Original Article

Association of socio-demographic factors with clinical outcome among hospitalized patients in first and second waves of COVID-19 pandemic: Study from the developing world

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Abstract

Background: Recent disease resurgence in China indicates that corona virus infectious disease is still a pertinent public health problem. We stand at a juncture where we are still unsure about the initial dilemmas regarding its birth, therapies, and the emerging novel strains. Medical literature has focused on the clinical, laboratory, radiological, and therapeutic aspects of disease management. There is paucity of literature on the association between socio-demographic variables on disease severity and clinical outcome. **Materials and Methods:** This retrospective observational study analyzing the socio-demographic variables was performed at a dedicated COVID care center in western Maharashtra, India. Electronic records of all individuals who were admitted to this hospital from July 29 2020, to June 14, 2021, and diagnosed COVID-19 positive by reverse transcriptase polymerase chain reaction (RT-PCR) were identified after due institutional ethical clearance. Patients admitted from July 29, 2020, to February 27, 2021, were categorized as patients presenting during the 'first wave of viral pandemic'. Those admitted from March 01, 2021, to June 14, 2021, have been included as patients admitted during 'second wave of viral pandemic'. The following outcome parameters were collected (presenting symptoms, duration of symptoms before the individual presented for diagnostic RT-PCR, total duration of symptoms, severity of disease at onset, duration of hospital stay, the final outcome (discharge/death) and Charlson's comorbidity index). The linear regression model was used to establish association between socio-demographic factors and disease severity at onset (mild/moderate/severe/critical). **Results:** A total of 37033 patients were screened, and the positivity rate with RT-PCR was 16.99% (n = 6275) during the study period. Out of which 45% (n = 2824) of the patients had mild disease requiring home isolation and the remaining 55% of patients required admission. 1590 patients from the first wave and 910 from the second wave of COVID-19 were hospitalized and included in the study after exclusion. The mean age of patients in first wave was 49 years and that in second wave was 54 years with 77.6% and 70.6% males in two waves, respectively. The burden of critical cases was higher in second wave as computed to first wave (10% vs 8%). The second wave had more outreach in the rural population as compared to second one (17.8% vs 12.2%). The mean duration from the onset of symptoms to hospitalization was 03 and 04 days, respectively, in two waves.

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Mortality associated in two waves was 11.9% and 24%, respectively ($P < 0.05$). Higher Charlson's comorbidity index was associated with higher mortality, and the cumulative survival from urban area was more as compared to the rural population (log rank - 9.148, $P = 0.0002$). **Conclusion:** The second COVID-19 wave had significantly higher case mortality. It affected elderly patients and those with rural background. The factors associated with higher mortality during COVID-19 pandemic were rural background, higher Charlson's comorbidity index and late presentation to the hospital. Ongoing vaccine campaigns, thus, should focus on rural areas and individuals with comorbidities especially in developing and least developed countries.

Keywords: COVID-19, cumulative survival, rural background, socio-demographic factors

Introduction

Corona virus infectious disease (COVID-19) pandemic is arguably the worst pandemic affecting mankind. Our response to the pandemic, the economic, and social upheaval in its aftermath would possibly be taught in the textbooks in times to come. This disease began in a largely urban area. The urban population bore the initial onslaught. As the pandemic raged across the globe, developing countries like India witnessed socioeconomic setbacks notably economic recession and human migration. This, in particular, played a part in the disease spread across the length and breadth of the country. A number of demographic risk factors especially old age, male gender, and patients with underlying comorbidities have statistically significant association with disease mortality.[1-4]

Recent evidence from the developed world has suggested that racial and ethnic minorities are disproportionately affected by COVID-19. Black and Hispanic individuals are more likely to test positive for SARS-CoV-2 and are at an increased risk of hospital admission for COVID-19 compared to white individuals.[5-7] The United States Centers for Disease Control and Prevention (CDC) has suggested that racial disparities in COVID-19 outcomes may be due, in part, to socioeconomic disadvantages that place low-income individuals at a higher risk of infection.[8] Disadvantaged socioeconomic status (SES) has previously been associated with an increased risk of hospital admissions for respiratory infections.[9-11] A recent study from Chennai, an Indian megacity, found that low-SES areas experienced a higher incidence of COVID-19 infections, suggesting that COVID-19 may disproportionately affect low-income individuals, although this study did not examine SES as a risk factor for COVID-19 morbidity and mortality.[12] Understanding the influence of social factors on the incidence and clinical outcomes of COVID-19 has been deemed a research priority, in order to further elucidate the epidemiological burden of SARS-CoV-2 within developed nations.[13]

Socio-demographic factors that influence human behaviour are closely associated with access to health care, nutrition, and disease outcomes. It is well documented that the risk of death was greater in areas with the worst social conditions throughout the study period.[14] There is also a group of researchers that claims the importance of taking occupation into account in public policy to deal with the pandemic.[15-17] Understanding the impact of socio-demographic variables is important, particularly for practicing primary care physicians across developing countries where vaccination outreach is poor. They are the first contact with individuals often presenting with symptoms of viral infection varying from mild fever to severe respiratory tract infection. Moreover, such studies in the present digital age will be of benefit in planning preventive programs for newer pandemics that may affect humankind in future. Involving primary care physicians in vaccine outreach programs is imperative for successful outcomes. Hence, this retrospective observational study was conducted with the aim to analyze the impact of socio-demographic variables on morbidity and mortality across the time period covering two prominent COVID-19 waves in India.

Materials and Methods

This is a retrospective record-based observational study comparing the socio-demographic variables of the first and second waves carried out at a dedicated tertiary COVID center in western Maharashtra. Electronic records of all individuals who were admitted to this hospital from July 29, 2020, to June 14, 2021, and diagnosed COVID-19 positive by reverse transcriptase polymerase chain reaction (RT-PCR) were identified after due institutional ethical clearance. The patients with incomplete records were excluded from the study. The various definitions used in the study were taken from the standard source. Rural area was defined as 'those areas with a population of less than 49,000 (tier-3 to tier-6 cities and the others as urban area as per the Reserve Bank Of India (RBI)".[18]

We used the Indian Council of Medical Research (ICMR) and Ministry of Health and Family Welfare (MOHFW) case definitions of COVID-19 for the stratification of the cases in the two waves[19] *'Asymptomatic or Presymptomatic Infection:* cases who test positive for SARS-CoV-2 using a virologic test (i.e., RT-PCR) but who have no symptoms that are consistent with COVID-19'. *'Mild Disease: cases* who have any of the various signs and symptoms of COVID-19 with positive RT-PCR (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging'. *'Moderate disease:* cases who show evidence of lower respiratory disease during clinical assessment or imaging and who had respiratory rate >24/min and oxygen saturation (SpO_2) ≥90 <93% on room air at sea level' with positive RTPCR. *'Severe disease:* individuals who have SpO_2 <90% on room air at sea level and respiratory rate >30/min, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) <300 mm Hg, or lung infiltrates >50%'

with positive RT-PCR. *'Critical Illness:* Cases who have features of acute respiratory distress syndrome, sepsis or septic shock, and/or multiple organ dysfunction' with positive RT-PCR. The following demographic parameters were noted: date of RT-PCR testing, age, gender, place of residence (urban/rural), facility at home to maintain social distancing, h/o travel two weeks prior to the onset of symptoms and history of contact with a COVID-19-positive patient elaborate study design depicted in [Figure 1].

Patients admitted from July 29, 2020, to February 27, 2021, were categorized as patients presenting during the 'first wave of viral pandemic'. Those admitted from 01 March 2021 to June 14, 2021, have been included as patients admitted during 'second wave of viral pandemic'. This categorization was based on the fact that the peak number of cases of the two waves was during these periods and the demarcation period was characterized by the lowest number of cases of COVID-19 between the two waves. This demarcation has also been taken in other studies.[20] The patients presenting after June 14, 2021, were not included in this analysis as the second wave of the pandemic was almost over. The following outcome parameters were collected (presenting symptoms, duration of symptoms before the individual presented for diagnostic RT-PCR, total duration of symptoms, severity of disease at onset, duration of hospital stay and the final outcome (discharge/death) and Charlson's comorbidity index).[21]

Management of COVID-19 patients

Patients with mild to moderate disease were advised home isolation. Those with severe illness and those high risk were admitted and managed as in patients. All hospitalized patients were managed as per institutional protocol for COVID-19 infection (empirical antibiotic, low molecular weight heparin, antiviral: favipiravir, supplemental oxygen, Inj. Dexamethasone ± Convalescent plasma/Inj. Remdesivir/Inj. Tocilizumab depending upon

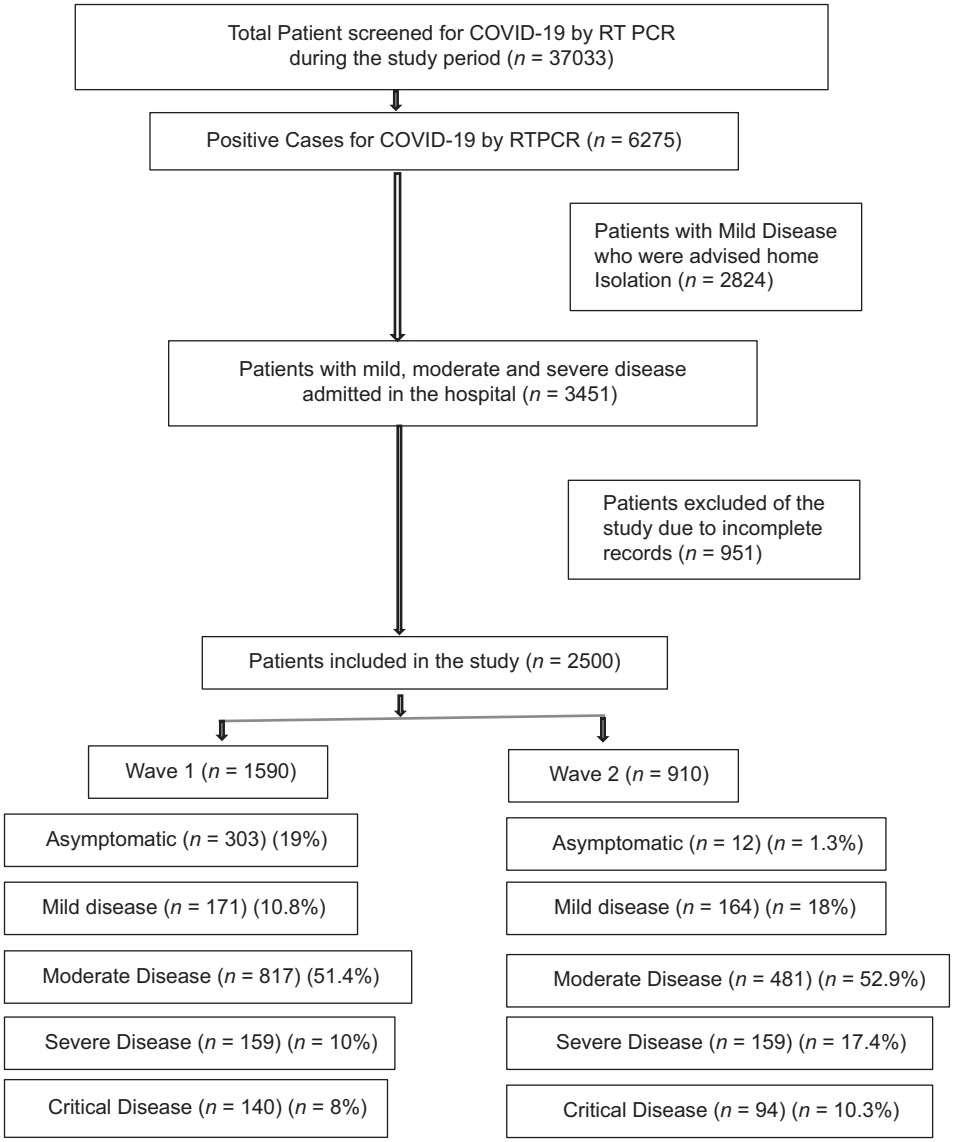

Figure 1: Study design: Impact of socio-demographic factors on clinical outcomes in the two waves of COVID-19 pandemic in western Maharashtra

their clinical condition). The treatment protocols were regularly updated in accordance with the guidelines issued by the Indian Council of Medical Research (ICMR) and Ministry of health and family welfare (MOHFW). An institutional committee would meet fortnightly to reassess the treatment protocols, update, and approve any changing treatment guidelines in view of emerging situations.

Statistics

The data were initially entered into 'Excel sheet' format. 'SPSS Statistic 22.0' (IBM SPSS Statistics, New York, United States) was used for statistical analysis. Descriptive statistics (demography, clinical features at presentation, history of contact with COVID positive patient) were calculated. Continuous variables were described by means and standard deviations, whereas categorical variables were described using frequencies and percentages. The linear regression model was used to establish an association between socio-demographic factors and the severity at onset (mild/moderate/severe/critical). Descriptive statistics for hospitalized patients were computed separately and correlation with duration between symptom onset and hospitalization, clinical, radiological features, duration of hospital stay, and final outcome (discharge/death) was determined using linear regression model. All tests were two-tailed. $P < 0.05$ was considered as significant. All tests were two-tailed. $P < 0.05$ was considered as significant.

Results

A total of 37033 patients were screened during the study period. The positivity rate with RT PCR was 16.99% ($n = 6275$). Out of which 45% ($n = 2824$) of the patients had mild disease and they were advised home Isolation. The remaining 55% of patients required admission to the hospital based on the existing national guidelines at that point of time. However, 15.15% ($n = 951$) patients were excluded from the study as their electronic health records were incomplete. Hence, a total of 2500 patients were included in the study from the two waves of the COVID-19 pandemic.

We found that the mean age patients were 49 years in the first wave and 54 years in the wave of pandemic. Majority of the admitted patients were males 77.6% ($n = 1235$) in first wave and 70.6% ($n = 643$) in the second wave. About 87.7% ($n = 1395$) in the first wave belonged to urban background and 82.2% ($n = 748$) belonged to urban background in second wave. Most of patients were educated up to XII standard 50.3% ($n = 800$) and 54.7 ($n = 498$) in first and second waves, respectively *[Table 1 highlights the socio-demographic variables in the first and second waves of viral pandemic]*. Fever (57.4%), cough (37.6%), and progressive breathlessness (08.9%) were the three most common clinical symptoms. The majority of patients admitted in first wave ($n = 81751.4\%$) and second wave ($n = 481$, 52.9%) had moderate illness. The mean duration from the onset of symptoms to hospitalization was 03 and 04 days for first and second waves, respectively.

A total of 88.7% ($n = 1401$) patients were discharged from the hospital after clinical recovery, whereas 11.9% ($N = 189$) patients succumbed to their illness during first wave; however, in the second wave, only 76% ($n = 692$) were discharged from the hospital and 24.0% ($n = 218$) of the patients succumbed to their illness. Mortality was significantly higher in the second wave as compared to the first wave.

Association of demographic variables with final outcome

Bivariate analysis showed that patients' age ($P < 0.0001$), place of residence (urban/rural), ($P < 0.0001$), presence of co-morbidity ($P < 0.0001$) Charlson's comorbidity index ($P < 0.0001$), and admission during first/second wave ($P < 0.0001$) had statistically significant correlation with final outcome (discharge/death). On the other hand, gender ($P = 0.935$) and educational status ($P = 0.119$) did not find any significant correlation with final outcome *[Table 2 depicts the association of socio-demographic variables with final outcome, i.e., discharge/death]*.

To further establish association of these socio-demographic variables, binary logistic regression was used. Place of residence ($P = 0.004$) and Charlson's comorbidity index ($P < 0.0001$) were significantly correlated with final outcome *[Table 3 depicts the regression analyses of socio-demographic factors with clinical outcome]*.

Table 1: Socio-demographic characteristics of patients

Characteristics	Wave 1		Wave 2	
Age (years)	Minimum	01	Minimum	01
	Maximum	102	Maximum	94
	Mean	49	Mean	54
Gender (*n*=Number Percentage:%)	Male	1235 (77.6%)	Male	643 (70.6%)
	Female	355 (22.3%)	Female	267 (29.3%)
Residence (*n*=Number Percentage:%)	Urban	1395 (87.7%)	Urban	748 (82.2%)
	Rural	195 (12.2%)	Rural	162 (17.8%)
Educational status	Illiterate	41 (25.7%)	Illiterate	30 (32.9%)
	Matriculate	380 (23.9%)	Matriculate	142 (15.6%)
	Higher secondary	800 (50.3%)	Higher secondary	498 (54.7%)
	Graduate	294 (18.5%)	Graduate	144 (15.8%)
	Postgraduate	75 (47.1%)	Postgraduate	96 (10.5%)

Table 2: Bivariate analysis showing association between socio-demographic factors and final outcome among COVID-19 patients

Variable	Pearson chi-square correlation	*P*
Age (years)	11.758	0.000
Gender (Male/Female)	0.000	0.935
Place of residence urban/rural	24.817	0.000
Presence of comorbidity	47.844	0.000
Educational status	7.343	0.119
Admission in wave 1/wave 2	66.747	0.000
Charlson's comorbidity index	35.576	0.000

The Chi-square statistic is significant at the 0.05 level

Kaplan–Meir survival curve, *Figure 2,* clearly shows improved survival in COVID-19 patients residing in urban areas vs. those residing in rural areas (log rank - 9.148, $P = 0.0002$).

Discussion

There is a paucity of data from developing countries on the effect of socio-demographic variables on clinical outcomes in patients in the two waves of COVID-19 pandemic. Studies in the United States have identified ethnic disparities predisposing the risk to COVID-19 with Asian, Hispanics, and Black Americans have an increased risk of contracting disease.[22] People living in crowded localities and single parents have been found to have increased incidence of developing disease besides increased disease-associated mortality.[23,24]

Interestingly, a study by Acharya *et al.* from India has proposed a 'vulnerability index', which computes the vulnerability of a community to develop disease based on five different indices: socioeconomic and demographic condition, availability of housing and hygienic conditions, access to health care in addition to COVID-19-related epidemiological factors. The state of Maharashtra had a high vulnerability of 0.829, which is in concordance with high case load in the state. However, another Indian state like Kerala, which has a large contribution to country's total COVID-19 case load, fares much better with a vulnerability index of 0.314.[25] This dichotomy, thus, supports our hypothesis that much needs to be done to study the effect of socio-demographic variables and patient profile of COVID-19 patients related to disease outcomes. A recent study has emphasized the importance of socio-demographic factors in disease containment and vaccination strategies.[26]

Table 3: Binary logistic regression showing association between socio-demographic factors and outcome among COVID-19 patients

Variable	SE	df	Sig
Age	0.005	1	0.031
Place of residence (Urban/Rural)	0.145	1	0.004
Presence of comorbidity	0.132	1	0.124
Charlson's comorbidity index	0.048	1	0.000

Df=Degree of freedom, SE=Standard error, $P<0.005$ is significant

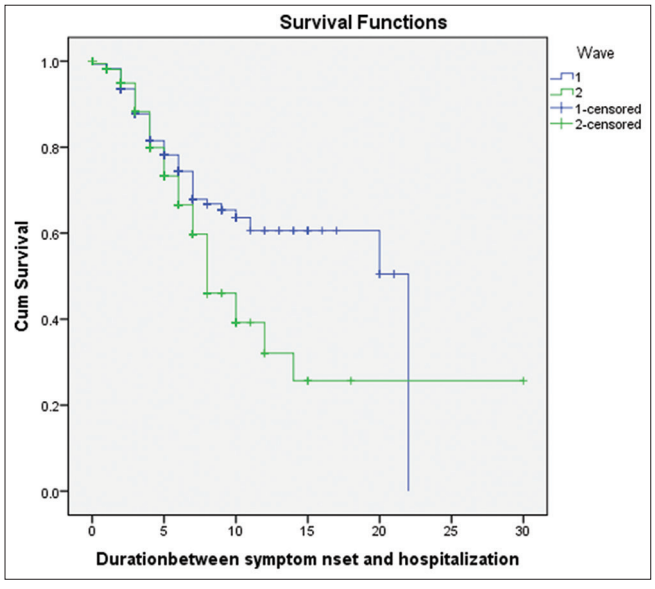

Figure 2: Cumulative survival of patients from urban areas compared to rural area

We have analyzed a meticolously organized large data base of hospitalized patients spread across different time span: the two waves of COVID-19 pandemic. The present study clearly establishes increased severity and higher mortality associated with India's second wave of COVID-19, which is consistent with the ICMR data. It is statistically proven that the compounding effect of increasing age and comorbidity (as determined by higher Charlson's comorbidity index) is associated with increased mortality in the present study as well as several other studies. Those residing in rural areas had higher disease-related mortality in the second wave as compared to those residing in the urban area as this may be attributable to multiple factors like delay in reaching the healthcare facility, delayed presentation of the disease. The study was carried out at a tertiary care referral center; hence, a number of patients were referred from different places including rural areas from within the state and even neighboring states hence a better representation of both urban and rural population. There are only few studies comparing the clinical and socioeconomic profile of the patient in the two major wave of the COVID-19 pandemic in western Maharashtra and India.[23] Majority of these studies have only covered clinical profile of the patient in two waves rather than socio-demographic profile, which is the peculiarity of the study.

Our study also has its share of limitations: It is a single-center retrospective observational study; hence, generalization cannot be made for population at large. We did not analyze the economic factors affecting the disease and its outcome as the study population was authorized free of cost medical care and the economic variables were not available in our database. Moreover, the study population in the present study had better access to healthcare facilities compared to others across the country. Thus, the aspect pertaining to access to health care may not be inferred from our results. Our study may be of special interest to primary care physicians, especially in rural/semi-urban areas who are often the first medical providers to majority of the patients.

Conclusion

The second COVID-19 wave had significantly higher case mortality. It affected elderly patients and those with rural background. The factors associated with higher mortality during COVID-19 pandemic were rural background and higher Charlson's comorbidity index. Patients residing in urban area had better cumulative survival as compared to the rural population.

Key points

This study includes large data base of COVID-19 patients spread over a period of 01 year and 02 months with a fair representation of patients residing in rural areas.

This study is among very few studied from India, which have analyzed not only clinical profile but also often-neglected socio-demographic factors affecting clinical outcomes.

Key take home message

Early access to medical facilities in severe COVID infection particularly to those residing in rural areas in developing countries may result in better clinical outcome. This study may be of importance to those planning vaccine outreach programs particularly in developing and least developed countries. Such campaigns thus should focus on rural areas and individuals with comorbidities.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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