

COVID-19 Mortality in Malaria Endemic Countries: An Ecological Study

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Research Article

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Abstract

Introduction

The number of persons infected with COVID-19 continue to increase with deaths reported daily across the globe. High income countries such as the US, the UK, Italy and Belgium have reported high COVID-19 related deaths but low-and-middle-income countries have recorded fewer deaths despite having poor healthcare system. This study aimed to investigate the association between malaria prevalence and COVID-19 mortality.

Methods

This is an ecological study with data from 195 countries. Spearman's correlation was used to test the association between the population variables and COVID-19 mortality. Generalized linear model with Poisson distribution was used to determine the significant predictors of COVID-19 mortality.

Results

There was a significant positive correlation between median age, life expectancy, 65+ mortality and COVID-19 mortality while malaria prevalence, sex ratio and cardiovascular mortality were negatively correlated with COVID-19 mortality. Malaria prevalence, life expectancy and mortality rate were significant on multivariate regression analysis.

Conclusion

The results of this study support the hypotheses that there is reduced COVID-19 deaths in malaria endemic countries, although the results need to be proved further by clinical trials.

Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease which is caused by a new coronavirus known as SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) (1). The outbreak began in Hubei province of China in December 2019, and it was announced as a Public Health Emergency of International Concern on January 2020, and later on March 2020, proclaimed a pandemic by the World Health Organization (WHO) after more than 4291 deaths were recorded in many countries (2). COVID-19 is transmitted through close contact with infected droplets from sneezing, coughing, talking or breathing (3). The signs and symptoms includes fever or chills, cough, shortness of breath or difficulty in breathing, fatigue, headaches, new loss of taste or smell, sore throat among others (3). Hand hygiene, social distancing, isolation and use of face masks have been recommended by WHO as well as other preventive measures such as local and international travel restrictions and lockdowns in order to stop the spread of COVID-19 (4).

As at December 25, 2020, there were about 1,736,752 COVID-19 related deaths reported globally (5). In various countries, differences in COVID-19 mortality has been observed with most Western countries having high mortality per million populations (6). For example, the mortality per million populations in the USA is 977, the United Kingdom (1025), France (948) and Belgium (1642). However, in developing nations, low COVID-19 mortality have been reported with Nigeria having a mortality per million populations of 6, Kenya (30), India (106) and Venezuela (35). This is in contrast to what was speculated in low-and-middle income countries where the morbidity and mortality of COVID-19 was expected to be high compared to Western countries (7). Epidemiological studies have identified several factors associated with COVID-19 mortality. A study reported that the mean age, life expectancy and other population characteristics in African countries account for the low COVID-19 mortality (8). Another ecological study of COVID-19 mortality across 173 countries showed that median age of the population and life expectancy were associated with COVID-19 mortality (6). Pre-existing conditions have also been found to be associated with COVID-19 deaths. The Chinese Centre for Disease Control and

Prevention reported in a study that cardiovascular disease, diabetes, hypertension and cancers were associated with an increased risk of covid-19 death (9).

There has been widespread speculation that hydroxychloroquine a drug used to treat malaria can be used to prevent and treat COVID-19. Although some studies reported that it may inhibit COVID-19 virus, other studies showed that it has no positive effect on COVID-19. Scientists have argued that its use in some countries is responsible for the low COVID-19 deaths in those countries, and studies conducted during the early period of the pandemics revealed that there is reduced spread of COVID-19 in malaria endemic countries (10). Following this assumption, the hypotheses that immune response against malaria in malaria endemic countries may have protective effects against COVID-19 was proposed.

Materials And Methods

Study Design

This is an ecological study which compared population variables of 195 countries.

Data Resources

All data were obtained from open resources. Information on COVID-19 was obtained from the WHO Coronavirus Disease Situation Dashboard (5). Malaria data was obtained from the World Malaria Report 2020 (11). All data regarding the population variables were obtained from the United Nations database (12), and data regarding cardiovascular mortality rate was culled from 'Our World in Data' (13).

Dependent Variable

The dependent variable evaluated in this study was COVID-19 mortality (total COVID-19 related deaths per million population) in each county obtained from the WHO Coronavirus Disease Situation Dashboard on 25th December, 2020 (5).

Independent Variable

Malaria prevalence was converted to total malaria cases per million population in each country. The data on malaria morbidity was culled from the World Malaria Report 2020 (11).

Covariates

The covariates assessed in this study were median age, life expectancy at birth, mortality rate per 1000 population, 65 + mortality rate, sex ratio and cardiovascular mortality per 100,000 obtained from the United Nations database and 'Our World in Data' (12, 13).

Statistical Analysis

STATA Version 12 was used for all statistical analysis. Spearman's correlation was used to test the association between COVID-19 mortality and the population variables. Generalized linear model (GLM) with Poisson distribution and log link was used to determine the significant predictors of COVID-19 mortality rate (deaths per million population). The Generalized linear model was used by reason of the zero values and non-parametric distribution of the dependent variable.

Ethics Approval

Approval from institutional review board was not sought for this study due to the use of publicly available data from open resources.

Results

A total of 195 countries that have data on COVID-19 deaths, malaria cases and population variables were included in the study. Table 1 and Table 2 shows the countries with the highest and lowest COVID-19 deaths per million populations and their population characteristics. Belgium (1643), Slovenia (1212), Bosnia and Herzegovina (1182) and Italy (1173) have the highest COVID-19 deaths per million population while Samoa (0), Turkmenistan (0) and Seychelles are among the countries with no COVID-19 mortality. Among malaria endemic countries, Benin (391065), Burkina Faso (371174), Liberia (353937) and Rwanda (352794) have the highest malaria cases per million population.

Table 1
Population Characteristics of Countries with Highest COVID-19 Mortality Per Million Population

Country	Covid Deaths	Malaria Prevalence	Median Age	Sex Ratio	Life Expectancy	Mortality Rate	65+ Mortality	CVD Mortality
Belgium	1643	0	42	98	81	10	84	114
Slovenia	1212	0	45	99	81	10	83	153
Bosnia and Herzegovina	1182	0	43	96	77	11	78	329
Italy	1173	0	47	95	83	11	89	113
North Macedonia	1140	0	39	100	76	10	77	322
Peru	1129	1378	31	99	76	6	60	85
Spain	1066	0	45	97	83	9	86	99
Montenegro	1033	0	39	98	77	11	79	387
UK	1026	0	41	98	81	9	84	122
Czechia	1014	0	43	97	79	11	82	227
Bulgaria	1011	0	45	94	75	15	79	424
USA	977	0	38	98	79	9	74	151
France	948	0	42	94	82	9	84	86
Argentina	936	0	31	95	76	8	72	191
Mexico	933	5	29	96	75	6	57	152

Table 2
Population Characteristics of Countries with Lowest COVID-19 Mortality Per Million Population

Country	Covid Deaths	Malaria Prevalence	Median Age	Sex Ratio	Life Expectancy	Mortality Rate	65+ Mortality	CVD Mortality
Vanuatu	0	3371	21	103	70	5	54	546
Tonga	0	0	22	100	71	7	61	227
Grenada	0	0	32	102	72	10	68	243
North Korea	0	186	35	96	72	9	65	321
St. Vincent & the Grenadines	0	0	33	103	72	9	63	252
Micronesia	0	0	24	103	68	7	47	454
Samoa	0	0	22	107	73	5	60	348
Laos	0	1434	24	101	67	7	41	368
Solomon Island	0	236540	20	104	73	4	44	459
Turkmenistan	0	0	27	97	67	7	40	536
Timor-Leste	0	0	21	102	69	6	46	335
Seychelles	0	0	34	105	73	8	58	242
Mongolia	0	0	28	97	70	6	40	460
Bhutan	0	3	28	113	71	6	44	217
Cambodia	0	8323	26	95	69	6	44	270

COVID-19 mortality per million population has a significant negative correlation with malaria prevalence ($r=-0.459$, $p < 0.001$), cardiovascular deaths per 100,000 ($r=-0.310$, $p < 0.001$) and sex ratio (-0.219 , $p = 0.003$). There was a significant positive correlation between COVID-19 mortality and median age ($r = 0.595$, $p < 0.001$), life expectancy ($r = 0.582$, $p < 0.001$) and 65 + mortality rate ($r = 0.583$, $p < 0.001$). Details are shown in Table 3.

Malaria prevalence and all the covariates were significant in bivariate analysis, however, multivariate analysis showed that malaria prevalence ($p < 0.001$; CI = 0.99–0.99), mortality rate ($p = 0.006$; CI = 1.06–1.46) and life expectancy ($p = 0.021$; CI = 1.02–1.29) were significantly associated with COVID-19 mortality. Details of the regression analysis are shown in Table 4.

Table 3
Spearman's Correlation of COVID-19 Mortality, Malaria Prevalence and Population Variables

Variables		Covid Cases	Covid Deaths	Malaria Prevalence	Median Age	Sex Ratio	LE	Mortality Rate	65+ Mortality	CVD Mortality
Covid Cases	R	1								
	p									
Covid Deaths	R	0.929	1							
	p	0.000								
Malaria Prevalence	R	-0.544	-0.459	1						
	p	0.000	0.000							
Median Age	R	0.660	0.595	-0.775	1					
	p	0.000	0.000	0.000						
Sex Ratio	R	-0.219	-0.279	0.144	-0.317	1				
	p	0.003	0.000	0.050	0.000					
Life Expectancy	R	0.644	0.582	-0.744	0.860	-0.118	1			
	p	0.000	0.000	0.000	0.000	0.109				
Mortality Rate	R	0.115	0.141	-0.009	0.283	-0.494	-0.080	1		
	p	0.119	0.056	0.908	0.000	0.000	0.281			
65+ Mortality	R	0.635	0.583	-0.790	0.925	-0.274	0.913	0.192	1	
	p	0.000	0.000	0.000	0.000	0.000	0.000	0.009		
CVD Mortality	R	-0.333	-0.310	0.192	-0.385	0.063	-0.586	0.104	-0.432	1
	p	0.000	0.000	0.009	0.000	0.398	0.000	0.161	0.000	

Table 4
Regression Analysis of Predictors of COVID-19 Mortality

Variable	Crude			Adjusted		
	IRR	p value	95% CI	IRR	p value	95% CI
Median Age	1.09	< 0.001	1.07–1.11	0.96	0.238	0.90–1.03
Sex Ratio	0.99	0.035	0.97–0.99	1.00	0.939	0.99–1.01
Life Expectancy	1.13	< 0.001	1.10–1.15	1.14	0.021	1.02–1.29*
Mortality Rate	1.12	< 0.001	1.06–1.18	1.24	0.006	1.06–1.46**
65+ Mortality	1.04	< 0.001	1.03–1.05	0.99	0.687	0.96–1.03
CVD Mortality	0.99	< 0.001	0.99–0.99	0.99	0.253	0.99–1.00
Malaria Prevalence	0.99	< 0.001	0.99–0.99	0.99	< 0.001	0.99–0.99***
*p < 0.05; **p < 0.01; ***p < 0.001						

IRR = Incidence Rate Ratio

Discussion

This ecological study aimed to determine the association between COVID-19 mortality and malaria prevalence. After adjusting for the population dynamics, malaria prevalence was significantly associated with COVID-19 mortality. The results of this study is consistent with previous studies which revealed that malaria endemic countries have reduced COVID-19 morbidity and mortality (10, 14, 15).

The association between COVID-19 and malaria prevalence could be as a result of immune response against malaria in malaria endemic countries, and the extensive use of chloroquine drugs and its derivatives. Several studies have revealed that it is plausible to have cross immunity, where one pathogen can provide immunity against another pathogen (16, 17). For example, prior exposure to *Plasmodium* has been shown to have protective effects against Chikungunya (18). Studies have discovered that SARS-CoV-2 uses the angiotensin-converting enzyme 2 (ACE2) receptor to invade the host cells (19). Similarly, studies have revealed that ACE1 and ACE2 polymorphisms protects the host from susceptibility to malaria (20, 21). Furthermore, studies have indicated that interferons generated by lymphocytes as an immune response to malaria have in vitro and in vivo efficacy against the coronavirus responsible for COVID-19 (22, 23). The therapeutic role of chloroquine and its derivatives in COVID-19 infection remains unclear. Although, studies have reported the antiviral and anti-inflammatory role of these drugs, however, clinical trial is still ongoing with early results showing no difference between these drugs and standard care (24–27). The relationship between malaria and COVID-19 is complicated considering that malaria and COVID-19 have common symptoms, despite the fact that COVID-19 is more aggressive in adults while malaria affects more children (28).

There are several limitations to this study. First, this is an ecological study and the outcome is limited with a high potential of bias. Second, the effect of lock downs, restriction of internal and international movement, restriction of public gatherings and public events, healthcare systems and other population covariates were not adjusted in this study. Third, the COVID-19 pandemics is still ongoing and the results may be different few months from now.

Conclusion

The results of this study support the hypotheses that there is reduced COVID-19 deaths in malaria endemic countries. Given the evidence from this ecological study, it may worth conducting laboratory experiments and clinical trials in order to validate the results of this study.

Declarations

Ethics approval and consent to participate

Approval from institutional review board was not sought for this study due to the use of publicly available data from open resources.

Consent for publication

Not Applicable

Availability of data and materials

The datasets used and/or analyzed during this study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

AMU was the sole author involved in the conceptualization, data collection, and writing of this article.

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