

# Inter-State Heterogeneity of The Burden of Novel Coronavirus Disease In India: An Analysis of the Correlating Factors

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**Abstract**—The number of cases of novel coronavirus 2019 (COVID-19) in India has been increasing since March 2020. However, a significant inter-state heterogeneity is evident. The present study was aimed at analysing the various factors that could correlate with this heterogeneity. This analytical cross-sectional study included the COVID-19 related data of various Indian states as on 14th Oct 2020. Data of the demographic factors and other infectious diseases were extracted from various websites. Correlation between these factors and COVID-19 confirmed cases and deaths was assessed (Pearson's correlation coefficient). After a check for multi-collinearity, a stepwise linear regression analysis using R software was done for the final model of confirmed cases as well as deaths due to COVID-19. Pearson's correlation coefficient showed a significant correlation between COVID-19 cases and deaths due to dengue while COVID-19 deaths demonstrated correlation with number of chikungunya cases and deaths due to dengue. The linear regression analysis gave the final model explaining COVID-19 deaths with total population, population density, other infectious diseases, average minimum temperature, and population above 60 years. The present study highlights a possible association between COVID-19 epidemiology and population density as well as with other infections like chikungunya, dengue, and malaria in India. Number of COVID-19 deaths are also related to population above 60 years. Knowledge of these related factors will help in prediction of health care need of states and better management of pandemic.

**Keywords**— Novel corona virus, multiple linear regression, statistical model, heterogeneity, India

## I. INTRODUCTION

The entire world is reeling under the effect of the novel coronavirus 2019 (COVID-19) pandemic that has affected almost all the countries. The first case in India was detected on January 30, 2020. Since mid-March 2020, the cases of COVID-19 in India have been increasing steadily across the country. However, a closer analysis lays open the heterogeneity of the burden of COVID-19 among the various states. Studies have been conducted in many countries to understand the factors associated with the burden of COVID-19 cases and/ or deaths. The effect of climatic conditions like temperature and humidity and factors like population density have been demonstrated on disease burden in some studies [1-3].

Recently, interest has generated regarding the association or correlation of infectious diseases like tuberculosis, dengue, chikungunya and malaria with COVID-19. A modelling study has shown that co-infection with tuberculosis and COVID-19 could lead to a more severe disease with higher death rates [4]. Similarly, co-infection with malaria and COVID-19 is assumed to portend a poor prognosis due to the cytokine storm-like phenomenon in malaria [5]. On the other hand, antimalarial drugs like

hydroxychloroquine have shown beneficial effects in COVID-19 prophylaxis as well as treatment and may contribute to lower mortality rates in endemic zones [5,6]. The relationship of COVID-19 infection with dengue, chikungunya and other arboviral diseases is not clear yet. However, so far there has been no study to evaluate the association of various demographic factors and endemicity of other infectious diseases with the burden of COVID-19 in Indian states. Hence, the present study aimed to achieve this objective and provide the initial evidence for such an association if it exists.

Rest of the paper is organized as follows, Section I contains the introduction of COVID-19 pandemic, Section II contains the related work, Section III contains the methodology and modelling strategies used in this study, Section IV contains the results along with discussion, section V concludes research work with future directions.

## II. RELATED WORK

A study entitled "Containment measures limit environmental effects on COVID-19 early outbreak dynamics" evaluated the effect of environmental parameters on COVID-19 dynamics during the early phase

of pandemic and reported that environmental factors may have impacted the variation in spread of the pandemic [1]. Another study "Impact of meteorological factors on the COVID-19 transmission: A multi-city study in China" assessed the association of COVID-19 case load and environmental conditions in cities of China to demonstrate that conditions such as low temperature and humidity may favour COVID-19 transmission [2].

### III. METHODOLOGY

The present study was an analytical cross-sectional study of the COVID 19 data of various Indian states (as on 14th Oct 2020) obtained from a crowd-sourced website [<https://www.covid19india.org>]. The most recent available data for these states, like population (total population, geographical area, and population density of the year 2017), number of chikungunya cases (2019), number of dengue cases as well as deaths (2019), total tuberculosis (TB) notification rate (per lakh population in the year 2017), total number of malaria cases, falciparum cases and deaths due to malaria (2019), average maximum and minimum temperature of the state (Oct 2020), gross domestic product (GDP) of the state (2013-14) and percentage of population above 60 years (2011) was obtained from various websites [<http://www.tbcindia.nic.in/showfile.php?lid=3314>; <https://nvbdcp.gov.in/index4.php?lang=1&level=0&linkid=486&lid=3765>; <https://nvbdcp.gov.in/index4.php?lang=1&level=0&linkid=431&lid=3715>; <http://www.tbcindia.nic.in/showfile.php?lid=3314>; <https://nvbdcp.gov.in/WriteReadData/1892s/41082350651617959011.pdf>; <https://www.currentresults.com/Weather/India/temperature-may.ph>; <https://m.rbi.org.in/scripts/PublicationsView.aspx?id=2000>; Census of India (2011). Population Composition. Office of the Registrar General & Census Commissioner, New Delhi, 27-12-2013. Available at [https://censusindia.gov.in/vital\\_statistics/SRS\\_Report/9Chap%20%20-%202011.pdf](https://censusindia.gov.in/vital_statistics/SRS_Report/9Chap%20%20-%202011.pdf)]. These were used as independent variables in the present study. Permission to use the data was obtained from the sources, wherever applicable.

In the first step, a Farrar Chi-Square test was performed to check for multi-collinearity between the independent variables. Variables with high variance inflation factor (VIF) were removed. This was followed by calculation of the correlation between dependent variables (number of confirmed coronavirus cases and deaths) and the independent variables using the Pearson's correlation coefficient.

A stepwise multiple linear regression analysis was performed to select the final statistical model based on lowest Akaike Information Criterion (AIC) obtained. Student's t-test was used to assess the significance of coefficients of variables and the overall significance of model was assessed using f-test.

Open-sourced statistical software "R" (version-3.6.0) in combination with R studio (version-1.1.463) was used for statistical modelling. A P value of <0.05 was taken as statistically significant.

### IV. RESULTS AND DISCUSSION

Data of 35 Indian states were analysed in the present study.

**Test for multi-collinearity:** The correlation matrix illustrating correlation among various independent variables is tabulated in Table 1. The highest VIF was of total malaria cases (VIF=24.18). The initial VIF and those after stepwise removal of total malaria cases are listed in Table 2.

**Correlation between dependent and independent variables:** Pearson's correlation coefficient gave a significant correlation between number of confirmed coronavirus cases and deaths due to dengue (P=0.012) and Chikungunya cases (P=0.021) similarly deaths due to coronavirus infection showed significant correlation with deaths due to dengue (P=0.009) and Chikungunya cases (P=0.041), as seen in Table 3.

#### Multiple Linear regression model

**Modelling of Confirmed Corona Cases:** To identify the variables affecting the burden of corona cases in various states a stepwise linear regression analysis was performed. The models were selected until the lowest AIC was obtained. The final linear regression and model obtained was as follows:

Confirmed corona cases = 486314.4 + 239.7 \* Population density + 194.2 \* Chikungunya Cases - 18.2 \* Total Falciparum Malaria Cases + 92821.5 \* Deaths Due to Malaria - 29780.8 \* GDP

The detail of intercept and coefficient are tabulated in Table 4. R<sup>2</sup> of the model was 0.661. The final model was overall statistically significant (F-statistic: 4.29 on 5 and 11 DF, p-value: 0.0207).

**Modelling of Deaths due to Corona:** For identification of the variables affecting the deaths due to corona cases in various states a stepwise linear regression analysis was performed. The models were selected until the lowest AIC was obtained. The final linear regression and model obtained was as follows:

Deaths due to corona = -8339.685 + 9.42 \* Population + 0.824 \* Population Density + 3.969 \* Chikungunya Cases - 0.490 \* Total Falciparum Malaria Cases + 3368.412 \* Deaths Due to Malaria - 548.876 \* Avg Min Temp + 1651.531 \* Population Above 60

The detail of intercept and coefficient are tabulated in Table 5. R<sup>2</sup> of the model was 0.779. The final model was overall statistically significant (F-statistic: 4.52 on 7 and 9 DF, p-value: 0.0199).

Table 1. Correlation among independent variables. Lower triangle (shaded) shows p values

	Population	Area	Population Density	Chikungunya Cases	Dengue Cases	Deaths Due to Dengue	Total Tuberculosis Notification Rate	Total Malaria Cases	Total Falciparum Malaria Cases	Deaths Due to Malaria	Avg Max Temp	Avg Min Temp	GDP	Population Above 60y
Population	1.00	0.61	-	0.18	0.49	0.62	-	0.69	0.17	0.06	0.32	0.201	-	-0.116
	0	3	9	6	8	0	0	4	8	6	6		0.1	52
Area	0.00	1.00	-	0.33	0.59	0.59	-	0.28	0.10	0.29	0.17	0.015	-	-
	9	0	1	2	9	1	0.31	7	6	0	6		0.1	0.009
Population Density	0.21	0.03	1.00	-	-	-	0.84	-	-	-	0.12	0.005	0.2	-
	2	6	0	8	4	6	9	0.17	0.18	0.24	7		0.73	0.336
Chikungunya Cases	0.47	0.19	0.73	1.00	0.60	0.40	-	-	-	0.03	-	0.100	0.0	0.068
	6	3	7	0	9	0	0.09	0.15	0.18	6	0.07		0.19	
Dengue Cases	0.04	0.01	0.32	0.00	1.00	0.73	-	0.08	-	-	0.36	0.185	-	0.197
	2	1	6	9	0	3	0.13	9	0.16	0.00	5		0.2	76
Deaths Due to Dengue	0.00	0.01	0.32	0.11	0.00	1.00	-	0.30	-	0.14	0.27	0.155	-	0.366
	8	2	1	2	1	0	0.18	5	0.08	2	2		0.3	00
Total Tuberculosis Notification Rate	0.24	0.22	0.00	0.73	0.60	0.48	1.00	-	-	-	0.30	0.006	0.2	-0.313
	2	2	0	1	0	9	0	0.12	0.11	0.11	2		0.60	
Total Malaria Cases	0.00	0.26	0.49	0.56	0.73	0.23	0.63	1.00	0.67	0.18	0.17	0.127	-	-0.153
	2	3	5	1	4	3	9	0	8	0	0		0.3	08
Total Falciparum Malaria Cases	0.49	0.68	0.46	0.48	0.52	0.75	0.65	0.00	1.00	0.60	0.00	0.250	-	0.032
	5	4	9	2	9	4	2	3	0	2	8		0.4	06
Deaths Due to Malaria	0.80	0.25	0.35	0.89	0.98	0.58	0.66	0.48	0.01	1.00	0.05	0.225	-	0.109
	1	9	3	2	0	5	0	9	0	0	0		0.3	18
Avg Max Temp	0.20	0.50	0.62	0.77	0.15	0.29	0.23	0.51	0.97	0.84	1.00	0.572	0.0	-0.169
	1	0	7	4	0	2	9	4	6	8	0		0.0	59
Avg Min Temp	0.44	0.95	0.98	0.70	0.47	0.55	0.98	0.62	0.33	0.38	0.01	1.000	0.0	0.074
	0	5	4	1	8	1	2	8	4	5	6		0.0	53
GDP	0.56	0.62	0.28	0.94	0.28	0.24	0.31	0.22	0.10	0.21	0.82	0.839	1.0	-0.323
	1	2	8	1	4	2	4	8	6	3	2		0.0	
Population Above 60y	0.65	0.97	0.18	0.79	0.44	0.14	0.22	0.55	0.90	0.67	0.51	0.778	0.2	1.000
	8	3	8	4	9	8	2	8	2	6	6		0.05	

Table 2. VIF after step wise removal of variables with VIF > 7

Variable	Initial VIF	VIF After Falciparum Malaria Removal
Population	9.23	3.84
Area	5.25	3.84
Population Density	7.37	6.14
Chikungunya Cases	3.10	2.74
Dengue Cases	6.07	5.92
Deaths Due to Dengue	11.01	5.08
Total Tuberculosis Notification Rate	6.75	5.83
Total Malaria Cases	24.18	-
Total Falciparum Malaria Cases	20.52	2.93
Deaths Due to Malaria	4.88	2.31
Avg Max Temp	3.77	3.67

Avg Min Temp	2.68	2.44
GDP	2.27	2.22
Population Above 60y	4.08	2.51

Table 3. Correlation between dependent (total corona cases and deaths) and independent variables

Variable	With Covid-19 Cases		With Deaths due to Covid-19	
	Correlation	p value	Correlation	p value
Population	0.404	0.108	0.372	0.142
Area	0.439	0.078	0.442	0.076
Population Density	-0.156	0.551	-0.082	0.756
Chikungunya Cases	0.553	0.021	0.499	0.041
Dengue Cases	0.466	0.059	0.466	0.059
Deaths Due to Dengue	0.592	0.012	0.613	0.009
Total Tuberculosis Notification Rate	-0.137	0.601	-0.029	0.911
Total Malaria Cases	0.038	0.884	0.010	0.970
Total Falciparum Malaria Cases	-0.044	0.866	-0.093	0.723
Deaths Due to Malaria	0.386	0.126	0.440	0.077
Avg Max Temp	0.101	0.699	0.133	0.612
Avg Min Temp	0.187	0.473	-0.019	0.943
GDP	-0.286	0.265	-0.218	0.400
Population Above 60y	0.257	0.320	0.193	0.459

Table 4. Statistical significance of coefficients of the final model explaining total Covid-19 cases

	Estimate	Std. Error	t value	Pr(> t )
(Intercept)	486314.4	350479.8	1.39	0.193
Population Density	239.7	130.3	1.84	0.093
CCG.19	194.2	93.3	2.08	0.061
MPF.19	-18.2	9.4	-1.94	0.078
Deaths Due to Malaria	92821.5	38071.7	2.44	0.033
GDP	-29780.8	22392.0	-1.33	0.210

Table 5. Statistical significance of coefficients of the final model explaining deaths due to Covid-19

	Estimate	Std. Error	t value	Pr(> t )
(Intercept)	-8339.685	10797.411	-0.77	0.460
Population	9.420	3.254	2.89	0.018
Population Density	0.824	0.505	1.63	0.137
CCG.19	3.969	2.133	1.86	0.096
MPF.19	-0.490	0.208	-2.35	0.043
Deaths Due to Malaria	3368.412	877.854	3.84	0.004
Avg Min Temp	-548.876	400.723	-1.37	0.204
Population above 60y	1651.531	1021.431	1.62	0.140

## Discussion

The pandemic caused by novel coronavirus 2019 (SARS-CoV-2) has affected almost all the countries of the world with total number of cases surpassing 38 million [<https://covid19.who.int>]. As on 14th Oct 2020 confirmed cases in world stood at 38,668,215 cases. In the same

timeframe, the number of confirmed cases in India stood at 7,241,517 with 110,645 deaths attributable to COVID-19. A closer look at the Indian data brings out the stark heterogeneity of COVID-19 burden among the various states with few (Maharashtra and Andhra Pradesh) affected badly while others (like Mizoram) faring better since the

arrival of the pandemic at our shores [https://www.covid19india.org]. Since India is a country with diverse geographical landscape and is endemic for diseases such as tuberculosis, malaria, and dengue, it was thought prudent to evaluate the correlates of COVID-19 burden as applicable to the Indian scenario in the present study.

Due to the magnitude of this pandemic, numerous studies have been conducted to delineate the factors associated with high or low burden of the COVID-19 cases and/or deaths. The relationship between weather and COVID-19 transmission has been investigated with variable results. One study concluded a higher growth rate of COVID-19 cases in temperate regions of Northern hemisphere with mean temperature of about 5°C and relative humidity of 17-26% [1]. Another study reported that lower ambient temperatures, low humidity levels and mild diurnal temperature variation favored COVID-19 transmission [2]. Population density has also been shown to affect the contact rates and thus have a bearing on the transmission of COVID-19 [3]. A study by Dan et al reported that temperature variation and humidity may not influence the COVID-19 mortality [7]. In the present study, average minimum temperature demonstrated correlation with number of deaths due to coronavirus infection, though the correlation with confirmed cases was not significant. In addition, the number of deaths due to malaria showed correlation with both the number of confirmed coronavirus cases as well as deaths. Since the deaths due to malaria are an indirect reflection of the availability and accessibility of health services in each area, its correlation with COVID-19 related deaths could also reflect the same.

A logistic regression analysis from the USA showed that proportion of black residents, temperature in addition to comorbidities, poverty and access to health services were risk factors for cases as well as deaths due to COVID-19 [8]. Our stepwise linear regression analysis showed that for Indian states, the population density, number of cases of chikungunya, number of falciparum malaria cases, and deaths due to malaria were significant factors contributing to the number of confirmed coronavirus cases. The model for deaths due to coronavirus infection included population size and density, number of cases of chikungunya, number of falciparum malaria cases, deaths due to malaria, average minimum temperature, and the population above 60 years of age. The relationship between coronavirus infection and other endemic infectious diseases such as malaria and chikungunya are interesting topics for research. Malaria, an endemic parasitic infection in India, is associated with changes in immune system functions. Malaria infection has also been shown to induce a cytokine storm-like cascade leading to severe symptoms, like that reported for COVID-19 [5]. Hence, co-infection is presumed to result in poor prognosis. Malaria-induced immunomodulation may also offer protection against severe disease in respiratory viral diseases through suppression of pulmonary cytokine production and reduced recruitment of inflammatory cells in the lungs [9]. Thus, the relationship between malaria and

COVID-19 appears to be complex requiring further evaluation. Antimalarial drugs like hydrochloroquine (HCQ) have been demonstrated to possess antiviral activity in addition to immunomodulatory effects [10]. The regular use of HCQ in malaria-endemic areas may also contribute to lower mortality rates in such zones [6].

Chikungunya, an arthropod-borne disease, shares the clinical presentation with COVID-19 in the presence of fever, chills, myalgia and fatigue [11]. This similarity has been linked to the misdiagnosis of cases either way – Chikungunya as COVID-19 and COVID-19 as Chikungunya. The problem is compounded by the cross-reactivity in antibody-based tests for COVID-19 and arboviral diseases [11,12]. Though no studies have been conducted so far on the association of Chikungunya and COVID-19 as a cause-and-effect relationship or predisposition by one to the other, healthcare professionals do need to exercise care in diagnosing Chikungunya on serology in the wake of COVID-19 pandemic and vice-versa.

Over the last year of COVID-19 pandemic, studies have demonstrated a higher incidence of severe disease and mortality among elderly patients. A retrospective study from Saudi Arabia showed that elderly patients had higher neutrophil counts, D-dimer, lactate dehydrogenase and lower lymphocyte counts. A significant association was reported between death due to COVID-19 and old age [13]. Another study from United States also demonstrated that older age was associated with higher mortality in COVID-19 patients [14]. Similarly, in the present analysis, the model of COVID-19 deaths included the factor of population above the age of 60 years

## V. CONCLUSION AND FUTURE SCOPE

The models obtained in the present study suggest that public health measures related to control of malaria and chikungunya should continue in addition to a focus on the prevention of infection of the elderly population and the containment procedures for COVID-19. Moreover, knowledge of the related factors will help in prediction of health care need of states and better management of pandemic in the times to come.

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