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Socioeconomic Status and COVID-19 Related Outcomes in India: Hospital Based Study

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ABSTRACT

Objective: Association of socioeconomic status with COVID-19 outcomes has not been well studied. We performed an observational study to determine association of educational status with COVID-19 in-hospital outcomes.

Methods: Successive patients of COVID-19 presenting at government hospital were recruited. Demographic and clinical details were obtained. Cohort was classified according to educational status into Group 1:illiterate or ≤primary, Group 2:higher secondary, and Group 3:college. To compare intergroup outcomes we performed logistic regression.

Results: 4645 patients(men 3386,women 1259) with confirmed COVID-19 were recruited. Mean age was 46±18y, most lived in large households and 30.5% had low educational status. Smoking or tobacco use was in 29.5%, co-morbidities in 28.6% and low oxygen concentration(SpO_2<95%) at admission in 30%. Average length of hospital stay was 6.8±3.7 days, supplemental oxygen was provided in 18.4%, high flow oxygen or non-invasive ventilation 7.1%, and mechanical ventilation 3.6%, 340 patients(7.3%) died. Group 1 patients had more tobacco use, hypoxia at admission, lymphocytopenia, liver and kidney dysfunction. In Group 1 vs Groups 2 and 3 requirement of oxygen (21.6vs16.7 and 17.0%), non-invasive ventilation (8.0vs5.9 and 7.1%), invasive ventilation (4.6vs3.5 and 3.1%) and deaths (10.0vs6.8 and 5.5%) were significantly greater (p<0.05). Odds ratio for deaths were higher in Group 1(1.91,1.46-2.51) and Group 2(1.24,0.93-1.66) compared to Group 3. Adjustment for demographic and comorbidities led to attenuation in Groups 1(1.44,1.07-1.93) and 2(1.38,1.02-1.85) that persisted with adjustments for clinical parameters and oxygen support in Groups 1(1.38,0.99-1.93) and 2(1.52,1.01-2.11).

Conclusion: Low educational status patients with COVID-19 in India have significantly greater adverse in-hospital outcomes and mortality.

KEYWORDS: SARS-CoV-2; Epidemiology; Registry; Risk factors; Socioeconomic status; Social determinants;

Strengths and limitations:

- Studies in high-income countries have reported that low socioeconomic status is a risk factor for adverse outcomes in COVID-19. Similar studies are not available in lower-middle and low-income countries.
- This study in India shows that low socioeconomic status patients, evaluated using educational status, with COVID-19 have significantly higher in-hospital mortality compared to the better educated.
- Low educational status patients have more severe disease at presentation with greater requirement of oxygen and ventilation.
- Important limitations are lack of area-based measures, details of neighborhoods, biochemical and inflammatory markers of severity of illness and absence of medium- and long-term follow-up.

INTRODUCTION

COVID-19 pandemic continues to devastate human lives and livelihoods, especially in low and lower-middle income countries.[1] After the initial spread to the high-income countries in Europe and North America, the epidemic is now rapidly escalating in middle-income and low-income countries of South America, South Asia, South East Asia and Africa.[2] Epidemiological studies from China, Europe, UK and USA have shown greater disease burden in socioeconomically deprived neighborhoods and minority ethnic groups.[3] A review that included more than 18.7 million patients from 50 studies in UK and USA reported that individuals from Black and Asian ethnicities had 1.5-2.0 time greater risk of COVID-19 infection compared to White individuals and individuals of Asian ethnicity were at greater risk for intensive-care unit admission and death.[4] Multiple reasons have been postulated for these socioeconomic disparities and include factors such as poverty, racism and other structural factors, lower availability, access, affordability and utilization of healthcare and low value care.[5,6] Greater load of infection and longer exposure to the virus due to crowded environments, limited housing, large household sizes, low quality jobs, unsafe commute and undernutrition are also important.[6,7]

Educational status is an important marker of socioeconomic status and hundreds of studies in fields of communicable and non-communicable diseases have reported association of low educational status with adverse health-related events.[8,9,10] It is also an independent risk factor for morbidity and mortality from infectious diseases .[8,11] Association of socioeconomic status with COVID-19 related outcomes has not been well studied. A rapid review identified 42 studies that evaluated social determinants of COVID-19 incidence, clinical presentation, health service use and outcomes,[3] and reported significant associations of race, ethnicity and social deprivation with increased COVID-19 incidence and hospitalization. The review also reported that there was limited evidence regarding other key determinants including occupation, education, housing status and food security and suggested larger epidemiological studies to obtain high-quality evidence. A number of more recent studies have highlighted importance of socioeconomic inequalities in COVID-19 related morbidity and mortality,[12,13,14] and a review that included 34 studies has reported substantial racial, ethnic and socioeconomic variation in incidence of COVID-19 in USA with greater incidence among poorer communities.[15]

India has one of the largest burdens of COVID-19 cases and deaths.[16] A macrolevel study reported that Indian states with greater human development index and other socioeconomic indices had higher per capita COVID-19 incidence and deaths.[17] Although anecdotal evidence and modelling data exist,[1,18] there are no significant data on association of individual level socioeconomic status with disease incidence and outcomes. Therefore, to examine association of educational status, as a marker of

socioeconomic status, in confirmed COVID-19 cases successively admitted to a dedicated COVID-19 government hospital in India we performed a prospective registry-based study.

METHODS

We conducted a hospital based prospective observational study on patients with laboratory confirmed COVID-19 admitted to a 1200-bed dedicated COVID-19 government university hospital from April to mid-September 2020. Initial data on patients have been reported earlier.[19,20] The registry has been approved by the college administration and institutional ethics committee (CDSCO Registration Number: CR/762/Inst/RJ/2015). Individual patient consent was waivered by the ethics committee as anonymized data have been used with no patient identifiers. It is registered with Clinical Trials Registry of India at www.ctri.nic.in with registration number REF/2020/06/ 034036. Patients and/or the public were not involved in the design, or conduct, or reporting of this research. The preprint (*medRxiv preprints.* https://doi.org/10.1101/2021.05.17.21257364) has been shared with the administrative authorities of Government of Rajasthan.

Patient data: Successive patients presenting to the hospital for admission with suspicion of COVID-19 infection were enrolled in the study and those who tested positive for COVID-19 on nasopharyngeal and oropharyngeal RT-PCR test were included. A questionnaire was developed and details of sociodemographic, clinical, laboratory, treatments and outcomes variables were recorded using patients' history and medical files.[19] Educational status was self-reported and patients were classified into three groups: Group 1- illiterate or ≤ primary education, Group 2- > primary to higher-secondary school education, and Group 3- any graduate or post graduate college education.

Statistical analyses: The data were computerized and data processing was performed using commercially available statistical software, SPSS v.20.0. Numerical data are expressed as numbers ±1 SD and categorical data as percent. Significance of intergroup differences were calculated using either unpaired t-test or χ^2 test as appropriate. To evaluate association of educational status with clinical outcomes we performed a stepwise logistic regression analysis. Univariate and multivariate odds ratios (OR) and 95% confidence intervals (95% CI) were calculated. P value of <0.05 is considered significant.

RESULTS

Data were obtained from March 2020 to mid-September 2020 and we enrolled successive patients presenting to the hospital. A total of 7349 patients were hospitalized with confirmed or suspected COVID-19 during this period, 5103 patients (69.0%) tested positive for the disease on reverse transcriptase-polymerase chain reaction (RT-PCR) test and for the present study 4645 individuals (91.0%

of confirmed cases), men 3386 (72.9%) and women 1259 (27.1%), in whom detailed clinical data were available have been included (Table 1). The mean age of the cohort was 45.9+18 years, 54% were less than 50 years and about half lived in large family households. Prevalence of low educational status was high and greater in women while tobacco use was more in men (Table 1). Comorbidities were present in 28.6% with hypertension and diabetes being the most common. Details of symptoms, laboratory investigations and clinical status at admission is shown in Table 1. Data on hematological investigations were available in 4456 (95.9%) and for biochemical tests in 867 (18.7%) patients. All patients received standard treatment according to guidelines available from Indian Council of Medical Research and local government.[21] Management included oral or intravenous hydration, paracetamol and oral or intravenous antibiotics if required. A number of patients also received hydroxychloroquine, ivermectin, azithromycin, doxycycline, lopinavir-ritonavir, favipiravir, etc. The average length of stay in hospital was 6.8±3.7 days, and was significantly greater in men (6.9±3.8 days) than in women (6.5±3.6 days) (p= 0.004). Oxygen requirement was significantly greater in women but other outcomes such as requirement of high flow oxygen, non-invasive or invasive ventilation were not significantly different. Number of in-hospital deaths were significantly greater in men (n=282, 8.3%) as compared to women (n=58, 4.6%) (p<0.001).

The cohort was divided into the three groups based on educational status. Important demographic and clinical characteristics and in-hospital outcomes are shown in Table 2. Low educational status (Group 1 and 2) was more common in women while more men had college education. Family size was larger among the less literate group and tobacco use and smoking greater. Prevalence of co-morbidities, especially hypertension and diabetes, was significantly greater among the more literate, similar to previous studies in India.[22] No significant differences were observed in complaints or clinical findings (data not shown). Low SpO_2 (<90% as well as <95%), lymphopenia, higher transaminases and higher creatinine values at admission were observed among the less literate. The length of hospital stay was not significantly different in the three groups. Various clinical outcomes are shown in Figure 1 and compared to Group 3, in Group 1 there was greater oxygen requirement (unadjusted OR 1.34, 95% CI 1.12-1.61) , non-invasive ventilation (1.14, 0.87-1.49) and invasive ventilation (1.54, 1.06-2.23) (Table 2). Compared to Group 3 (deaths n=92, 5.5%), deaths were significantly greater in Group 1 (n=143, 10.0%, unadjusted OR 1.91, CI 1.46-1,51) and Group 2 (n=104, 6.8%, unadjusted OR 1.24, CI 0.93-1.66) (p<0.001).

We performed a stepwise logistic regression analysis to identify influence of various sociodemographic, risk factor, clinical and treatment variables on outcomes. Compared to Group 3,

unadjusted OR for deaths were higher in less literate Groups 1 and 2 (Table 3). Following adjustments for age, sex, household size, risk factors and comorbidities the ORs declined but remained significant in both Groups 1 (1.44, 1.07-1.93) and 2 (1.38, 1.02-1.85). However, after addition of clinical features at admission and laboratory investigations the risks attenuated to marginally significant in Group 1 (1.39, 0.99-1.93) and significant in Group 2 (1.53, 1.10-2.11) and remain the same after further adjustments for oxygenation (Table 3). OR for other outcomes assessed in the cohort (need for invasive ventilation and non-invasive ventilation) are shown in Table 3 and demonstrate a marginal significance.

DISCUSSION

The study shows that illiterate and less literate COVID-19 patients in India have significantly greater mortality compared to the better educated. The higher risk of death among the less literate persists after adjustment for various sociodemographic factors (age, sex, household size), lifestyle factors and comorbidities but attenuates after adjustment for clinical features at presentation, investigations and oxygen treatment. This suggests that more adverse features at presentation (hypoxia, deranged liver and kidney functions) could be responsible for higher deaths among the less educated (low socioeconomic status) COVID-19 patients in India.

Clinical and epidemiological studies from most developed countries in Europe and North America have consistently reported higher communicable disease-related mortality among the less literate and lower socioeconomic individuals.[11] In the COVID-19 pandemic, studies from most developed countries have reported greater COVID-19 related mortality and adverse outcomes among the ethnic minorities.[3,4,5] However, association of mortality among low socioeconomic or less educational status individuals are inconclusive.[3,4,12,13,14] In England, OpenSAFELY platform evaluated ethnic differences in COVID-19 related hospitalization, intensive care unit admission and death in 17 million adults from the National Health Service.[23] As compared to British White group, deaths were higher in South Asians in the first wave (OR 1.08, CI 1.07-1.09), and the second wave of COVID-19 epidemic (OR 1.87, CI 1.68-2.07) as well as in the overall cohort (OR 1.26, CI 1.15-1.37). Deaths were the highest in the most deprived groups.[23] A study from Brazil reported that those with low education attainment were more likely to die from COVID-19 (OR 1.13, CI 1.07-1.19).[24] Increased deaths among the poor and low educational status patients has also been reported in recent studies from USA,[25] South Korea,[26] and African countries.[27] An epidemiological study in Santiago, Chile report a strong association between socioeconomic status and mortality, measured either by COVID-19 attributed deaths or excess deaths with greater caser-fatality rates in the young people in deprived localities.[28] Our study is one of the first reports from India that has evaluated socioeconomic difference in COVID-19 related mortality and shows a 1.4 to 1.9 fold

greater mortality among low educational status men and women and is similar to the recent international studies. Our study also shows that greater mortality among low educational status individuals could be due to delayed presentation and more severe disease (lower oxygen, greater impaired liver and renal functions) and greater need of oxygen and non-invasive and invasive ventilation in these patients (Table 2). We did not obtain exact information regarding use of various non-evidence based empirical therapies (hydroxychloroquine, ivermectin, lopinavir-ritonavir, favipiravir, etc)[29] or proven evidence-based therapies such as corticosteroids, remdesivir and tocilizumab,[30] and this is a study limitation.

A variety of approaches to conceptualization and measurement of socioeconomic status have been used. Four measures are consistently associated with greater risk: low education, low income, lower employment status, and neighborhood socioeconomic factors.[31] Low education or socioeconomic status is well known as a leading modifiable risk factor for overall as well as infectious disease mortality and is an important social determinant of health.[32] Previous studies in India and other low and lower middle income countries have reported strong correlation of educational status with measures of income, household wealth, occupation, etc.[33,34] There are multiple social, clinical and system level contributors that lead to greater disease risk among the poor and include structural barriers to good health, particularly among the less literate and poor, increased risk of exposure (unhygienic working conditions and crowded housing), unequal access to testing and high-quality care, higher rates of associated medical conditions and less access to vaccination.[7] In the present study we observed some of these barriers among our patients (crowded housing , greater tobacco use, and delayed presentation with more severe disease). COVID-19 in India could act as a catalyst to improve overall healthcare systems with opportunities for policymakers, advocacy groups and researchers for evaluation of various interventions.[36] It is hoped that COVID-19 would lead to global focus on creation of health equity by influencing coaxing politicians towards the right direction.[37]

The study has some strengths and many limitations. This is the largest case-series from India, we used data from a government hospital which is more representative of general population, there are substantial number of less literate patients reflecting local educational status. This has led to data granularity and robust evaluation of outcomes. Limitations include lack of many sociodemographic factors (occupation, income, working conditions, etc.), clinical parameters (pulmonary findings, radiological evaluation, chest computerized tomographic scans, and blood biomarkers- C-reactive protein, interleukins, d-Dimer, ferritin, etc), and type of therapy the patients received. We also did not evaluate cardiovascular biomarkers (troponins, n-terminal pro-brain natriuretic peptide) that are

important in prognostication. There could be multiple causes of deaths in COVID-19 (acute respiratory distress syndrome, myocardial infarction, acute heart failure, pulmonary embolism, sepsis, acute renal failure, etc) and we did not have data on specific causes of death. About 2.5% persons were transferred from our hospital to other centres and although we have obtained information on death in these patients using telephonic interview with families, details of specific outcomes are not available. And finally, data from a single hospital with about 4500 patients and 340 deaths may not be applicable to the whole country which has the second largest burden of COVID-19 in the world.[16] In view of the massive second wave of COVID-19 in India,[16] we should strive for larger multicentric studies for identifying reasons for greater mortality among the low socioeconomic status patients with this disease in the country.

In conclusion, our study shows a significantly greater mortality from COVID-19 in less educated (lower socioeconomic status) individuals in India. This is in contrast to the general impression that COVID-19 is more among the middle-class urban population in the country.[18] Less educated COVID-19 patients have more severe disease at presentation to hospital and need greater oxygen and ventilatory support. Strategies to increase early diagnosis and access to care for these patients are important and should include public health measures for early detection of disease and early referral to treatment centres for appropriate therapeutic measures.

Data availability statement

All the data obtained from patients have been reported in the enclosed article. Individual-level anonymised patient data are not available to all, but can be shared after permission from institutional ethics committee.

Ethics statements

Patient consent for publication

Not required.

Ethics approval

Ethics clearance for the study proposal was obtained from the Institutional Ethics Committee at RUHS College of Medical Sciences, Rajasthan University of Health Sciences, Jaipur, India. CDSCO Registration Number: CR/762/Inst/RJ/2015. Individual patient consent was waivered by the ethics committee as anonymized data have been used with no patient identifiers. The study is registered with Clinical Trials Registry of India at www.ctri.nic.in with registration number REF/2020/06/ 034036.

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Contributors

- AKS, RG, WNB, TVS, SC, JPS and SPS had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
- AKS, RG, VNB, RBP and VMK contributed to the plan and design of the study.
- AKS and VNB developed the study protocol and case-report forms.
- AKS, VNB, TVS, SC, JPS, PD and SPS led the data collection.
- AKS and RG performed the data analyses and along with RBP and VMK participated in the interpretation of the results.
- RG and AKS drafted the manuscript.
- AKS, RG, RBP and VMK contributed to the critical revision of the manuscript for important intellectual content.
- All authors approved the final version of the manuscript.
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- **Competing interests** None declared.

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LEGEND TO FIGURES:

Figure 1: Clinical outcomes in various educational status groups

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Table 1: Demographic and Clinical Characteristics of the Study Cohort

Variables	Total [N=4645]	Men (n=3386)	Women (N=1259)	P value
Age (mean, yr)	45.9±18.0	45.5±17.8	47.1±18.5	0.226
Age groups				
<30	1125[24.2]	838[24.7]	287[22.8]	0.008
30-49	1397[30.1]	1052[31.1]	345[27.4]	
50-69	1650[35.5]	1161[34.3]	489[38.8]	
70+	473[10.2]	335[9.9]	138[11.0]	
Family members/house				
1-4	2395[51.2]	656[51.7]	1739[51.1]	0.834
5-9	2000[42.8]	535[42.1]	1465[43.0]	
≥10	281[6.0]	79[6.2]	202[5.9]	
Educational status *				
Illiterate or Primary	1424[30.5]	980[28.8]	444[35.0]	<0.001
Secondary school/ Higher secondary	1538[32.9]	1061[31.2]	477[35.0]	
Graduate	1667[35.7]	1339[39.3]	328[25.8]	
Tobacco or smoking (ever)	1369[29.5]	1045[30.9]	324[25.7]	0.001
	1335[28.6]	1020[29.9]	315[24.8]	0.001
Medical co-morbidities	831[17.8]	658[19.3]	173[13.6]	<0.001
Hypertension	193[4.1]	135[4.0]	58[4.6]	0.364
Pulmonary disease	777[16.6]	666[19.6]	111[8.7]	<0.001
Type 2 Diabetes	38[0.8]	27[0.8]	11[0.9]	0.855
Thyroid disease	75[1.6]	51[1.5]	24[1.9]	0.360
Heart disease	15[0.3]	6[0.2]	9[0.7]	0.008
Neurological disease	106[2.3]	78[2.3]	28[2.3]	0.874
Current or past tuberculosis	112[2.4]	55[1.6]	57[4.5]	<0.001
Other				
Clinical findings				
Pulse rate /min	83.9±11.4	83.91±11.2	84.1±11.8	0.715
Systolic BP mmHg	125.4±12.2	125.12±11.9	126.0±12.9	0.028
Diastolic BP mmHg	82.8±8.1	82.71±7.9	83.1±8.4	0.155
Respiratory rate/min	19.0±3.7	19.0±3.7	19.1±3.9	0.313
SpO_2 at admission				
≥95%	2144[70.0]	1554[70.5]	590[68.7]	0.601
90-94%	561[18.3]	397[18.0]	164[19.1]	
<90%	357[11.7]	252[11.4]	105[12.2]	
Laboratory Investigations (Biochemistry n=867; Hematology n=4456)				
Creatinine, mg/dl	0.95±0.50	0.94±0.47	0.97±0.56	0.378
SGOT, IU	44.9±96.5	45.0±108.9	44.8±44.5	0.531
SGPT, IU	43.4±56.2	42.7±59.7	45.6± 44.2	0.096
Sodium, mEq/L	136.1±12.5	136.6±9.4	134.8±17.8	0.144
Potassium, mEq/L	5.4±10.1	5.1±8.9	5.9±12.6	0.112
Hb (gm/dl)	12.7±2.3	12.7±2.3	12.6±2.2	0.411
White cells (10^9 cells/L)	7527±3830	7585±3894	7370±3651	0.099
Lymphocytes (10^9 cells/L)	1589±1325	1607±1355	1534±1225	0.089
Lymphocyte/Neutrophil ratio	0.36±0.32	0.36±0.27	0.35±0.46	0.346
Outcome measures				
Mean duration of hospital stay[days]	6.8±3.7	6.9±3.8	6.5±3.6	0.004
Oxygen requirement	861[18.4]	600[17.6]	261[20.6]	0.022
High flow O_2/non-invasive ventilation	334[7.1]	236[6.9]	98[7.7]	0.371

Mechanical ventilation	169[3.6]	123[3.6]	46[3.6]	1.000
Recovered	4217[90.2]	3020[88.7]	1197[94.3]	<0.001
Referred	119[2.5]	104[3.0]	15[1.2]	<0.001
Deaths	340[7.3]	282[8.3]	58[4.6]	<0.001
Numbers ± indicate 1 SD; Numbers in parentheses are percent; BP blood pressure; SpO_2 saturation of peripheral oxygen; SGOT serum glutamic oxalate transferase; SGPT serum glutamic pyruvate transferase				

Table 2: Clinical characteristics and outcomes according to educational status (Group 1= none/primary; Group 2= higher secondary; Group 3= college)

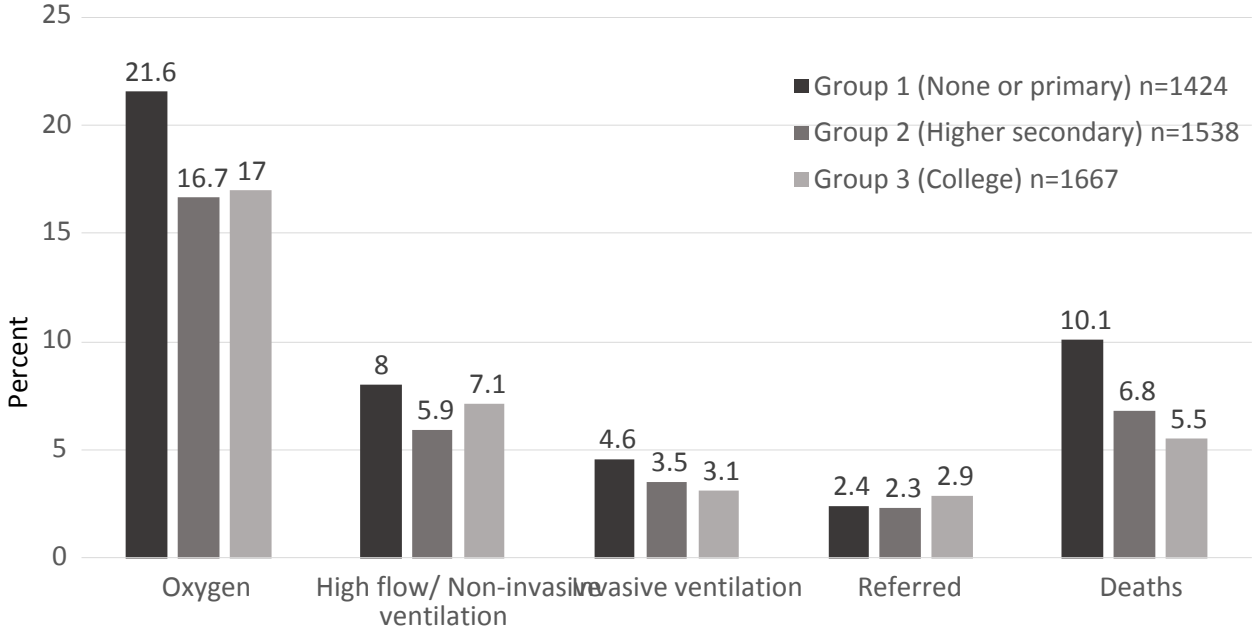
Variables	Group 1 (n=1424)	Group 2 (n=1538)	Group 3 (n=1667)	Odds Ratio/ Mean Difference (95% CI) Group 2vs3	Odds Ratio/ Mean Difference (95% CI) Group 1vs3
Age groups					
<30y	353[25.0]	414[27.1]	348[21.0]	1.39[1.18-1.64]***	1.25[1.05-1.47]***
30-49	416[29.4]	459[30.0]	510[30.8]	0.97[0.83-1.12]	0.93[0.80-1.09]
50-69	509[36.0]	501[32.8]	620[37.4]	0.81[0.70-0.94]**	0.94[0.81-1.08]
70+	136[9.6]	154[10.1]	179[10.8]	0.85[0.67-1.06]	0.87[0.69-1.11]
Age mean (yr)	45.8±17.9	44.6± 18.4	47.1± 17.6	1.84 (0.69-2.99)	-5.92 (-7.10--4.69)
Men	980[29.0]	1061[31.4]	1339[39.6]	0.54[0.46-0.64]***	0.54[0.45-0.64]***
Women	444[35.5]	477[38.2]	328[26.3]	1.83[1.56-2.15]**	1.85{1.57-2.18]**
Members/house					
1-4	710[49.9]	769[50.0]	893[53.6]	0.87[0.75-0.99]*	0.86[0.75-0.99]*
5-9	624[43.8]	652[42.4]	703[42.2]	1.00[0.87-1.16]	1.07[0.93-1.23]
≥10	90[6.3]	117[7.6]	71[4.3]	1.85[1.37-2.51]***	1.52[1.10-2.08]*
Tobacco or smoking	496[34.6]	485[31.5]	375[22.5]	1.58[1.35-1.85]***	1.79***[1.52-2.09]
Medical co-morbidities	391[27.5]	411[26.7]	531[31.9]	0.78[0.67-0.91]**	0.81[0.69-0.95]**
Hypertension	248[17.4]	218[14.2]	365[21.9]	0.59[0.49-0.71]***	0.75[0.63-0.90]**
Pulmonary disease	44[3.1]	59[3.8]	89[5.3]	0.71[0.50-0.99]*	0.56[0.39-0.82]**
Type 2 Diabetes	220[15.4]	232[15.1]	325[19.5]	0.73[0.61-0.88]**	0.75[0.62-0.91]**
Thyroid disease	18[1.3]	13[0.8]	7[0.4]	2.02[0.80-5.08]	3.04[1.26-07.29]*
Coronary heart disease	18[1.3]	20[1.3]	36[2.2]	0.59[0.34-1.03]	0.58[0.33-1.03]
Clinical findings					
Systolic BP mmHg (mean±SD)	125.4±12.6	124.7±11.6	125.9±12.4	1.21[0.37-2.03]**	0.51[-0.38-1.38]
Respiratory rate (mean±SD)	19.1±3.7	18.9±3.5	19.1±3.9	0.20[-0.05-0.45]	0.00[-0.26-0.27]
SpO2 <90%	173[12.1]	165[10.7]	168[10.1]	1.07[0.85-1.34]	1.23[0.98-1.55]
SpO2 90-94%	273[19.2]	272[17.7]	270[16.2]	1.11[0.92-1.33]	1.22[1.02-1.45]*
Investigations (mean±SD)					
Haemoglobin, g/dl	12.8±2.2	12.6±2.4	12.7±2.2	0.10[-0.05-0.26]	-0.1[-0.25-0.05]
White cells, 10^9 cells/L	7559±3917	7611±3759	7419±3832	-192[-455-71]	-140[-414-134]
Lymphocyte, 10^9 cells/L	1574±1269	1561±1187	1631±1489	70[-23-163]	57[-41-155]
Lymphocyte/neutrophil ratio	0.35±0.35	0.36±0.35	0.36±0.27	0.00[-0.02-0.02]	0.01[-0.01-0.03]
SGPT, units	46.9±72.6	43.0±50.1	38.5±29.2	-4.5[-7.3--1.7]**	-8.4[-12.2--4.6]***
SGOT, units	50.8±143.5	43.6±59.02	38.3±26.9	-5.3[-8.4--2.2]***	-12.5[-19.5--5.5]***
Sodium, mEq/L	135.1±15.3	136.4±10.9	136.6±11.1	0.29[-0.47-1.05]	1.61[0.67-2.53]***
Creatinine, mg/dl	0.96±0.57	0.90±0.51	0.90±0.32	0.00[-0.02-0.02]	-0.06[-0.09--0.02]**
Clinical Outcomes					
Oxygen requirement	308[21.6]	257[16.7]	284[17.0]	0.97[0.81-1.17]	1.34[1.12-1.61]**
Non-invasive ventilation	114[8.0]	91[5.9]	118[7.1]	0.82[0.62-1.09]	1.14[0.87-1.49]
Invasive ventilation	66[4.6]	54[3.5]	51[3.1]	1.15[0.78-1.70]	1.54[1.06-2.23]*
In-hospital outcomes					
Recovered	1247[87.6]	1400[91.0]	1526[91.5]	0.94[0.73-1.19]	0.65[0.51-0.82]***
Referred	34[2.4]	34[2.3]	49[2.9]	0.75[0.47-1.16]	0.81[0.52-1.26]
Deaths	143[10.0]	104[6.8]	92[5.5]	1.24[0.93-1.66]	1.91[1.46-2.51]***

Numbers ± indicate 1 SD; Numbers in parentheses are percent;
Odds ratios and 95% CI calculated for categorical variables; Mean difference and 95% CI calculated for numerical variables;
95% CI 95% confidence intervals; BP blood pressure; SpO_2 saturation of peripheral oxygen; SGOT serum glutamic oxalate transferase; SGPT serum glutamic pyruvate transferase;
* p<0.05, ** p<0.01, *** p<0.001

Table 3: Stepwise Multivariate Logistic Regression Analyses and Odds Ratio for Adverse Outcomes in Educational Status Groups 1 (≤primary education) and 2 (>primary-higher secondary education) compared to Group 3 (any college education)

	Educational status groups (Reference 3)	Unadjusted Odds Ratios	Age and Sex adjusted	Plus household size	Plus risk factors, comorbidities	Plus clinical factors, investigations	Plus oxygenation
Deaths	Group 1	1.91(1.46-2.51)	1.33[0.99-1.83]	1.37[1.01-1.83]	1.44[1.07-1.93]	1.39[0.99-1.93]	1.38[0.99-1.93]
	Group 2	1.24(0.93-1.66)	1.31[0.91-1.82]	1.32[0.98-1.78]	1.38[1.02-1.85]	1.53[1.10-2.11]	1.52[10.1-2.11]
Invasive ventilation	Group 1	1.54(1.06-2.23)	1.19[0.80-1.81]	1.21[0.81-1.79]	1.29[0.86-1.92]	1.34[0.86-2.11]	1.39[0.88-2.19]
	Group 2	1.15(0.78-1.70)	1.06[0.71-1.59]	1.07[0.71-1.60]	1.11[0.74-1.67]	1.31[0.84-2.04]	1.33[0.85-2.07]
Non-invasive	Group 1	1.14(0.87-1.49)	0.95[0.71-1.32]	0.96[0.72-1.27]	1.03[0.77-1.36]	0.79[0.56-1.12]	0.78[0.54-1.13]
ventilation	Group 2	0.82(0.62-1.09)	1.01[0.76-1.33]	1.00[0.76-1.33]	1.02[0.77-1.35]	0.88[0.63-1.22]	0.91[0.64-1.29]
Data are in odds ratios and 95% confidence intervals; OR odds ratios;							

Figure 1: Clinical outcomes in various educational status groups



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Educational Status and COVID-19 Related Outcomes in India: Hospital Based Cross Sectional Study

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ABSTRACT

Objective: Association of educational status, as marker of socioeconomic status, with COVID-19 outcomes has not been well studied. We performed a hospital based cross-sectional study to determine its association with outcomes.

Methods: Successive patients of COVID-19 presenting at government hospital were recruited. Demographic and clinical details were obtained at admission and in-hospital outcomes assessed. Cohort was classified according to educational status into Group 1: illiterate or ≤primary, Group 2: higher secondary, and Group 3: some college. To compare intergroup outcomes, we performed logistic regression.

Results: 4645 patients (men 3386, women 1259) with confirmed COVID-19 were recruited. Mean age was 46±18y, most lived in large households and 30.5% had low educational status. Smoking or tobacco use was in 29.5%, co-morbidities in 28.6% and low oxygen concentration (SpO_2<95%) at admission in 30%. Average length of hospital stay was 6.8±3.7 days, supplemental oxygen was provided in 18.4%, high flow oxygen or non-invasive ventilation 7.1%, and mechanical ventilation 3.6%, 340 patients (7.3%) died. Group 1 patients had more tobacco use, hypoxia at admission, lymphocytopenia and liver and kidney dysfunction. In Group 1 vs Groups 2 and 3 requirement of oxygen (21.6vs16.7 and 17.0%), non-invasive ventilation (8.0vs5.9 and 7.1%), invasive ventilation (4.6vs3.5 and 3.1%) and deaths (10.0vs6.8 and 5.5%) were significantly greater (p<0.05). Odds ratio for deaths were higher in Group 1(1.91,1.46-2.51) and Group 2(1.24,0.93-1.66) compared to Group 3. Adjustment for demographic and comorbidities led to some attenuation in Groups 1(1.44,1.07-1.93) and 2(1.38,1.02-1.85), this persisted with adjustments for clinical parameters and oxygen support in Groups 1(1.38,0.99-1.93) and 2(1.52,1.01-2.11).

Conclusion: Low educational status patients with COVID-19 in India have significantly greater adverse in-hospital outcomes and mortality.

KEYWORDS: SARS-CoV-2; Epidemiology; Registry; Risk factors; Socioeconomic status; Social determinants;

Strengths and limitations:

- Studies in high-income countries have reported that low socioeconomic status is a risk factor for adverse outcomes in COVID-19. Similar studies are not available in lower-middle and low-income countries.
- This study shows that low educational status patients with COVID-19 in India have significantly higher in-hospital mortality compared to the better educated.
- Low educational status patients have more severe disease at presentation with greater requirement of oxygen and ventilation.
- Important limitations are lack of area-based measures, neighborhood details, biochemical and inflammatory markers of severity of illness, and absence of long-term follow-up.

INTRODUCTION

COVID-19 pandemic continues to devastate human lives and livelihoods, especially in low and lower-middle income countries.[1] After the initial spread to the high-income countries in Europe and North America, the epidemic is now rapidly escalating in middle-income and low-income countries of South America, South Asia, South East Asia and Africa.[2] Epidemiological studies from China, Europe, UK and USA have shown greater disease burden in socioeconomically deprived neighborhoods and minority ethnic groups.[3] A review that included more than 18.7 million patients from 50 studies in UK and USA reported that individuals from Black and Asian ethnicities had 1.5-2.0 time greater risk of COVID-19 infection compared to White individuals and individuals of Asian ethnicity were at greater risk for intensive-care unit admission and death.[4] Multiple reasons have been postulated for these socioeconomic disparities and include factors such as poverty, racism and other structural factors, lower availability, access, affordability and utilization of healthcare and low value care.[5,6] Greater load of infection and longer exposure to the virus due to crowded environments, limited housing, large household sizes, low quality jobs, unsafe commute and undernutrition are also important.[6,7]

Educational status is an important marker of socioeconomic status and hundreds of studies in fields of communicable and non-communicable diseases have reported association of low educational status with adverse health-related events.[8,9,10] It is also an independent risk factor for morbidity and mortality from infectious diseases .[8,11] Association of socioeconomic status with COVID-19 related outcomes has not been well studied. A rapid review identified 42 studies that evaluated social determinants of COVID-19 incidence, clinical presentation, health service use and outcomes,[3] and reported significant associations of race, ethnicity and social deprivation with increased COVID-19 incidence and hospitalization. The review also reported that there was limited evidence regarding other key determinants including occupation, education, housing status and food security and suggested larger epidemiological studies to obtain high-quality evidence. A number of more recent studies have highlighted importance of socioeconomic inequalities in COVID-19 related morbidity and mortality,[12,13,14] and a review that included 34 studies has reported substantial racial, ethnic and socioeconomic variation in incidence of COVID-19 in USA with greater incidence among poorer communities.[15]

India has one of the largest burdens of COVID-19 cases and deaths.[16] A macrolevel study reported that Indian states with greater human development index and other socioeconomic indices had higher per capita COVID-19 incidence and deaths.[17] Although anecdotal evidence and modelling data exist,[1,18] there are no significant data on association of individual level socioeconomic status with disease incidence and outcomes. Therefore, to examine association of educational status, as a marker of

socioeconomic status, in confirmed COVID-19 cases successively admitted to a dedicated COVID-19 government hospital in India, we performed a prospective registry-based study.

METHODS

We conducted a hospital based prospective observational study on patients with laboratory confirmed COVID-19 admitted to a 1200-bed dedicated COVID-19 government hospital (Rajasthan University of Health Sciences Hospital, Jaipur) from April to mid-September 2020. Initial data on patients have been reported earlier.[19,20] The registry has been approved by the college administration and institutional ethics committee (CDSCO Registration Number: CR/762/Inst/RJ/2015). Individual patient consent was waivered by the ethics committee and anonymized data have been used with no patient identifiers. It is registered with Clinical Trials Registry of India at www.ctri.nic.in with registration number REF/2020/06/ 034036. Patients and/or the public were not involved in the design, or conduct, or reporting of this research. The preprint (*medRxiv preprints.* https://doi.org/10.1101/2021.05.17.21257364) has been shared with the administrative authorities of Government of Rajasthan.

Patient data: Successive patients aged 18 years or more, presenting to the hospital for admission with suspicion of COVID-19 infection were enrolled in the study. Only those who tested positive for COVID-19 on nasopharyngeal and oropharyngeal reverse transcriptase polymerase chain reaction (RT-PCR) test have been included. All RT-PCR positive patients admitted from 1 April to 15 September have been included. Patients recruited into the study in mid-September were followed up to discharge or death and outcome events were recorded.

A questionnaire was developed and details of sociodemographic, clinical, laboratory, treatments and outcomes variables were recorded using patients' history and medical records.[19] Demographic details were obtained at the time of admission. These included name, age, sex, residence address and educational status. Other sociodemographic variables were not available for majority of patients and are not reported. Although it is mandatory to obtain individual details of Aadhaar number or other identifiers of all the COVID-19 cases we did not use these data. All the COVID-19 RT-PCR reports along with the government identifier are uploaded on the official website of Indian Council of Medical Research at www.icmr.gov.in. Details of physical examination at the time of admission were obtained from patient case files. These included history of duration of symptoms at admission, pulse, blood pressure (BP), respiratory rate, and surface oxygen concentration (SpO2. Details of investigations at admission were obtained from the case files and biochemistry, microbiology and pathology departments

as reported earlier.[20] We do not have data on serial investigations. We obtained data on duration of hospital stay from medical record department. For patients discharged alive from the hospital, we obtained data on patients who required oxygen support (nasal prongs, facial mask or high-flow nasal cannula), non-invasive ventilation (CPaP or BiPaP support) or invasive ventilation after endotracheal intubation. Binary outcomes were obtained for all patients and included either recovery, referral to non-government hospitals on request of family, or death. All these data have also been sent to the Department of Health, Government of Rajasthan, India, but are not currently accessible.

Statistical analyses: The data were computerized and data processing was performed using commercially available statistical software, SPSS v.20.0. Educational status was self-reported and patients were classified into three groups: Group 1: illiterate or ≤ primary education, Group 2: > primary to higher-secondary school education, and Group 3: any graduate or post graduate college education. Numerical data are expressed as mean±1 standard deviation (SD) and categorical data as percent. Significance of intergroup differences were calculated using either χ^2 test or ANOVA as appropriate. χ^2 test residuals were determined for categorical variables in various groups and significant were age, sex, household size and some clinical parameters. Tests of normality for continuous variables was performed in the statistical program and all followed a normal Gaussian distribution. The variables where significant residuals identified were adjusted using logistic regression. We also compared mean and proportionate differences in Groups 1 and 2 as compared to Group 3 using unpaired t-test or χ^2 test as appropriate. To evaluate association of educational status with clinical outcomes we performed stepwise logistic regression. Univariate and multivariate odds ratios (OR) and 95% confidence intervals (95% CI) were calculated for Group 1 and Group 2 compared to Group 3 for outcomes of in-hospital death, invasive ventilation and non-invasive ventilation. We initially calculated the univariate ORs and subsequently performed a stepwise logistic regression with sequential adjustment with (i) age and sex, (ii) household size, (iii) cardiovascular risk factors and comorbidities, (iv) clinical features and investigations at presentation and finally with (v) oxygenation during hospital stay, and determined multivariate ORs. P value of <0.05 is considered significant.

RESULTS

Patients were enrolled from March 2020 to mid-September 2020. A total of 7349 patients were hospitalized with confirmed or suspected COVID-19 during this period, 5103 patients (69.0%) tested positive for the disease on RT-PCR test and for the present study 4645 individuals (91.0% of confirmed cases), men 3386 (72.9%) and women 1259 (27.1%), in whom detailed clinical data were available have been included (Table 1). The mean age of the cohort was 45.9±18 years, 54% were less than 50 years

and about half lived in large family households. Prevalence of low educational status was high and greater in women while tobacco use was more in men (Supplementary Table 1). Comorbidities were present in 28.6% with hypertension and diabetes being the most common. Details of symptoms, laboratory investigations and clinical status at admission is shown in Table 1. Data on hematological investigations were available in 4456 (95.9%) and for biochemical tests in 867 (18.7%) patients. All patients received standard treatment according to guidelines available from Indian Council of Medical Research and the state government.[21] Management included oral or intravenous hydration, paracetamol and oral or intravenous antibiotics if required. A number of patients also received hydroxychloroquine, ivermectin, azithromycin, doxycycline, lopinavir-ritonavir, favipiravir, etc. The average length of stay in hospital was 6.8±3.7 days, and was significantly greater in men (6.9±3.8 days) than in women (6.5±3.6 days) (p= 0.004). Oxygen requirement was significantly greater in women but other outcomes such as requirement of high flow oxygen, non-invasive or invasive ventilation were not significantly different (Supplementary Table 1). Number of in-hospital deaths were significantly greater in men (n=282, 8.3%) as compared to women (n=58, 4.6%) (p<0.001).

The cohort was divided into the three groups based on educational status. Important demographic and clinical characteristics and in-hospital outcomes are shown in Table 2. Low educational status (Group 1 and 2) was more common in women while more men had college education. Family size was larger among the less literate group. Tobacco use and smoking was also greater in Group 1. Prevalence of co-morbidities, especially hypertension and diabetes, was significantly greater among the more literate, similar to previous studies in India.[22] No significant differences were observed in complaints or clinical findings (data not shown). Data on duration of illness prior to admission were not available. Low SpO_2 (<90% as well as <95%), lymphopenia, higher transaminases and higher creatinine values at admission were observed among the less literate. The length of hospital stay was not significantly different in the three groups.

Univariate ORs (categorical variables) and mean differences (continuous variables) in less literate Groups 1 and 2 compared to the more literate Group 3 are shown in Table 3. Patients in less literate groups were younger, more women and lived in larger households (>10 persons/house). Presence of tobacco use was greater while cardiovascular risk factors were lower. Various clinical outcomes are shown in Figure 1 and compared to Group 3, in Group 1 there was greater oxygen requirement (unadjusted OR 1.34, 95% CI 1.12-1.61), non-invasive ventilation (1.14, 0.87-1.49) and invasive ventilation (1.54, 1.06-2.23) (Table 3). Compared to Group 3 (deaths n=92, 5.5%), deaths were

significantly greater in Group 1 (n=143, 10.0%, unadjusted OR 1.91, CI 1.46-1,51) as well as in Group 2 (n=104, 6.8%, unadjusted OR 1.24, CI 0.93-1.66) (p<0.001).

We performed a stepwise logistic regression analysis to identify influence of various sociodemographic, risk factor, clinical and treatment variables on outcomes. Compared to the most literate Group 3, unadjusted OR for deaths were higher in less literate Groups 1 and 2 (Table 4). Following adjustments for age, sex, household size, risk factors and comorbidities the ORs attenuated but remained significant in both Group 1 (1.44, 1.07-1.93) and Group 2 (1.38, 1.02-1.85). However, after addition of clinical features at admission and laboratory investigations the risks attenuated to marginally significant in Group 1 (1.39, 0.99-1.93) and significant in Group 2 (1.53, 1.10-2.11) and remain the same after further adjustments for oxygenation (Table 3). OR for other outcomes assessed in the cohort (need for invasive ventilation and non-invasive ventilation) are shown in Table 4 and demonstrate a marginal significance.

DISCUSSION

This study shows that illiterate and less literate COVID-19 patients have significantly greater in-hospital mortality compared to the better educated. The higher risk of death among the less literate persists after adjustment for various sociodemographic factors (age, sex, household size), lifestyle factors and comorbidities but attenuates after adjustment for clinical features at presentation, investigations and oxygen treatment. This suggests that more adverse features at presentation (hypoxia, deranged liver and kidney functions) could be responsible for higher deaths among the less educated COVID-19 patients in India.

Clinical and epidemiological studies from most developed countries in Europe and North America have consistently reported higher communicable disease-related mortality among the less literate and lower socioeconomic individuals.[11] In the COVID-19 pandemic, studies from most developed countries have reported greater COVID-19 related mortality and adverse outcomes among the ethnic minorities.[3,4,5] However, association of mortality among low socioeconomic or less educational status individuals are inconclusive.[3,4,12,13,14] In England, OpenSAFELY platform evaluated ethnic differences in COVID-19 related hospitalization, intensive care unit admission and death in 17 million adults from the National Health Service.[23] As compared to the British White patients, deaths were higher in South Asians in the first wave (OR 1.08, CI 1.07-1.09), and the second wave of COVID-19 epidemic (OR 1.87, CI 1.68-2.07) as well as in the overall cohort (OR 1.26, CI 1.15-1.37). Deaths were the highest in the most deprived groups.[23] A study from Brazil reported that those with low education attainment were more

likely to die from COVID-19 (OR 1.13, CI 1.07-1.19).[24] Increased deaths among the poor and low educational status patients has also been reported in recent studies from USA,[25] South Korea,[26] and African countries.[27] An epidemiological study in Santiago, Chile report a strong association between socioeconomic status and mortality, measured either by COVID-19 attributed deaths or excess deaths with greater case-fatality rates in the young COVID-19 patients in deprived localities.[28] A large meta-analysis, that combined population and hospital based data in the US, involving 4.3 million patients from 68 studies reported that disease incidence was more in African-American and Hispanic-American individuals, risk of hospitalization greater in Asian Americans. Mortality rates in Hispanics and Asian Americans correlated positively with residence in more deprived locations.[29] In this study influence of individual level socioeconomic factors was not reported. Our study is one of the first reports from India that has evaluated socioeconomic difference in COVID-19 related mortality and shows a 1.4 to 1.9 fold greater mortality among low educational status men and women and is similar to the recent international studies. Our study also shows that greater mortality among low educational status individuals could be due to delayed presentation and more severe disease (lower oxygen, greater impaired liver and renal functions) and greater need of oxygen and non-invasive and invasive ventilation in these patients (Table 2). We did not obtain exact information regarding use of various non-evidence based empirical therapies (hydroxychloroquine, ivermectin, lopinavir-ritonavir, favipiravir, etc)[30] or proven evidence-based therapies such as corticosteroids, remdesivir and tocilizumab,[31] and this is a study limitation.

A variety of approaches to conceptualization and measurement of socioeconomic status have been used. Four measures are consistently associated with greater risk: low education, low income, lower employment status, and neighborhood socioeconomic factors.[32] Low education or socioeconomic status is well known as a leading modifiable risk factor for overall as well as infectious disease mortality and is an important social determinant of health.[33] Our previous studies in India and other low and lower middle income countries have reported strong correlation of educational status with measures of income, household wealth, occupation, etc.[34,35] There are multiple social, clinical and system level contributors that lead to greater disease risk among the poor and include structural barriers to good health, particularly among the less literate and poor, increased risk of exposure (unhygienic working conditions and crowded housing), unequal access to testing and high-quality care, higher rates of associated medical conditions and less access to vaccination.[7,36] In the present study we observed some of these barriers among our patients (crowded housing , greater tobacco use, and delayed presentation with more severe disease). COVID-19 in India could act as a catalyst to improve overall healthcare

systems with opportunities for policymakers, advocacy groups and researchers for evaluation of various interventions.[37] It is hoped that COVID-19 would lead to global focus on creation of health equity by influencing coaxing politicians towards the right direction.[38]

The study has strengths as well as limitations. This is the largest case-series from India, we used data from a government hospital which is more representative of general population, there are substantial number of less literate patients reflecting local educational status. This has led to data granularity and robust evaluation of outcomes. Limitations include lack of many sociodemographic factors (housing, neighborhoods, occupation, income, working conditions, etc.), clinical parameters (detailed history, pulmonary findings, radiological evaluation, chest computerized tomographic scans, and blood biomarkers- C-reactive protein, interleukins, d-Dimer, ferritin, lactic dehydrogenase, etc.), and type of therapy the patients received. We also did not evaluate cardiovascular biomarkers (troponins and n-terminal pro-brain natriuretic peptide) that are important in prognostication.[29] These are due to lack of guidelines regarding routine measurement of many of these variables,[21] and low healthcare funding in the country.[1] There could be multiple causes of deaths in COVID-19 (acute respiratory distress syndrome, myocardial infarction, acute heart failure, pulmonary embolism, secondary chest infection, sepsis, acute renal failure, etc.)[29] and we did not have data on specific causes of death. About 2.5% persons were transferred from our hospital to other centres and although we have obtained information on death in these patients using telephonic interview with families, details of specific outcomes are not available. And finally, data from a single hospital with about 4500 patients and 340 deaths may not be applicable to the whole country which has one of the largest burden of COVID-19 in the world.[16] In view of the massive second wave of COVID-19 in India,[39] we should strive for larger multicentric studies for identifying reasons for greater mortality among the low socioeconomic status patients with this disease in the country.

In conclusion, our study shows a significantly greater mortality from COVID-19 in less educated (lower socioeconomic status) individuals in India. Khalatbari-Soltani et al have suggested that low educational status is associated with increased prevalence of smoking and poor nutrition leading to more severe disease, prevalence of comorbidities is high in these individuals and low health literacy results in increased disease incidence and severity due to poor understanding pf public health preventive measures and delayed healthcare seeking behaviours.[40] Our study shows that the less educated COVID-19 patients have more severe disease at presentation to hospital with need for greater oxygen and ventilatory support. Strategies to increase early diagnosis and access to care for these

patients are important and should include public health measures for early detection of disease and early referral to treatment centres for appropriate therapeutic measures.

Data availability statement: All the data obtained from patients have been reported in the enclosed article. No additional data available.

Ethics statements:

Patient consent for publication: Individual patient consent was waivered by the ethics committee and anonymized data have been used with no patient identifiers. Patients and/or the public were not involved in the design, or conduct, or reporting of this research.

Ethics approval: Ethics clearance for the study proposal was obtained from the Institutional Ethics Committee at RUHS College of Medical Sciences, Rajasthan University of Health Sciences, Jaipur, India. CDSCO Registration Number: CR/762/Inst/RJ/2015.

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Contributors

- AKS, RG, WNB, TVS, SC, JPS and SPS had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
- AKS, RG, VNB, RBP and VMK contributed to the plan and design of the study.
- AKS and VNB developed the study protocol and case-report forms.
- AKS, VNB, TVS, SC, JPS, PD and SPS led the data collection.
- AKS and RG performed the data analyses and participated in interpretation of the results.
- RG and AKS drafted the manuscript.
- AKS, RG, RBP and VMK contributed to the critical revision of the manuscript for important intellectual content.
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LEGEND TO FIGURES

Figure 1: Clinical outcomes in various educational status groups

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Table 1: Clinical characteristics of the study cohort at admission to hospital and outcomes

Variables	Total [N=4645]
Men	3386[72.9]
Women	1259[27.1]
Age (mean, years)	45.9±18.0
Age groups	
<30	1125[24.2]
30-49	1397[30.1]
50-69	1650[35.5]
70+	473[10.2]
Family members/house	
1-4	2395[51.2]
5-9	2000[42.8]
≥10	281[6.0]
Educational status	
Illiterate or up to primary education	1424[30.5]
Secondary school and/or higher secondary education	1538[32.9]
Some college	1667[35.7]
Tobacco or smoking (ever)	1369[29.5]
Medical co-morbidities	1335[28.6]
Hypertension	831[17.8]
Pulmonary disease	193[4.1]
Type 2 Diabetes	777[16.6]
Thyroid disease	38[0.8]
Heart disease	75[1.6]
Neurological disease	15[0.3]
Current or past tuberculosis	106[2.3]
Duration of symptoms at admission (days)	
Clinical findings	
Pulse rate /min	83.9±11.4
Systolic BP mmHg	125.4±12.2
Diastolic BP mmHg	82.8±8.1
Respiratory rate/min	19.0±3.7
SpO_2 at admission	
≥95%	2144[70.0]
90-94%	561[18.3]
<90%	357[11.7]
Laboratory Investigations (Biochemistry n=867; Hematology n=4456)	
Creatinine, mg/dl	0.95±0.50
SGOT, IU	44.9±96.5
	43.4±56.2

SGPT, IU	136.1±12.5
Sodium, mEq/L	5.4±1.1
Potassium, mEq/L	12.7±2.3
Hb (gm/dl)	7527±3830
White cells (10^9 cells/L)	1589±1325
Lymphocytes (10^9 cells/L)	0.36±0.32
Lymphocyte/Neutrophil ratio	
Outcome measures	
Mean duration of hospital stay[days]	6.8±3.7
Oxygen requirement	861[18.4]
High flow O_2/non-invasive ventilation	334[7.1]
Mechanical ventilation	169[3.6]
Recovered	4217[90.2]
Referred	119[2.5]
Deaths	340[7.3]

Numbers ± indicate 1 SD; Numbers in parentheses are percent; BP blood pressure; SpO_2 saturation of peripheral oxygen; SGOT serum glutamic oxalate transferase; SGPT serum glutamic pyruvate transferase

Table 2: Clinical characteristics and outcomes according to educational status (Group 1= < primary education; Group 2= >primary to higher secondary education; Group 3= some college). χ^2 test used for categorical variables and ANOVA for continuous variables.

Variables	Group 1 (n=1424)	Group 2 (n=1538)	Group 3 (n=1667)	χ^2 test or ANOVA-F (p value)
Age groups				<0.001
<30y	353[25.0]	414[27.1]	348[21.0]	
30-49	416[29.4]	459[30.0]	510[30.8]	
50-69	509[36.0]	501[32.8]	620[37.4]	
70+	136[9.6]	154[10.1]	179[10.8]	
Age mean (yr)	45.8±17.9	44.6± 18.4	47.1± 17.6	<0.001
Men	980[29.0]	1061[31.4]	1339[39.6]	<0.001
Women	444[35.5]	477[38.2]	328[26.3]	
Members/house				<0.001
1-4	710[49.9]	769[50.0]	893[53.6]	
5-9	624[43.8]	652[42.4]	703[42.2]	
≥10	90[6.3]	117[7.6]	71[4.3]	
Tobacco or smoking	496[34.6]	485[31.5]	375[22.5]	<0.001
Medical co-morbidities	391[27.5]	411[26.7]	531[31.9]	0.002
Hypertension	248[17.4]	218[14.2]	365[21.9]	0.000
Pulmonary disease	44[3.1]	59[3.8]	89[5.3]	0.006
Type 2 Diabetes	220[15.4]	232[15.1]	325[19.5]	0.001
Thyroid disease	18[1.3]	13[0.8]	7[0.4]	0.034
Coronary heart disease	18[1.3]	20[1.3]	36[2.2]	0.074
Clinical findings at admission				
Systolic BP mmHg (mean±SD)	125.4±12.6	124.7±11.6	125.9±12.4	0.021
Respiratory rate (mean±SD)	19.1±3.7	18.9±3.5	19.1±3.9	0.225
SpO2 <90%	173[12.1]	165[10.7]	168[10.1]	0.765
SpO2 90-94%	273[19.2]	272[17.7]	270[16.2]	0.312
Investigations (mean±SD)				
Haemoglobin, g/dl	12.8±2.2	12.6±2.4	12.7±2.2	0.056
White cells, 10^9 cells/L	7559±3917	7611±3759	7419±3832	0.340
Lymphocyte, 10^9 cells/L	1574±1269	1561±1187	1631±1489	0.282
Lymphocyte/neutrophil ratio	0.35±0.35	0.36±0.35	0.36±0.27	0.624
SGPT, units	46.9±72.6	43.0±50.1	38.5±29.2	<0.001
SGOT, units	50.8±143.5	43.6±59.02	38.3±26.9	<0.001
Sodium, mEq/L	135.1±15.3	136.4±10.9	136.6±11.1	0.002
	0.96±0.57	0.90±0.51	0.90±0.32	<0.001

Creatinine, mg/dl				
Clinical Outcomes				
Oxygen requirement	308[21.6]	257[16.7]	284[17.0]	<0.001
Non-invasive ventilation	114[8.0]	91[5.9]	118[7.1]	0.582
Invasive ventilation	66[4.6]	54[3.5]	51[3.1]	<0.001
In-hospital outcomes				
Recovered	1247[87.6]	1400[91.0]	1526[91.5]	<0.001
Referred	34[2.4]	34[2.3]	49[2.9]	0.582
Deaths	143[10.0]	104[6.8]	92[5.5]	<0.001

Numbers ± indicate 1 SD; Numbers in parentheses are percent;

Odds ratios and 95% CI calculated for categorical variables; Mean difference and 95% CI calculated for numerical variables; 95% CI 95% confidence intervals; BP blood pressure; SpO_2 saturation of peripheral oxygen; SGOT serum glutamic oxalate transferase; SGPT serum glutamic pyruvate transferase;

* p<0.05, ** p<0.01, *** p<0.001

Table 3: Odds ratios (categorical variables) or mean difference (continuous variables) and 95% confidence intervals among Group 1 and 2 patients compared with Group 3 (college education). Univariate logistic regression used for categorical variables and unpaired t-test for continuous variables.

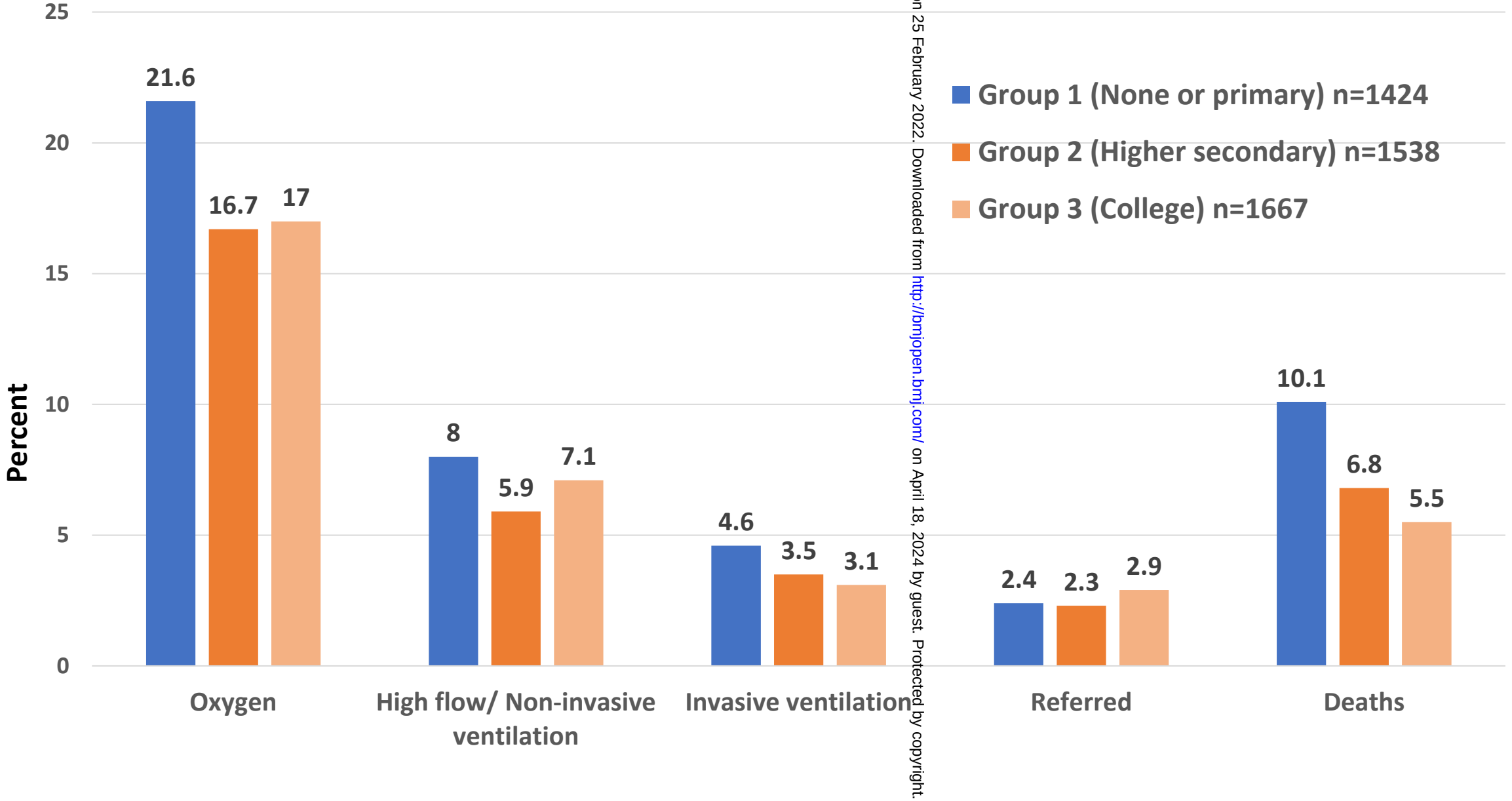
Variables	Odds Ratio/ Mean Difference (95% CI) Group 2vs3	p-Value	Odds Ratio/ Mean Difference (95% CI) Group 1vs3	p-Value
Age groups				
<30y	1.39[1.18-1.64]	0.0001	1.25[1.05-1.47]	0.0083
30-49	0.97[0.83-1.12]	0.6229	0.93[0.80-1.09]	0.3980
50-69	0.81[0.70-0.94]	0.0065	0.94[0.81-1.08]	0.4211
70+	0.85[0.67-1.06]	0.5178	0.87[0.69-1.11]	0.2729
Age mean (yr)	1.84 (0.69-2.99)	0.0001	-5.92 (-7.10--4.69)	0.0423
Men	0.54[0.46-0.64]	<0.0001	0.54[0.45-0.64]	<0.0001
Women	1.83[1.56-2.15]	<0.0001	1.85{1.57-2.18]	<0.0001
Members/house				
1-4	0.87[0.75-0.99]	0.0416	0.86[0.75-0.99]	0.0402
5-9	1.00[0.87-1.16]	0.9089	1.07[0.93-1.23]	0.3704
≥10	1.85[1.37-2.51]	0.0001	1.52[1.10-2.08]	0.0127
Tobacco or smoking	1.58[1.35-1.85]	<0.0001	1.79[1.52-2.09]	<0.0001
Medical co-morbidities	0.78[0.67-0.91]	0.0012	0.81[0.69-0.95]	0.0077
Hypertension	0.59[0.49-0.71]	<0.0001	0.75[0.63-0.90]	0.0018
Pulmonary disease	0.71[0.50-0.99]	0.0344	0.56[0.39-0.82]	0.0026
Type 2 Diabetes	0.73[0.61-0.88]	0.0010	0.75[0.62-0.91]	0.0029
Thyroid disease	2.02[0.80-5.08]	0.1403	3.04[1.26-07.29]	0.0055
Coronary heart disease	0.59[0.34-1.03]	0.0535	0.58[0.33-1.03]	0.0597
Clinical findings				
Systolic BP mmHg (mean±SD)	1.21[0.37-2.03]	0.0048	0.51[-0.38-1.38]	0.2674
Respiratory rate (mean±SD)	0.20[-0.05-0.45]	0.1278	0.00[-0.26-0.27]	1.0000
SpO2 <90%	1.07[0.85-1.34]	0.5781	1.23[0.98-1.55]	0.0768
SpO2 90-94%	1.11[0.92-1.33]	0.2579	1.22[1.02-1.45]	0.0290
Investigations (mean±SD)				
Haemoglobin, g/dl	0.10[-0.05-0.26]	0.2185	-0.1[-0.25-0.05]	0.2079
White cells, 10^9 cells/L	-192[-455-71]	0.1528	-140[-414-134]	0.3163
Lymphocyte, 10^9 cells/L	70[-23-163]	0.1433	57[-41-155]	0.2566
Lymphocyte/neutrophil ratio	0.00[-0.02-0.02]	1.000	0.01[-0.01-0.03]	0.3705
SGPT, units	-4.5[-7.3--1.7]	0.0017	-8.4[-12.2--4.6]	<0.0001
SGOT, units	-5.3[-8.4--2.2]	0.0009	-12.5[-19.5--5.5]	<0.0001
Sodium, mEq/L	0.29[-0.47-1.05]	0.7193	1.61[0.67-2.53]	0.0017
Creatinine, mg/dl	0.00[-0.02-0.02]	1.000	-0.06[-0.09--0.02]	0.0002

Clinical Outcomes				
Oxygen requirement	0.97[0.81-1.17]	0.8207	1.34[1.12-1.61]	0.0012
Non-invasive ventilation	0.82[0.62-1.09]	0.1694	1.14[0.87-1.49]	0.3442
Invasive ventilation	1.15[0.78-1.70]	0.5261	1.54[1.06-2.23]	0.0295
In-hospital outcomes				
Recovered	0.94[0.73-1.19]	0.6166	0.65[0.51-0.82]	0.0004
Referred	0.75[0.47-1.16]	0.2874	0.81[0.52-1.26]	0.3901
Deaths	1.24[0.93-1.66]	0.1252	1.91[1.46-2.51]	<0.0001

Numbers ± indicate 1 SD; Numbers in parentheses are percent; Mean difference and 95% CI calculated for numerical variables and odds ratios and 95% CI for categorical variables. 95% CI 95% confidence intervals; BP blood pressure; SGOT serum glutamic oxalate transaminase; SGPT serum glutamic pyruvate transaminase;

Table 4: Stepwise multivariate logistic regression analyses and odds ratio (95% confidence intervals) for adverse outcomes in educational status Group 1 (< primary education) and Group 2 (>primary to higher secondary education) compared to Group 3 (some college)

	Educational status groups (Reference 3)	Unadjusted Odds Ratios	Age and Sex adjusted	Plus household size	Plus risk factors, comorbidities	Plus clinical factors, investigations	Plus oxygenation
Deaths	Group 1	1.91(1.46-2.51)	1.33[0.99-1.83]	1.37[1.01-1.83]	1.44[1.07-1.93]	1.39[0.99-1.93]	1.38[0.99-1.93]
	Group 2	1.24(0.93-1.66)	1.31[0.91-1.82]	1.32[0.98-1.78]	1.38[1.02-1.85]	1.53[1.10-2.11]	1.52[10.1-2.11]
Invasive ventilation	Group 1	1.54(1.06-2.23)	1.19[0.80-1.81]	1.21[0.81-1.79]	1.29[0.86-1.92]	1.34[0.86-2.11]	1.39[0.88-2.19]
	Group 2	1.15(0.78-1.70)	1.06[0.71-1.59]	1.07[0.71-1.60]	1.11[0.74-1.67]	1.31[0.84-2.04]	1.33[0.85-2.07]
Non-invasive ventilation	Group 1	1.14(0.87-1.49)	0.95[0.71-1.32]	0.96[0.72-1.27]	1.03[0.77-1.36]	0.79[0.56-1.12]	0.78[0.54-1.13]
	Group 2	0.82(0.62-1.09)	1.01[0.76-1.33]	1.00[0.76-1.33]	1.02[0.77-1.35]	0.88[0.63-1.22]	0.91[0.64-1.29]
Data are in odds ratios and 95% confidence intervals; OR odds ratios;							



Educational Status and COVID-19 Related Outcomes in India: Hospital Based Cross Sectional Study

Supplementary Data

Supplementary Table 1: Demographic and clinical characteristics of men and women in the study cohort

Variables	Men (n=3386)	Women (N=1259)	P value
Age (mean, yr)	45.5±17.8	47.1±18.5	0.226
Age groups			
<30	838[24.7]	287[22.8]	0.008
30-49	1052[31.1]	345[27.4]	
50-69	1161[34.3]	489[38.8]	
70+	335[9.9]	138[11.0]	
Family members/house			
1-4	656[51.7]	1739[51.1]	0.834
5-9	535[42.1]	1465[43.0]	
≥10	79[6.2]	202[5.9]	
Educational status *			
Illiterate or Primary	980[28.8]	444[35.0]	<0.001
Secondary school/ Higher secondary	1061[31.2]	477[35.0]	
Graduate	1339[39.3]	328[25.8]	
Tobacco or smoking (ever)	1045[30.9]	324[25.7]	0.001
Medical co-morbidities	1020[29.9]	315[24.8]	0.001
Hypertension	658[19.3]	173[13.6]	<0.001
Pulmonary disease	135[4.0]	58[4.6]	0.364
Type 2 Diabetes	666[19.6]	111[8.7]	<0.001
Thyroid disease	27[0.8]	11[0.9]	0.855
Heart disease	51[1.5]	24[1.9]	0.360
Neurological disease	6[0.2]	9[0.7]	0.008
Current or past tuberculosis	78[2.3]	28[2.3]	0.874
Other	55[1.6]	57[4.5]	<0.001
Clinical findings			
Pulse rate /min	83.91±11.2	84.1±11.8	0.715
Systolic BP mmHg	125.12±11.9	126.0±12.9	0.028
Diastolic BP mmHg	82.71±7.9	83.1±8.4	0.155
Respiratory rate/min	19.0±3.7	19.1±3.9	0.313
SpO_2 at admission			
≥95%	1554[70.5]	590[68.7]	0.601
90-94%	397[18.0]	164[19.1]	
<90%	252[11.4]	105[12.2]	
Laboratory Investigations (Biochemistry n=867; Hematology n=4456)			
Creatinine, mg/dl	0.94±0.47	0.97±0.56	0.378
SGOT, IU	45.0±108.9	44.8±44.5	0.531
SGPT, IU	42.7±59.7	45.6± 44.2	0.096
Sodium, mEq/L	136.6±9.4	134.8±17.8	0.144
Potassium, mEq/L	5.1±8.9	5.9±12.6	0.112
Hb (gm/dl)	12.7±2.3	12.6±2.2	0.411
White cells (10^9 cells/L)	7585±3894	7370±3651	0.099
Lymphocytes (10^9 cells/L)	1607±1355	1534±1225	0.089
Lymphocyte/Neutrophil ratio	0.36±0.27	0.35±0.46	0.346
Outcome measures			
Mean duration of hospital stay[days]	6.9±3.8	6.5±3.6	0.004
Oxygen requirement	600[17.6]	261[20.6]	0.022

High flow O_2/non-invasive ventilation	236[6.9]	98[7.7]	0.371
Mechanical ventilation	123[3.6]	46[3.6]	1.000
Recovered	3020[88.7]	1197[94.3]	<0.001
Referred	104[3.0]	15[1.2]	<0.001
Deaths	282[8.3]	58[4.6]	<0.001

Numbers ± indicate 1 SD; Numbers in parentheses are percent; BP blood pressure; SpO_2 saturation of peripheral oxygen; SGOT serum glutamic oxalate transferase; SGPT serum glutamic pyruvate transferase

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4	
Objectives	3	State specific objectives, including any prespecified hypotheses	4,5	
Methods				
Study design	4	Present key elements of study design early in the paper	**5**	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	**5**	
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	**5,6**	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	**5,6**	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	**5,6**	
Bias	9	Describe any efforts to address potential sources of bias	--	
Study size	10	Explain how the study size was arrived at	**6**	Consecutive patients enrolled

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	**6**	Categorical and continuous variables
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6	
		(*b*) Describe any methods used to examine subgroups and interactions	6	
		(*c*) Explain how missing data were addressed	6	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy		
		(*e*) Describe any sensitivity analyses		Nil
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed		**6,7**
		(b) Give reasons for non-participation at each stage		**6,7**
		(c) Consider use of a flow diagram		Nil
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders		**7, Tables 1,2,3**
		(b) Indicate number of participants with missing data for each variable of interest		**7, Tables 1,2,3**
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)		
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time		
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures		**7,8, Tables 1,2,3,4**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included		**Tables 2,3,4**
		(*b*) Report category boundaries when continuous variables were categorized		**Tables 3,4**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		**Table 3**

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	**Table 4**
Discussion			
Key results	18	Summarise key results with reference to study objectives	**8**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	**10**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	**3,10,11**
Generalisability	21	Discuss the generalisability (external validity) of the study results	**3,10**
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	**11**

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Educational Status and COVID-19 Related Outcomes in India: Hospital Based Cross Sectional Study

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ABSTRACT

Objective: Association of educational status, as marker of socioeconomic status, with COVID-19 outcomes has not been well studied. We performed a hospital based cross-sectional study to determine its association with outcomes.

Methods: Successive patients of COVID-19 presenting at government hospital were recruited. Demographic and clinical details were obtained at admission and in-hospital outcomes assessed. Cohort was classified according to self-reported educational status into Group 1: illiterate or ≤primary, Group 2: higher secondary, and Group 3: some college. To compare intergroup outcomes, we performed logistic regression.

Results: 4645 patients (men 3386, women 1259) with confirmed COVID-19 were recruited. Mean age was 46±18y, most lived in large households and 30.5% had low educational status. Smoking or tobacco use was in 29.5%, co-morbidities in 28.6% and low oxygen concentration (SpO_2<95%) at admission in 30%. Average length of hospital stay was 6.8±3.7 days, supplemental oxygen was provided in 18.4%, high flow oxygen or non-invasive ventilation 7.1%, and mechanical ventilation 3.6%, 340 patients (7.3%) died. Group 1 patients had more tobacco use, hypoxia at admission, lymphocytopenia and liver and kidney dysfunction. In Group 1 vs Groups 2 and 3 requirement of oxygen (21.6vs16.7 and 17.0%), non-invasive ventilation (8.0vs5.9 and 7.1%), invasive ventilation (4.6vs3.5 and 3.1%) and deaths (10.0vs6.8 and 5.5%) were significantly greater (p<0.05). Odds ratio for deaths were higher in Group 1(1.91,1.46-2.51) and Group 2(1.24,0.93-1.66) compared to Group 3. Adjustment for demographic and comorbidities led to some attenuation in Groups 1(1.44,1.07-1.93) and 2(1.38,1.02-1.85), this persisted with adjustments for clinical parameters and oxygen support in Groups 1(1.38,0.99-1.93) and 2(1.52,1.01-2.11).

Conclusion: Low educational status patients with COVID-19 in India have significantly greater adverse in-hospital outcomes and mortality.

KEYWORDS: SARS-CoV-2; Epidemiology; Registry; Risk factors; Socioeconomic status; Social determinants;

Strengths and limitations:

- Studies in high-income countries have reported that low socioeconomic status is a risk factor for adverse outcomes in COVID-19. Similar studies are not available in lower-middle and low-income countries.
- This study shows that low educational status patients with COVID-19 in India have significantly higher in-hospital mortality compared to the better educated.
- Low educational status patients have more severe disease at presentation with greater requirement of oxygen and ventilation.
- Important limitations are lack of area-based measures, neighborhood details, biochemical and inflammatory markers of severity of illness, and absence of long-term follow-up.

INTRODUCTION

COVID-19 pandemic continues to devastate human lives and livelihoods, especially in low and lower-middle income countries.[1] After the initial spread to the high-income countries in Europe and North America, the epidemic is now rapidly escalating in middle-income and low-income countries of South America, South Asia, South East Asia and Africa.[2] Epidemiological studies from China, Europe, UK and USA have shown greater disease burden in socioeconomically deprived neighborhoods and minority ethnic groups.[3] A review that included more than 18.7 million patients from 50 studies in UK and USA reported that individuals from Black and Asian ethnicities had 1.5-2.0 time greater risk of COVID-19 infection compared to White individuals and individuals of Asian ethnicity were at greater risk for intensive-care unit admission and death.[4] Multiple reasons have been postulated for these socioeconomic disparities and include factors such as poverty, racism and other structural factors, lower availability, access, affordability and utilization of healthcare and low value care.[5,6] Greater load of infection and longer exposure to the virus due to crowded environments, limited housing, large household sizes, low quality jobs, unsafe commute and undernutrition are also important.[6,7]

Educational status is an important marker of socioeconomic status and hundreds of studies in fields of communicable and non-communicable diseases have reported association of low educational status with adverse health-related events.[8,9,10] It is also an independent risk factor for morbidity and mortality from infectious diseases .[8,11] Association of socioeconomic status with COVID-19 related outcomes has not been well studied. A rapid review identified 42 studies that evaluated social determinants of COVID-19 incidence, clinical presentation, health service use and outcomes,[3] and reported significant associations of race, ethnicity and social deprivation with increased COVID-19 incidence and hospitalization. The review also reported that there was limited evidence regarding other key determinants including occupation, education, housing status and food security and suggested larger epidemiological studies to obtain high-quality evidence. A number of more recent studies have highlighted importance of socioeconomic inequalities in COVID-19 related morbidity and mortality,[12,13,14] and a review that included 34 studies has reported substantial racial, ethnic and socioeconomic variation in incidence of COVID-19 in USA with greater incidence among poorer communities.[15]

India has one of the largest burdens of COVID-19 cases and deaths.[16] A macrolevel study reported that Indian states with greater human development index and other socioeconomic indices had higher per capita COVID-19 incidence and deaths.[17] Although anecdotal evidence and modelling data exist,[1,18] there are no significant data on association of individual level socioeconomic status with disease incidence and outcomes. Therefore, to examine association of self-reported educational

status,[9,10] as a marker of socioeconomic status, in confirmed COVID-19 cases successively admitted to a dedicated COVID-19 government hospital in India, we performed a prospective registry-based study.

METHODS

We conducted a hospital based prospective observational study on patients with laboratory confirmed COVID-19 admitted to a 1200-bed dedicated COVID-19 government hospital (Rajasthan University of Health Sciences Hospital, Jaipur) from April to mid-September 2020. Initial data on patients have been reported earlier.[19,20] The registry has been approved by the college administration and institutional ethics committee (CDSCO Registration Number: CR/762/Inst/RJ/2015). Individual patient consent was waivered by the ethics committee and anonymized data have been used with no patient identifiers. It is registered with Clinical Trials Registry of India at www.ctri.nic.in with registration number REF/2020/06/ 034036.

Patient data: Successive patients aged 18 years or more, presenting to the hospital for admission with suspicion of COVID-19 infection were enrolled in the study. Only those who tested positive for COVID-19 on nasopharyngeal and oropharyngeal reverse transcriptase polymerase chain reaction (RT-PCR) test have been included. All RT-PCR positive patients admitted from 1 April to 15 September have been included. Patients recruited into the study in mid-September were followed up to discharge or death and outcome events were recorded.

A questionnaire was developed and details of sociodemographic, clinical, laboratory, treatments and outcomes variables were recorded using patients' history and medical records.[19] Demographic details were obtained at the time of admission. These included name, age, sex, residence address and educational status. Status of highest educational level achieved was self-reported similar to most of the previous studies.[9,10] Other sociodemographic variables were not available for majority of patients and are not reported. Although it is possible to obtain individual details from unique identification number (Aadhaar number) or other identifiers of all the COVID-19 cases we did not use these data. All the COVID-19 RT-PCR reports along with the government identifier are uploaded on the official website of Indian Council of Medical Research at www.icmr.gov.in. Details of physical examination at the time of admission were obtained from patient case files. These included history of duration of symptoms at admission, pulse, blood pressure (BP), respiratory rate, and surface oxygen concentration (SpO2. Details of investigations at admission were obtained from the case files and biochemistry, microbiology and pathology departments as reported earlier.[20] We do not have data on serial investigations. We obtained data on duration of hospital stay from medical record department. For patients discharged alive from

the hospital, we obtained data on patients who required oxygen support (nasal prongs, facial mask or high-flow nasal cannula), non-invasive ventilation (CPaP or BiPaP support) or invasive ventilation after endotracheal intubation. Binary outcomes were obtained for all patients and included either recovery, referral to non-government hospitals on request of family, or death. All these data have also been sent to the Department of Health, Government of Rajasthan, India, but are not currently accessible.

Patient and public involvement: Patients and the public were not involved in the design, or conduct, or reporting of this research. The preprint (*medRxiv preprints.* https://doi.org/10.1101/2021.05.17.21257364) has been shared with the administrative authorities of Government of Rajasthan.

Statistical analyses: The data were computerized and data processing was performed using commercially available statistical software, SPSS v.20.0. Educational status was self-reported and patients were classified into three groups: Group 1: illiterate or ≤ primary education, Group 2: > primary to higher-secondary school education, and Group 3: any graduate or post graduate college education. Numerical data are expressed as mean±1 standard deviation (SD) and categorical data as percent. Significance of intergroup differences were calculated using either χ^2 test or ANOVA as appropriate. χ^2 test residuals were determined for categorical variables in various groups and significant were age, sex, household size and some clinical parameters. Tests of normality for continuous variables was performed in the statistical program and all followed a normal Gaussian distribution. The variables where significant residuals identified were adjusted using logistic regression. We also compared mean and proportionate differences in Groups 1 and 2 as compared to Group 3 using unpaired t-test or χ^2 test as appropriate. To evaluate association of educational status with clinical outcomes we performed stepwise logistic regression. Univariate and multivariate odds ratios (OR) and 95% confidence intervals (95% CI) were calculated for Group 1 and Group 2 compared to Group 3 for outcomes of in-hospital death, invasive ventilation and non-invasive ventilation. We initially calculated the univariate ORs and subsequently performed a stepwise logistic regression with sequential adjustment with (i) age and sex, (ii) household size, (iii) cardiovascular risk factors and comorbidities, (iv) clinical features and investigations at presentation and finally with (v) oxygenation during hospital stay, and determined multivariate ORs. P value of <0.05 is considered significant.

RESULTS

Patients were enrolled from March 2020 to mid-September 2020. A total of 7349 patients were hospitalized with confirmed or suspected COVID-19 during this period, 5103 patients (69.0%) tested

positive for the disease on RT-PCR test and for the present study 4645 individuals (91.0% of confirmed cases), men 3386 (72.9%) and women 1259 (27.1%), in whom detailed clinical data were available have been included (Table 1). The mean age of the cohort was 45.9±18 years, 54% were less than 50 years and about half lived in large family households. Prevalence of low educational status was high and greater in women while tobacco use was more in men (Supplementary File). Comorbidities were present in 28.6% with hypertension and diabetes being the most common. Details of symptoms, laboratory investigations and clinical status at admission is shown in Table 1. Data on hematological investigations were available in 4456 (95.9%) and for biochemical tests in 867 (18.7%) patients. All patients received standard treatment according to guidelines available from Indian Council of Medical Research and the state government.[21] Management included oral or intravenous hydration, paracetamol and oral or intravenous antibiotics if required. A number of patients also received hydroxychloroquine, ivermectin, azithromycin, doxycycline, lopinavir-ritonavir, favipiravir, etc. The average length of stay in hospital was 6.8±3.7 days, and was significantly greater in men (6.9±3.8 days) than in women (6.5±3.6 days) (p= 0.004). Oxygen requirement was significantly greater in women but other outcomes such as requirement of high flow oxygen, non-invasive or invasive ventilation were not significantly different (Supplementary Table 1). Number of in-hospital deaths were significantly greater in men (n=282, 8.3%) as compared to women (n=58, 4.6%) (p<0.001).

The cohort was divided into the three groups based on educational status. Important demographic and clinical characteristics and in-hospital outcomes are shown in Table 2. Low educational status (Group 1 and 2) was more common in women while more men had college education. Family size was larger among the less literate group. Tobacco use and smoking was also greater in Group 1. Prevalence of co-morbidities, especially hypertension and diabetes, was significantly greater among the more literate, similar to previous studies in India.[22] No significant differences were observed in complaints or clinical findings (data not shown). Data on duration of illness prior to admission were not available. Low SpO_2 (<90% as well as <95%), lymphopenia, higher transaminases and higher creatinine values at admission were observed among the less literate. The length of hospital stay was not significantly different in the three groups.

Univariate ORs (categorical variables) and mean differences (continuous variables) in less literate Groups 1 and 2 compared to the more literate Group 3 are shown in Table 3. Patients in less literate groups were younger, more women and lived in larger households (>10 persons/house). Presence of tobacco use was greater while cardiovascular risk factors were lower. Various clinical outcomes are shown in Figure 1 and compared to Group 3, in Group 1 there was greater oxygen

requirement (unadjusted OR 1.34, 95% CI 1.12-1.61), non-invasive ventilation (1.14, 0.87-1.49) and invasive ventilation (1.54, 1.06-2.23) (Table 3). Compared to Group 3 (deaths n=92, 5.5%), deaths were significantly greater in Group 1 (n=143, 10.0%, unadjusted OR 1.91, CI 1.46-1,51) as well as in Group 2 (n=104, 6.8%, unadjusted OR 1.24, CI 0.93-1.66) (p<0.001).

We performed a stepwise logistic regression analysis to identify influence of various sociodemographic, risk factor, clinical and treatment variables on outcomes. Compared to the most literate Group 3, unadjusted OR for deaths were higher in less literate Groups 1 and 2 (Table 4). Following adjustments for age, sex, household size, risk factors and comorbidities the ORs attenuated but remained significant in both Group 1 (1.44, 1.07-1.93) and Group 2 (1.38, 1.02-1.85). However, after addition of clinical features at admission and laboratory investigations the risks attenuated to marginally significant in Group 1 (1.39, 0.99-1.93) and significant in Group 2 (1.53, 1.10-2.11) and remain the same after further adjustments for oxygenation (Table 3). OR for other outcomes assessed in the cohort (need for invasive ventilation and non-invasive ventilation) are shown in Table 4 and demonstrate a marginal significance.

DISCUSSION

This study shows that illiterate and less literate COVID-19 patients have significantly greater in-hospital mortality compared to the better educated. The higher risk of death among the less literate persists after adjustment for various sociodemographic factors (age, sex, household size), lifestyle factors and comorbidities but attenuates after adjustment for clinical features at presentation, investigations and oxygen treatment. This suggests that more adverse features at presentation (hypoxia, deranged liver and kidney functions) could be responsible for higher deaths among the less educated COVID-19 patients in India.

Clinical and epidemiological studies from most developed countries in Europe and North America have consistently reported higher communicable disease-related mortality among the less literate and lower socioeconomic individuals.[11] In the COVID-19 pandemic, studies from most developed countries have reported greater COVID-19 related mortality and adverse outcomes among the ethnic minorities.[3,4,5] However, association of mortality among low socioeconomic or less educational status individuals are inconclusive.[3,4,12,13,14] In England, OpenSAFELY platform evaluated ethnic differences in COVID-19 related hospitalization, intensive care unit admission and death in 17 million adults from the National Health Service.[23] As compared to the British White patients, deaths were higher in South Asians in the first wave (OR 1.08, CI 1.07-1.09), and the second wave of COVID-19 epidemic (OR 1.87, CI 1.68-

2.07) as well as in the overall cohort (OR 1.26, CI 1.15-1.37). Deaths were the highest in the most deprived groups.[23] A study from Brazil reported that those with low education attainment were more likely to die from COVID-19 (OR 1.13, CI 1.07-1.19).[24] Increased deaths among the poor and low educational status patients has also been reported in recent studies from USA,[25] South Korea,[26] and African countries.[27] An epidemiological study in Santiago, Chile report a strong association between socioeconomic status and mortality, measured either by COVID-19 attributed deaths or excess deaths with greater case-fatality rates in the young COVID-19 patients in deprived localities.[28] A large meta-analysis, that combined population and hospital based data in the US, involving 4.3 million patients from 68 studies reported that disease incidence was more in African-American and Hispanic-American individuals, risk of hospitalization greater in Asian Americans. Mortality rates in Hispanics and Asian Americans correlated positively with residence in more deprived locations.[29] In this study influence of individual level socioeconomic factors was not reported. Our study is one of the first reports from India that has evaluated socioeconomic difference in COVID-19 related mortality and shows a 1.4 to 1.9-fold greater mortality among low educational status men and women and is similar to the recent international studies. Our study also shows that greater mortality among low educational status individuals could be due to delayed presentation and more severe disease (lower oxygen, greater impaired liver and renal functions) and greater need of oxygen and non-invasive and invasive ventilation in these patients (Table 2). We did not obtain exact information regarding use of various non-evidence based empirical therapies (hydroxychloroquine, ivermectin, lopinavir-ritonavir, favipiravir, etc)[30] or proven evidence-based therapies such as corticosteroids, remdesivir and tocilizumab,[31] and this is a study limitation.

A variety of approaches to conceptualization and measurement of socioeconomic status have been used. Four measures are consistently associated with greater risk: low education, low income, lower employment status, and neighborhood socioeconomic factors.[32] Use of self-reported educational status as marker of level of highest education achieved is similar to previous studies.[8,9,10] Low education or socioeconomic status is well known as a leading modifiable risk factor for overall as well as infectious disease mortality and is an important social determinant of health.[33] Our previous studies in India and other low and lower middle income countries have reported strong correlation of self-reported educational status with measures of income, household wealth, occupation, etc.[34,35] There are multiple social, clinical and system level contributors that lead to greater disease risk among the poor and include structural barriers to good health, particularly among the less literate and poor, increased risk of exposure (unhygienic working conditions and crowded housing), unequal access to testing and high-

quality care, higher rates of associated medical conditions and less access to vaccination.[7,36] In the present study we observed some of these barriers among our patients (crowded housing , greater tobacco use, and delayed presentation with more severe disease). COVID-19 in India could act as a catalyst to improve overall healthcare systems with opportunities for policymakers, advocacy groups and researchers for evaluation of various interventions.[37] It is hoped that COVID-19 would lead to global focus on creation of health equity by influencing coaxing politicians towards the right direction.[38]

The study has strengths as well as limitations. This is the largest case-series from India, we used data from a government hospital which is more representative of general population, there are substantial number of less literate patients reflecting local educational status. This has led to data granularity and robust evaluation of outcomes. We used self-reported educational status to determine the highest level of literacy achieved and this is a study limitation, however, most of the previous studies have used similar methods.[8,9,10] Other limitations include lack of other sociodemographic factors (housing, neighborhoods, occupation, income, working conditions, etc.), clinical parameters (detailed history, pulmonary findings, radiological evaluation, chest computerized tomographic scans, and blood biomarkers- C-reactive protein, interleukins, d-Dimer, ferritin, lactic dehydrogenase, etc.), and type of therapy the patients received. We also did not evaluate cardiovascular biomarkers (troponins and n-terminal pro-brain natriuretic peptide) that are important in prognostication.[29] These are due to lack of guidelines regarding routine measurement of many of these variables,[21] and low healthcare funding in the country.[1] There could be multiple causes of deaths in COVID-19 (acute respiratory distress syndrome, myocardial infarction, acute heart failure, pulmonary embolism, secondary chest infection, sepsis, acute renal failure, etc.)[29] and we did not have data on specific causes of death. About 2.5% persons were transferred from our hospital to other centres and although we have obtained information on death in these patients using telephonic interview with families, details of specific outcomes are not available. And finally, data from a single hospital with about 4500 patients and 340 deaths may not be applicable to the whole country which has one of the largest burden of COVID-19 in the world.[16] In view of the massive second wave of COVID-19 in India,[39] we should strive for larger multicentric studies for identifying reasons for greater mortality among the low socioeconomic status patients with this disease in the country.

In conclusion, our study shows a significantly greater mortality from COVID-19 in less educated (lower socioeconomic status) individuals in India. Khalatbari-Soltani et al have suggested that low educational status is associated with increased prevalence of smoking and poor nutrition leading to more severe disease, prevalence of comorbidities is high in these individuals and low health literacy

results in increased disease incidence and severity due to poor understanding pf public health preventive measures and delayed healthcare seeking behaviours.[40] Our study shows that the less educated COVID-19 patients have more severe disease at presentation to hospital with need for greater oxygen and ventilatory support. Strategies to increase early diagnosis and access to care for these patients are important and should include public health measures for early detection of disease and early referral to treatment centres for appropriate therapeutic measures.

Data availability statement: All the data obtained from patients have been reported in the enclosed article. No additional data available.

Ethics statements:

Patient consent for publication: Individual patient consent was waivered by the ethics committee and anonymized data have been used with no patient identifiers. Patients and/or the public were not involved in the design, or conduct, or reporting of this research.

Ethics approval: Ethics clearance for the study proposal was obtained from the Institutional Ethics Committee at RUHS College of Medical Sciences, Rajasthan University of Health Sciences, Jaipur, India. CDSCO Registration Number: CR/762/Inst/RJ/2015.

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Contributors

- AKS, RG, VNB, TVS, SC, JPS and SPS had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
- AKS, RG, VNB, RBP and VMK contributed to the plan and design of the study.
- AKS and VNB developed the study protocol and case-report forms.
- AKS, VNB, TVS, SC, JPS, PD and SPS led the data collection.
- AKS and RG performed the data analyses and participated in interpretation of the results.
- RG and AKS drafted the manuscript.
- AKS, RG, RBP and VMK contributed to the critical revision of the manuscript for important intellectual content.
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LEGEND TO FIGURES

Figure 1: Clinical outcomes in various educational status groups

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Table 1: Clinical characteristics of the study cohort at admission to hospital and outcomes

Variables	Total [N=4645]
Men	3386[72.9]
Women	1259[27.1]
Age (mean, years)	45.9±18.0
Age groups	
<30	1125[24.2]
30-49	1397[30.1]
50-69	1650[35.5]
70+	473[10.2]
Family members/house	
1-4	2395[51.2]
5-9	2000[42.8]
≥10	281[6.0]
Educational status	
Illiterate or up to primary education	1424[30.5]
Secondary school and/or higher secondary education	1538[32.9]
Some college	1667[35.7]
Tobacco or smoking (ever)	1369[29.5]
Medical co-morbidities	1335[28.6]
Hypertension	831[17.8]
Pulmonary disease	193[4.1]
Type 2 Diabetes	777[16.6]
Thyroid disease	38[0.8]
Heart disease	75[1.6]
Neurological disease	15[0.3]
Current or past tuberculosis	106[2.3]
Duration of symptoms at admission (days)	
Clinical findings	
Pulse rate /min	83.9±11.4
Systolic BP mmHg	125.4±12.2
Diastolic BP mmHg	82.8±8.1
Respiratory rate/min	19.0±3.7
SpO_2 at admission	
≥95%	2144[70.0]
90-94%	561[18.3]
<90%	357[11.7]
Laboratory Investigations (Biochemistry n=867; Hematology n=4456)	
Creatinine, mg/dl	0.95±0.50
SGOT, IU	44.9±96.5
	43.4±56.2

SGPT, IU	136.1±12.5
Sodium, mEq/L	5.4±1.1
Potassium, mEq/L	12.7±2.3
Hb (gm/dl)	7527±3830
White cells (10^9 cells/L)	1589±1325
Lymphocytes (10^9 cells/L)	0.36±0.32
Lymphocyte/Neutrophil ratio	
Outcome measures	
Mean duration of hospital stay[days]	6.8±3.7
Oxygen requirement	861[18.4]
High flow O_2/non-invasive ventilation	334[7.1]
Mechanical ventilation	169[3.6]
Recovered	4217[90.2]
Referred	119[2.5]
Deaths	340[7.3]

Numbers ± indicate 1 SD; Numbers in parentheses are percent; BP blood pressure; SpO_2 saturation of peripheral oxygen; SGOT serum glutamic oxalate transferase; SGPT serum glutamic pyruvate transferase

Table 2: Clinical characteristics and outcomes according to educational status (Group 1= < primary education; Group 2= >primary to higher secondary education; Group 3= some college). χ^2 test used for categorical variables and ANOVA for continuous variables.

Variables	Group 1 (n=1424)	Group 2 (n=1538)	Group 3 (n=1667)	χ^2 test or ANOVA-F (p value)
Age groups				<0.001
<30y	353[25.0]	414[27.1]	348[21.0]	
30-49	416[29.4]	459[30.0]	510[30.8]	
50-69	509[36.0]	501[32.8]	620[37.4]	
70+	136[9.6]	154[10.1]	179[10.8]	
Age mean (yr)	45.8±17.9	44.6± 18.4	47.1± 17.6	<0.001
Men	980[29.0]	1061[31.4]	1339[39.6]	<0.001
Women	444[35.5]	477[38.2]	328[26.3]	
Members/house				<0.001
1-4	710[49.9]	769[50.0]	893[53.6]	
5-9	624[43.8]	652[42.4]	703[42.2]	
≥10	90[6.3]	117[7.6]	71[4.3]	
Tobacco or smoking	496[34.6]	485[31.5]	375[22.5]	<0.001
Medical co-morbidities	391[27.5]	411[26.7]	531[31.9]	0.002
Hypertension	248[17.4]	218[14.2]	365[21.9]	0.000
Pulmonary disease	44[3.1]	59[3.8]	89[5.3]	0.006
Type 2 Diabetes	220[15.4]	232[15.1]	325[19.5]	0.001
Thyroid disease	18[1.3]	13[0.8]	7[0.4]	0.034
Coronary heart disease	18[1.3]	20[1.3]	36[2.2]	0.074
Clinical findings at admission				
Systolic BP mmHg (mean±SD)	125.4±12.6	124.7±11.6	125.9±12.4	0.021
Respiratory rate (mean±SD)	19.1±3.7	18.9±3.5	19.1±3.9	0.225
SpO2 <90%	173[12.1]	165[10.7]	168[10.1]	0.765
SpO2 90-94%	273[19.2]	272[17.7]	270[16.2]	0.312
Investigations (mean±SD)				
Haemoglobin, g/dl	12.8±2.2	12.6±2.4	12.7±2.2	0.056
White cells, 10^9 cells/L	7559±3917	7611±3759	7419±3832	0.340
Lymphocyte, 10^9 cells/L	1574±1269	1561±1187	1631±1489	0.282
Lymphocyte/neutrophil ratio	0.35±0.35	0.36±0.35	0.36±0.27	0.624
SGPT, units	46.9±72.6	43.0±50.1	38.5±29.2	<0.001
SGOT, units	50.8±143.5	43.6±59.02	38.3±26.9	<0.001
Sodium, mEq/L	135.1±15.3	136.4±10.9	136.6±11.1	0.002
	0.96±0.57	0.90±0.51	0.90±0.32	<0.001

Creatinine, mg/dl				
Clinical Outcomes				
Oxygen requirement	308[21.6]	257[16.7]	284[17.0]	<0.001
Non-invasive ventilation	114[8.0]	91[5.9]	118[7.1]	0.582
Invasive ventilation	66[4.6]	54[3.5]	51[3.1]	<0.001
In-hospital outcomes				
Recovered	1247[87.6]	1400[91.0]	1526[91.5]	<0.001
Referred	34[2.4]	34[2.3]	49[2.9]	0.582
Deaths	143[10.0]	104[6.8]	92[5.5]	<0.001

Numbers ± indicate 1 SD; Numbers in parentheses are percent;

Odds ratios and 95% CI calculated for categorical variables; Mean difference and 95% CI calculated for numerical variables; 95% CI 95% confidence intervals; BP blood pressure; SpO_2 saturation of peripheral oxygen; SGOT serum glutamic oxalate transferase; SGPT serum glutamic pyruvate transferase;

* p<0.05, ** p<0.01, *** p<0.001

Table 3: Odds ratios (categorical variables) or mean difference (continuous variables) and 95% confidence intervals among Group 1 and 2 patients compared with Group 3 (college education). Univariate logistic regression used for categorical variables and unpaired t-test for continuous variables.

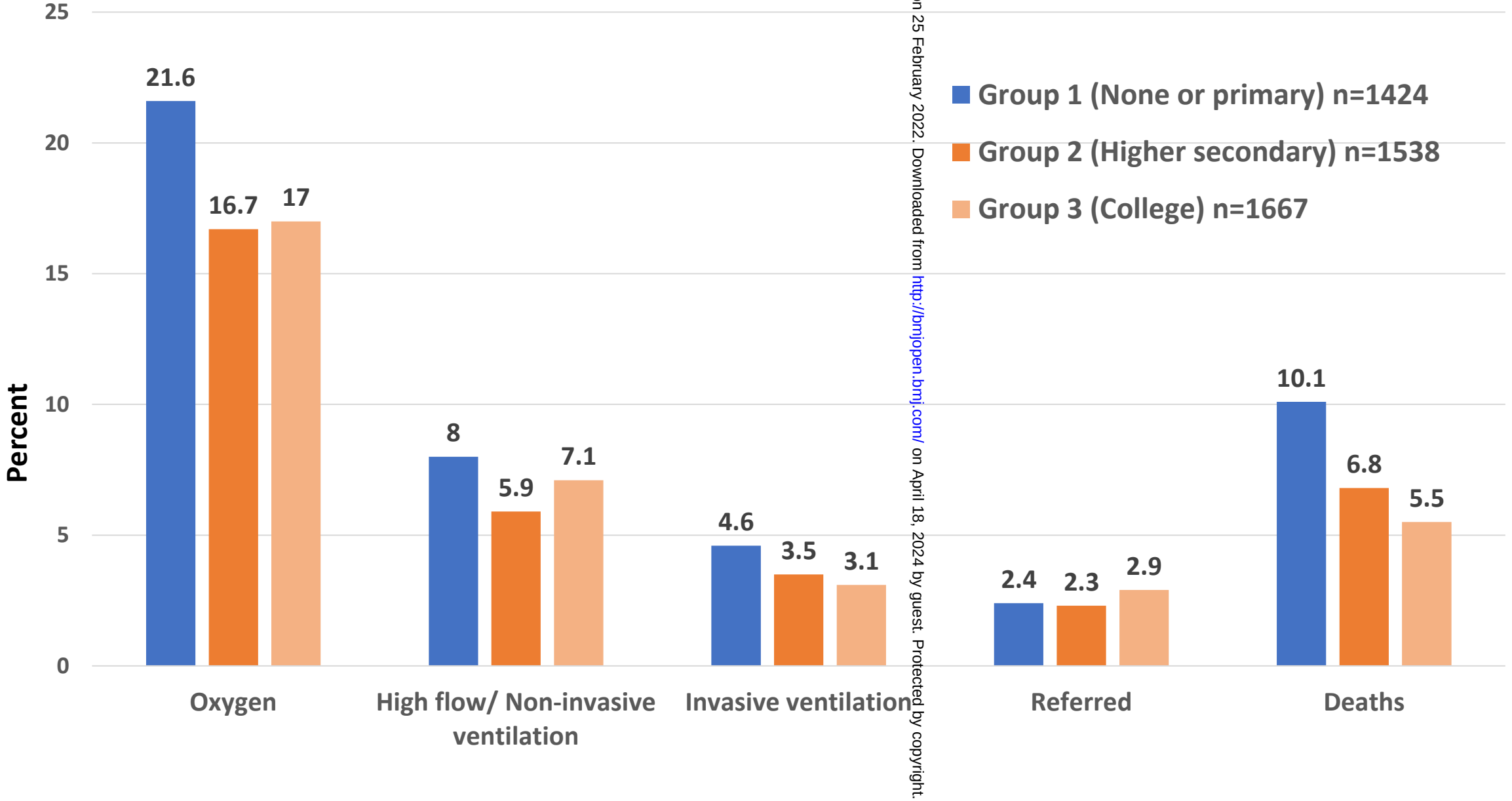
Variables	Odds Ratio/ Mean Difference (95% CI) Group 2vs3	p-Value	Odds Ratio/ Mean Difference (95% CI) Group 1vs3	p-Value
Age groups				
<30y	1.39[1.18-1.64]	0.0001	1.25[1.05-1.47]	0.0083
30-49	0.97[0.83-1.12]	0.6229	0.93[0.80-1.09]	0.3980
50-69	0.81[0.70-0.94]	0.0065	0.94[0.81-1.08]	0.4211
70+	0.85[0.67-1.06]	0.5178	0.87[0.69-1.11]	0.2729
Age mean (yr)	1.84 (0.69-2.99)	0.0001	-5.92 (-7.10--4.69)	0.0423
Men	0.54[0.46-0.64]	<0.0001	0.54[0.45-0.64]	<0.0001
Women	1.83[1.56-2.15]	<0.0001	1.85{1.57-2.18]	<0.0001
Members/house				
1-4	0.87[0.75-0.99]	0.0416	0.86[0.75-0.99]	0.0402
5-9	1.00[0.87-1.16]	0.9089	1.07[0.93-1.23]	0.3704
≥10	1.85[1.37-2.51]	0.0001	1.52[1.10-2.08]	0.0127
Tobacco or smoking	1.58[1.35-1.85]	<0.0001	1.79[1.52-2.09]	<0.0001
Medical co-morbidities	0.78[0.67-0.91]	0.0012	0.81[0.69-0.95]	0.0077
Hypertension	0.59[0.49-0.71]	<0.0001	0.75[0.63-0.90]	0.0018
Pulmonary disease	0.71[0.50-0.99]	0.0344	0.56[0.39-0.82]	0.0026
Type 2 Diabetes	0.73[0.61-0.88]	0.0010	0.75[0.62-0.91]	0.0029
Thyroid disease	2.02[0.80-5.08]	0.1403	3.04[1.26-07.29]	0.0055
Coronary heart disease	0.59[0.34-1.03]	0.0535	0.58[0.33-1.03]	0.0597
Clinical findings				
Systolic BP mmHg (mean±SD)	1.21[0.37-2.03]	0.0048	0.51[-0.38-1.38]	0.2674
Respiratory rate (mean±SD)	0.20[-0.05-0.45]	0.1278	0.00[-0.26-0.27]	1.0000
SpO2 <90%	1.07[0.85-1.34]	0.5781	1.23[0.98-1.55]	0.0768
SpO2 90-94%	1.11[0.92-1.33]	0.2579	1.22[1.02-1.45]	0.0290
Investigations (mean±SD)				
Haemoglobin, g/dl	0.10[-0.05-0.26]	0.2185	-0.1[-0.25-0.05]	0.2079
White cells, 10^9 cells/L	-192[-455-71]	0.1528	-140[-414-134]	0.3163
Lymphocyte, 10^9 cells/L	70[-23-163]	0.1433	57[-41-155]	0.2566
Lymphocyte/neutrophil ratio	0.00[-0.02-0.02]	1.000	0.01[-0.01-0.03]	0.3705
SGPT, units	-4.5[-7.3--1.7]	0.0017	-8.4[-12.2--4.6]	<0.0001
SGOT, units	-5.3[-8.4--2.2]	0.0009	-12.5[-19.5--5.5]	<0.0001
Sodium, mEq/L	0.29[-0.47-1.05]	0.7193	1.61[0.67-2.53]	0.0017
Creatinine, mg/dl	0.00[-0.02-0.02]	1.000	-0.06[-0.09--0.02]	0.0002

Clinical Outcomes				
Oxygen requirement	0.97[0.81-1.17]	0.8207	1.34[1.12-1.61]	0.0012
Non-invasive ventilation	0.82[0.62-1.09]	0.1694	1.14[0.87-1.49]	0.3442
Invasive ventilation	1.15[0.78-1.70]	0.5261	1.54[1.06-2.23]	0.0295
In-hospital outcomes				
Recovered	0.94[0.73-1.19]	0.6166	0.65[0.51-0.82]	0.0004
Referred	0.75[0.47-1.16]	0.2874	0.81[0.52-1.26]	0.3901
Deaths	1.24[0.93-1.66]	0.1252	1.91[1.46-2.51]	<0.0001

Numbers ± indicate 1 SD; Numbers in parentheses are percent; Mean difference and 95% CI calculated for numerical variables and odds ratios and 95% CI for categorical variables. 95% CI 95% confidence intervals; BP blood pressure; SGOT serum glutamic oxalate transaminase; SGPT serum glutamic pyruvate transaminase;

Table 4: Stepwise multivariate logistic regression analyses and odds ratio (95% confidence intervals) for adverse outcomes in educational status Group 1 (< primary education) and Group 2 (>primary to higher secondary education) compared to Group 3 (some college)

	Educational status groups (Reference 3)	Unadjusted Odds Ratios	Age and Sex adjusted	Plus household size	Plus risk factors, comorbidities	Plus clinical factors, investigations	Plus oxygenation
Deaths	Group 1	1.91(1.46-2.51)	1.33[0.99-1.83]	1.37[1.01-1.83]	1.44[1.07-1.93]	1.39[0.99-1.93]	1.38[0.99-1.93]
	Group 2	1.24(0.93-1.66)	1.31[0.91-1.82]	1.32[0.98-1.78]	1.38[1.02-1.85]	1.53[1.10-2.11]	1.52[10.1-2.11]
Invasive ventilation	Group 1	1.54(1.06-2.23)	1.19[0.80-1.81]	1.21[0.81-1.79]	1.29[0.86-1.92]	1.34[0.86-2.11]	1.39[0.88-2.19]
	Group 2	1.15(0.78-1.70)	1.06[0.71-1.59]	1.07[0.71-1.60]	1.11[0.74-1.67]	1.31[0.84-2.04]	1.33[0.85-2.07]
Non-invasive ventilation	Group 1	1.14(0.87-1.49)	0.95[0.71-1.32]	0.96[0.72-1.27]	1.03[0.77-1.36]	0.79[0.56-1.12]	0.78[0.54-1.13]
	Group 2	0.82(0.62-1.09)	1.01[0.76-1.33]	1.00[0.76-1.33]	1.02[0.77-1.35]	0.88[0.63-1.22]	0.91[0.64-1.29]
Data are in odds ratios and 95% confidence intervals; OR odds ratios;							



Educational Status and COVID-19 Related Outcomes in India: Hospital Based Cross Sectional Study

Supplementary Data

Supplementary Table 1: Demographic and clinical characteristics of men and women in the study cohort

Variables	Men (n=3386)	Women (N=1259)	P value
Age (mean, yr)	45.5±17.8	47.1±18.5	0.226
Age groups			
<30	838[24.7]	287[22.8]	0.008
30-49	1052[31.1]	345[27.4]	
50-69	1161[34.3]	489[38.8]	
70+	335[9.9]	138[11.0]	
Family members/house			
1-4	656[51.7]	1739[51.1]	0.834
5-9	535[42.1]	1465[43.0]	
≥10	79[6.2]	202[5.9]	
Educational status *			
Illiterate or Primary	980[28.8]	444[35.0]	<0.001
Secondary school/ Higher secondary	1061[31.2]	477[35.0]	
Graduate	1339[39.3]	328[25.8]	
Tobacco or smoking (ever)	1045[30.9]	324[25.7]	0.001
Medical co-morbidities	1020[29.9]	315[24.8]	0.001
Hypertension	658[19.3]	173[13.6]	<0.001
Pulmonary disease	135[4.0]	58[4.6]	0.364
Type 2 Diabetes	666[19.6]	111[8.7]	<0.001
Thyroid disease	27[0.8]	11[0.9]	0.855
Heart disease	51[1.5]	24[1.9]	0.360
Neurological disease	6[0.2]	9[0.7]	0.008
Current or past tuberculosis	78[2.3]	28[2.3]	0.874
Other	55[1.6]	57[4.5]	<0.001
Clinical findings			
Pulse rate /min	83.91±11.2	84.1±11.8	0.715
Systolic BP mmHg	125.12±11.9	126.0±12.9	0.028
Diastolic BP mmHg	82.71±7.9	83.1±8.4	0.155
Respiratory rate/min	19.0±3.7	19.1±3.9	0.313
SpO_2 at admission			
≥95%	1554[70.5]	590[68.7]	0.601
90-94%	397[18.0]	164[19.1]	
<90%	252[11.4]	105[12.2]	
Laboratory Investigations (Biochemistry n=867; Hematology n=4456)			
Creatinine, mg/dl	0.94±0.47	0.97±0.56	0.378
SGOT, IU	45.0±108.9	44.8±44.5	0.531
SGPT, IU	42.7±59.7	45.6± 44.2	0.096
Sodium, mEq/L	136.6±9.4	134.8±17.8	0.144
Potassium, mEq/L	5.1±8.9	5.9±12.6	0.112
Hb (gm/dl)	12.7±2.3	12.6±2.2	0.411
White cells (10^9 cells/L)	7585±3894	7370±3651	0.099
Lymphocytes (10^9 cells/L)	1607±1355	1534±1225	0.089
Lymphocyte/Neutrophil ratio	0.36±0.27	0.35±0.46	0.346
Outcome measures			
Mean duration of hospital stay[days]	6.9±3.8	6.5±3.6	0.004
Oxygen requirement	600[17.6]	261[20.6]	0.022

High flow O_2/non-invasive ventilation	236[6.9]	98[7.7]	0.371
Mechanical ventilation	123[3.6]	46[3.6]	1.000
Recovered	3020[88.7]	1197[94.3]	<0.001
Referred	104[3.0]	15[1.2]	<0.001
Deaths	282[8.3]	58[4.6]	<0.001
Numbers ± indicate 1 SD; Numbers in parentheses are percent; BP blood pressure; SpO_2 saturation of peripheral oxygen; SGOT serum glutamic oxalate transferase; SGPT serum glutamic pyruvate transferase			

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4	
Objectives	3	State specific objectives, including any prespecified hypotheses	4,5	
Methods				
Study design	4	Present key elements of study design early in the paper	**5**	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	**5**	
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	**5,6**	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	**5,6**	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	**5,6**	
Bias	9	Describe any efforts to address potential sources of bias	--	
Study size	10	Explain how the study size was arrived at	**6**	Consecutive patients enrolled

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	**6**	Categorical and continuous variables
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6	
		(*b*) Describe any methods used to examine subgroups and interactions	6	
		(*c*) Explain how missing data were addressed	6	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy		
		(*e*) Describe any sensitivity analyses		Nil
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed		**6,7**
		(b) Give reasons for non-participation at each stage		**6,7**
		(c) Consider use of a flow diagram		Nil
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders		**7, Tables 1,2,3**
		(b) Indicate number of participants with missing data for each variable of interest		**7, Tables 1,2,3**
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)		
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time		
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures		**7,8, Tables 1,2,3,4**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included		**Tables 2,3,4**
		(*b*) Report category boundaries when continuous variables were categorized		**Tables 3,4**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		**Table 3**

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	**Table 4**
Discussion			
Key results	18	Summarise key results with reference to study objectives	**8**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	**10**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	**3,10,11**
Generalisability	21	Discuss the generalisability (external validity) of the study results	**3,10**
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	**11**

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.