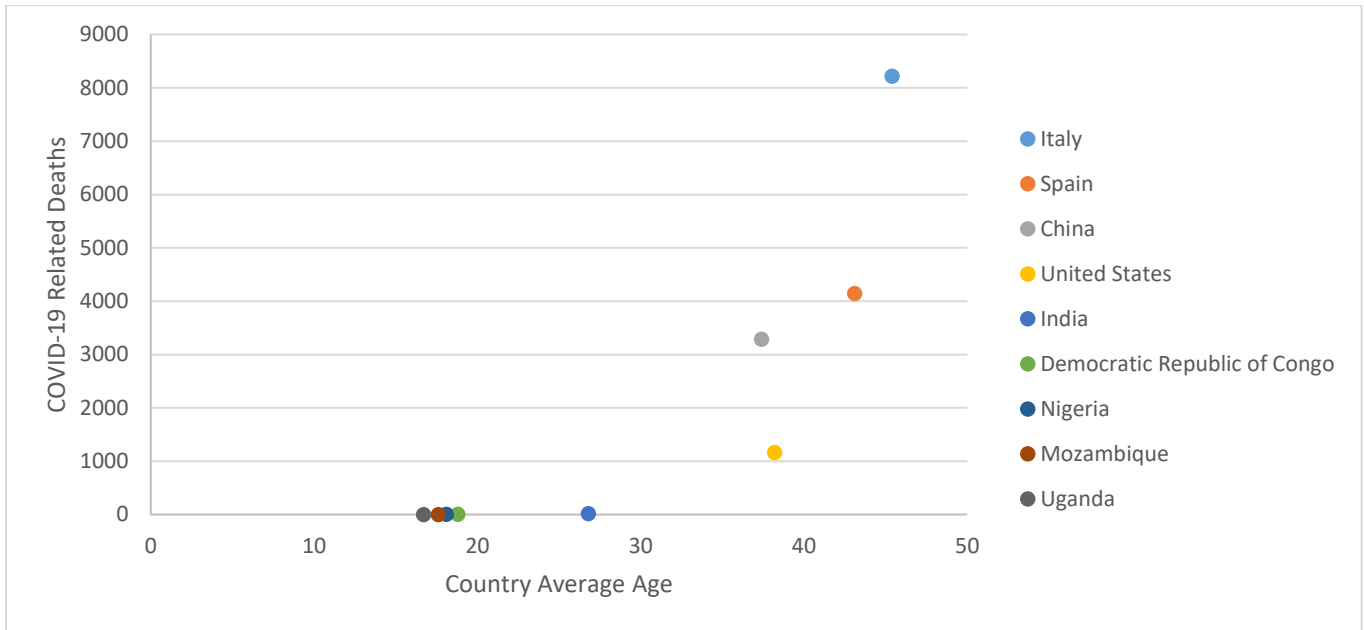


Figure 2

Scatterplot of COVID-19 related death compared to country average age, showing slight correlation between the two with a coefficient of determination (R^2) of 0.711.

deaths in malaria prevalent countries as other countries with low average age appear to still have many cases of COVID-19, such as Pakistan.^{1,9} In evaluations of the pandemic in its early stages, researchers projected that countries in Africa would be hard hit due, based on the rapid spread of other viruses in Africa as Ebola.¹¹ However, it can be seen that many of the countries in Africa are not affected, further supporting the predicted correlation between countries taking the 4-aminoquinolones anti-malarial drugs, chloroquine and hydroxychloroquine, and prevention of COVID-19. The majority of people in countries where malaria is prevalent take anti-malaria drugs regularly,⁶ which could serve as a reason as to why COVID-19 is hardly prevalent in countries where malaria is exceedingly prevalent.

This statistical analysis points to the fact that malaria-stricken countries have both less cases of COVID-19 and less COVID-19 related deaths. This study provides further evidence that anti-malaria drugs may prove essential to breaking the spread of SARS-CoV-2 and preventing COVID-19 and COVID-19

related mortality.⁴ As the pandemic continues to evolve and doctors and researchers across the globe try to attenuate or stop the spread of SARS-Cov-2, the medical community should not overlook the potential role of the 4-aminoquinolones anti-malarial drugs, chloroquine and hydroxychloroquine, and 8-aminoquinolone anti-malaria drugs, tafenoquine and primaquine, as a prophylaxis.

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