Clinical profile and risk factors for mortality among COVID-19 in patients at a tertiary care centre in Bengaluru, India

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Abstract

COVID-19 is an emerging viral disease affecting more than 200 countries worldwide and it present with varied clinical profile throughout the world. Without effective drugs to cure COVID-19, early identification and control of risk factors are important measures to combat COVID-19. This study was conducted to determine the clinical profile and risk factors associated with mortality among COVID-19 patients in a tertiary care hospital in South India. This record-based longitudinal study was conducted by reviewing the case records of COVID-19 patients admitted for treatment from June 2020 to September 2020 in a tertiary care centre in South India. The clinical details, discharge/death details, were collected and entered in MS Excel. Potential risk factors for COVID-19 mortality were analysed using univariate binomial logistic regression, generalized linear models (GLM) with Poisson distribution. Survival curves were made using the Kaplan-Meier method. Log-rank test was used to test the equality of survivor functions between the groups. Out of 854 COVID-19 patients, 56.6% were men and the mean (standard deviation) age was 45.3(17.2) years. The median survival time was significantly lesser in male COVID-19 patients (16 days) as compared to female patients (20 days). Increasing age, male gender, patients presenting with symptoms of fever, cough, breathlessness, smoking, alcohol consumption, comorbidities were significantly associated with mortality among COVID-19 patients. Patients with older age, male gender, breathlessness, fever, cough, smoking and alcohol and comorbidities need careful observation and early intervention. Public health campaigns aimed at reducing the prevalence of risk factors like diabetes, hypertension, smoking and alcohol use are also needed.

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Introduction

Severe acute respiratory syndrome-related coronavirus-2 (SARS-CoV-2) infection emerged in Wuhan, China, and has spread rapidly worldwide [1]. Currently COVID-19 pandemic has affected 51,848,261cases and 1,280,868 deaths till 10th November 2020 [2]. India is currently burdened with 8,728,795 cases and 1,28,668 deaths as of 13th November whereas Karnataka is affected with 8,55,912 cases and 11,474 deaths [3]. The clinical presentation and the mortality pattern is widely varied across the countries. In countries like India with diversity, the presentation of COVID-19 is different even among different States.

Thirty percent of SARS-CoV-2 infection presents without any symptoms and usually recovers without immediate complications [4]. Evidence shows that 80% of the COVID-19 patients present with mild to moderate disease in which symptoms such as mild upper respiratory tract illness fever, cough, myalgia, fatigue, anosmia, breathlessness and pneumonia were present.[5]

Around 20% of the COVID-19 patients present with severe acute respiratory illness and most of these severe patients succumb to death [5-7]. Severity of COVID-19 disease among patients infected with SARS-CoV-2 virus varies widely between different countries.

In Italy the proportion of severe cases was 37% [8], in China it was 13.8% [9] and in the USA 12% of COVID-19 patients had severe cases. In India, most people with SARS CoV-2 infections develop mild or uncomplicated illnesses [5]. Only 14% of the patients develop the severe disease that requires hospitalization and oxygen support, and 5% require admission to an intensive care unit [5.] The risk factors for severe COVID-19 disease and mortality need to be identified to find out who are at higher risk of having severe disease and death.

Studies in other countries have identified that older age, male gender, presence of comorbidities like diabetes, hypertension, obesity, chronic kidney disease, smoking have positively associated with severity and mortality for COVID-19 [10-13]. Literature regarding risk factors for COVID-19 mortality is very limited in the Indian setting. Without effective drugs for COVID-19 and some vaccines which are under trial [14], the public health interventions like identification and control of risk factors, social distancing, wearing masks, performing hand hygiene remain the mainstay of management to combat COVID-19. For effective implementation of the above public interventions, early identification and management of risk factors for mortality due to COVID-19 is the need of the hour. With this background, this study was conducted to determine the risk factors associated with mortality among COVID-19 patients in a tertiary care hospital in South India.

Methods

A record-based longitudinal study was carried out by reviewing the case sheets of COVID-19 patients admitted for treatment in the tertiary care centre in Bengaluru. This tertiary care institution is equipped with around 500 beds and was designated as Dedicated COVID Health Centre (DCHC) in the last week of June 2020. Since then COVID-19 patients were given inpatient care in this institute. Standard care is being provided free of cost to COVID patients seeking care at the hospital as per the Ministry of Health and Family Welfare, Government of Karnataka guidelines.

Each COVID-19 patient's clinical details were maintained in the case records which were collected by the study investigators. The data related to the clinical and socio-demographic details were collected and entered in MS Excel. The data collected were anonymous and confidentiality of information was maintained throughout the study. A total of 854 case records of the confirmed COVID-19 patients admitted from June 2020 to September 2020 were collected and analysed. Patients were followed till discharge or death from the hospital.

The variables collected from the case record and used for the analysis were age, gender, symptoms like fever, cough, breathlessness, sore throat, loose stools, chest pain, headache, myalgia, epidemiological details like the history of contact, history of travel to foreign countries, personal history like smoking, alcohol consumption, comorbidities like diabetes, hypertension, respiratory diseases, chronic kidney disease (CKD), malignancies, tuberculosis, hypothyroidism. The outcomes were classified into discharge from hospital, death of the COVID-19 patient. The continuous variable age is categorized in 10 years intervals.

Operational definitions

History of contact

A person who is involved in any works related to providing direct care without proper personal protective equipment for COVID-19 patients or staying in the same close environment of a COVID-19 patient in the last 14 days before the onset of symptoms [15].

History of travel

A person who has travelled to any foreign countries in the last 14 days before the onset of symptoms.

History of smoking

A person who is a current smoker or former smoker is considered as having a positive history of smoking [16].

History of alcohol consumption

Use of alcoholic beverages either on individual occasions (binge drinking) or as a regular practice is considered a positive history of alcohol consumption [17].

Statistical analysis

Data were entered using Microsoft Excel and analysis was done using STATA statistical software v. 14 (StataCorp LCC, College Station, TX, USA) [18]. The continuous variables age and duration of stay are summarized as mean with standard deviation (SD) or median with an interquartile range based on the distribution of data. The categorical variables are summarized as frequencies and proportions. Chi-square tests and Fischer's exact tests are used to test the statistical significance for the association of categorical data as appropriate. Univariate analysis was done using binomial logistic regression to identify the factors associated with mortality of COVID-19 patients. The strength of association is expressed as relative risk (RR) with 95% confidence interval (95% CI). The variables which were included in the multivariate regression model were selected based on the statistical significance of association ($p<0.05$) and clinical significance. Multivariate analysis was done using generalized linear models (GLM) with Poisson distribution to calculate adjusted relative risk (aRR) along with the 95% CI. A p-value less than 0.05 was considered statistically significant. Survival curves were made using the Kaplan-Meier method. Log-rank test was used to test the equality of survivor functions between the groups.

Results

A total of 854 COVID-19 patients were included in the study with a mean (SD) age of 45.3 (17.2) years. Among them, 371 (43.4%) were women and 483 (56.6%) were men. Symptoms with which the COVID-19 patients presented to the hospital were fever (48.24%), cough (39.9%), difficulty in breathing (29%), myalgia (21.9%), sore throat (8.9%), headache (8.7%), loose stools (4%) and chest pain (2.9%). The median (IQR) duration of stay in the hospital was 5 (3-8) days. The median survival time of COVID-19 patients in the hospital was 20 (95% CI: 16-23) days. The median survival time was lesser in male COVID-19 patients (16 days) as

compared to female patients (20 days) and the difference was statistically significant (=0.054) (Figure 1).

History of contact with positive COIVD-19 cases was present in 208 (24.3%) patients and the history of travel to foreign countries was present in 126 (14.7%) of the COVID-19 patients. History of smoking was there in 10 (1.1%) and a history of alcohol consumption was present in 14 (1.6%) of the COVID-19 patients. Out of the COVID-19 patients presented during the study period, 73 (8.5%) were pregnant. Co-morbidity was present in 348 (40.7%) of the COVID-19 patients presented to the hospital. The comorbidities with which they presented were hypertension (23.4%), diabetes (23%), hypothyroidism (5.3%), chronic obstructive pulmonary disease (1.5%), asthma (1.4%), chronic kidney disease (1.1%), cardiac illnesses (4.3%), malignancy (1.1%) and tuberculosis (1.1%).

Our results have depicted that as the age increased, the risk of death due to COVID-19 also increased and the association was statistically significant. As compared to COVID-19 patients in the 31-40-year age group, the patients in the 41-50 years age group had 1.4 (95% CI: 0.6- 3.0) times increased risk of mortality (Table 1). Patients in the 51-60 years age group had 2.2 (95% CI: 1.1-5.2) times increased risk of death, 61-70 years age group had 2.8 (95% CI: 1.5- 6.9) times increased risk of dying and 71-80 years age group had 3.4 (95% CI: 1.7-9.8) times increased risk of dying. Male COVID-19 patients had 1.7 (95% CI: 1.1-2.6) times increased risk of death as compared to female patients. COVID-19 patients who presented with fever had

2.0 (95% CI: 1.3-3.1) times increased risk of mortality whereas patients who presented with cough had 1.4 (95% CI: 0.94-2.1) times increased risk. Patients presented with breathlessness had 15.2 (95% CI: 8.4-27.4) times increased risk of mortality as compared to patients without breathlessness symptoms (Figure 2). The symptoms like loose stools, chest pain, headache and myalgia were not significantly associated with mortality.

COVID-19 patients with a history of smoking had 6.2 (95% CI: 3.6-10.8) times increased risk of death and patients with a history of alcohol consumption had 5.2 (95% CI: 2.9-9.2) times increased risk of mortality (Table 2). COVID-19 patients with comorbidities had 4.0 (95% CI: 2.5-6.3) times increased risk of death as compared to patients without comorbidities. These associations were statistically significant. Hypertension and diabetes were the common comorbidities with which COVID-19 patients presented to the hospital which increased the risk of mortality by 2.2 (95% CI: 1.4-3.3) times and 4.0 (95% CI: 2.7-5.9) times respectively. Respiratory comorbidities like COPD, Asthma and Tuberculosis increased the risk of mortality by 3.1 (95% CI: 1.3-7.3), 2.5 (95% CI: 0.95-7.0) and 4.0 (95% CI: 1.8-8.9) times respectively.

Other co-morbidities that significantly increased the risk of mortality in COVID-19 patients were CKD (RR=6.2 (95% CI: 3.6-10.8)) and cardiac illnesses [RR=3.5 (95% CI: 2.1-5.9)].

The variables included in the multivariate analysis were age, gender, presence of symptoms like fever, cough, breathlessness, history of smoking, history of alcohol consumption, presence of any comorbidity. In the multivariate analysis the variables age of the patient (aRR for 71-80 years=2.1 (95% CI: 1.1-4.4)), presence of breathlessness during admission (aRR=10.6 (95% CI: 5.8-19.6)), and presence of any comorbidity (aRR=1.9 (95% CI: 1.2-3.1)) were significantly associated with mortality among COIVD-19 patients admitted in the tertiary care centre.

Discussion

The results of our analysis have shown that increasing age, male gender, patients presenting with symptoms of fever, cough, breathlessness, smoking, alcohol consumption, presence of comorbidities like diabetes, hypertension, respiratory disease, chronic kidney disease, cardiac illness and malignancy were significantly associated with mortality among COVID-19 patients. A systematic review and meta-analysis done by Galbadage *et al.* have identified that male sex is a significant risk factor for severe disease and COVID-19 mortality [19]. The immunological, biological, cultural

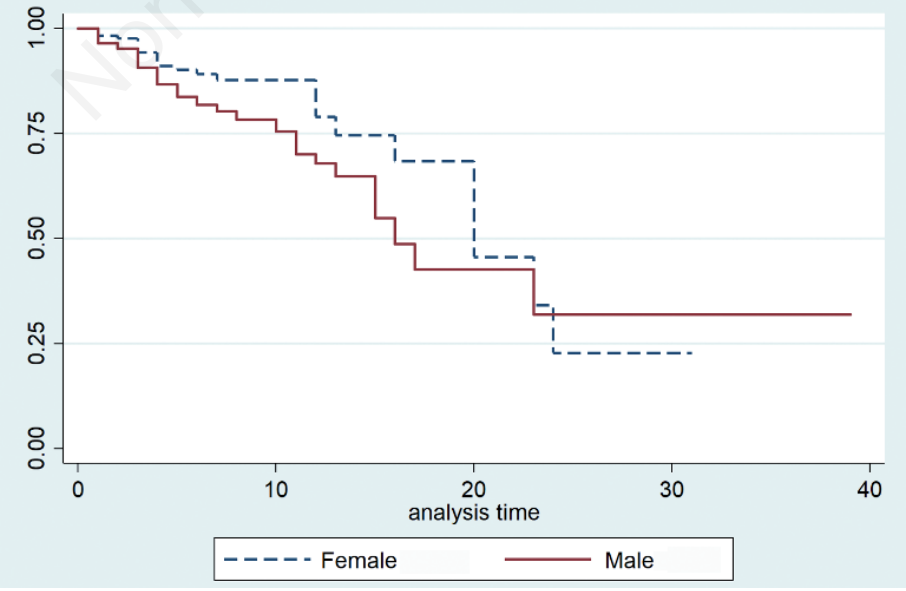

Figure 1. Kaplan-Meier survival estimates.

Table 1. Association of demographic and clinical characteristics with mortality among COVID-19 patients admitted to the tertiary care centre (n=854).

Characteristics	Categories	Discharged (n=767) Frequency (%)	Died (n=87) Frequency (%)	RR (95% CI)*	aRR (95% CI)°	p-value
Age	0-10	14 (100%)	0 (0.0%)	-		
	11-20	31 (100%)	0 (0.0%)	-		
	21-30	151 (98.7%)	2 (1.3%)	0.2 (0.04-0.84)	0.41 (0.09-1.7)	0.030
	31-40	153 (93.3%)	11 (6.7%)	1	1	
	41-50	140 (90.3%)	15 (9.7%)	1.4 (0.6-3.0)	1.0 (0.49-2.0)	0.336
	51-60	130 (84.9%)	23 (15.1%)	2.2 (1.1-5.2)	1.2 (0.63-2.2)	0.021
	61-70	99 (81.1%)	23 (18.9%)	2.8 (1.5-6.9)	1.4 (0.73-2.7)	0.003
	71-80	41 (77.3%)	12 (22.7%)	3.4 (1.7-9.8)	2.1 (1.1-4.4)	0.002
	81-90	8 (88.9%)	1 (11.1%)	1.6 (0.19-15.1)	1.2 (0.54-2.8)	0.609
Sex	Female	344 (92.7%)	27 (7.3%)	1	1	
	Male	423 (87.6%)	60 (12.4%)	1.7 (1.1-2.6)	1.1 (0.77- 1.7)	0.016
Fever	No	412 (93.2%)	30 (6.8%)	1	1	
	Yes	355 (86.2%)	57 (13.8%)	2.0 (1.3-3.1)	1.3 (0.91- 2.0)	0.001
Cough	No	468 (91.2%)	45 (8.8%)	1	1	
	Yes	299 (87.7%)	42 (12.3%)	1.4 (0.94-2.1)	0.67 (0.46- 0.97)	0.094
Breathlessness	No	593 (98.0%)	12 (2.0%)	1	1	
	Yes	174 (69.9%)	75 (30.1%)	15.2 (8.4-27.4)	10.6 (5.8-19.6)	<0.001
Loose stools	No	736 (89.9%)	83 (10.1%)	1	-	
	Yes	31 (88.6%)	4 (11.4%)	1.1 (0.43-2.9)	-	0.803
Chest pain	No	747 (90.1%)	82 (9.9%)	1	-	
	Yes	20 (80%)	5 (20%)	2.0 (0.89 – 4.5)	-	0.189
Headache	No	696 (89.3%)	83 (10.7%)	1	-	
	Yes	71 (94.7%)	4 (5.3%)	0.50 (0.18-1.3)	-	0.164
Myalgia	No	599 (89.8%)	68 (10.2%)	1	-	
	Yes	168 (89.8%)	19 (10.2%)	0.99 (0.61-1.61)	-	0.989
Sore throat	No	691 (88.8%)	87 (11.2%)	-	-	-
	Yes	76 (100%)	0 (0.0%)	-	-	-

*RR, relative risk; °aRR, adjusted relative risk.

Table 2. Association of epidemiologic and clinical characteristics with mortality among COVID-19 patients admitted to the tertiary care centre (n=854).

Factor	Categories	Discharge	Death	RR (95% CI)*	aRR (95%CI)°	p-value
History of contact	No	564 (87.3%)	82 (12.7%)	1	-	
	Yes	203 (97.6%)	5 (2.4%)	0.18 (0.07-0.46)	-	<0.001
History of travel	No	643 (88.3%)	85 (11.7%)	1	-	
	Yes	124 (98.4%)	2 (1.6%)	0.13 (0.03-0.54)	-	0.005
History of smoking	No	763 (90.4%)	81 (9.6%)	1	1	
	Yes	4 (40%)	6 (60%)	6.2 (3.6-10.8)	1.4 (0.56- 3.6)	<0.001
History of alcoholconsumption	No	760 (90.5%)	80 (9.5%)	1	1	
	Yes	7 (50%)	7 (50%)	5.2 (2.9 – 9.2)	1.3 (0.51-3.5)	<0.001
Pregnancy	No	694 (88.9%)	87 (11.1%)	-	-	-
	Yes	73 (100%)	0 (0.0%)	-	-	-
Co-morbidity	No	483 (95.5%)	23 (4.5%)	1	1	
	Yes	284 (81.6%)	64 (18.4%)	4.0 (2.5-6.3)	1.9 (1.2- 3.1)	<0.001
Hypertension	No	602 (92.1%)	52 (7.9%)	1	-	
	Yes	163 (82.5%)	35 (17.5%)	2.2 (1.4-3.2)	-	<0.001
Diabetes	No	615 (94.0%)	39 (6.0%)	1	-	
	Yes	152 (76.0%)	48 (24.0%)	4.0 (2.7-5.9)	-	<0.001
Respiratory disease	No	749 (90.3%)	80 (9.6%)	1	-	
	COPD	9 (69.2%)	4 (30.8%)	3.1 (1.3-7.3)	-	0.007
	Asthma	9 (75.0%)	3 (25.0%)	2.5 (0.95-7.0)	-	0.063
Tuberculosis	No	761 (90.2%)	83 (9.8%)	1	-	
	Yes	6 (60.0%)	4 (40.0%)	4.0 (1.8-8.9)	-	<0.001
Chronic kidney disease	No	763 (90.4%)	81 (9.6%)	1	-	
	Yes	4 (40.0%)	6 (60.0%)	6.2 (3.6-10.8)	-	<0.001
Cardiac illnesses	No	742 (90.8%)	75 (9.2%)	1	-	
	Yes	25 (67.6%)	12 (32.4%)	3.5 (2.1-5.9)	-	<0.001
Malignancy	No	759 (89.9%)	85 (10.1%)	1	-	
	Yes	8 (80.0%)	2 (20.0%)	1.9 (0.56-6.9)	-	0.284
Hypothyroidism	No	725 (89.6%)	84 (10.4%)		-	
	Yes	42 (93.3%)	3 (6.7%)	0.64 (0.2-1.9)	-	0.435

*RR, relative risk; °aRR- adjusted relative risk; COPD, chronic obstructive pulmonary disease.

and socio-behavioural aspects might have led to the unfavourable situation for the male sex [20,21].

Our study depicted that older age increased the risk of COVID-19 mortality in the Indian population which was similar to other studies in the Mexican and Chinese populations [10,11,17]. Age-related decrease in clearance of inhaled particles in the airway, immunosenescence (a gradual decline in immune function due to aging), the change in quantity and quality of mucins and protective glycoproteins found in mucosal barriers, presence of comorbidities might be the reasons for the increased risk of COVID-19 mortality among older individuals [22,23].

Smoking and alcohol are significantly associated with COVID-19 mortality in our study which is similar to the results from other studies [10,11]. The reasons for increased mortality among patients with alcohol consumption might be immunological changes, malnutrition, alcohol- related liver diseases and changes in the amount of Angiotensin-converting enzyme 2 [24], which is a target enzyme for SARS-CoV-2 [25]. Increased COVID-19 mortality among smokers might be due to the detrimental action of tobacco smoke on the immune system, direct lung injury, up-regulation of SARS-CoV-2 receptor, Angiotensin-converting enzyme 2 (ACE2) in human cells [26] due to smoking [25].

Among the various symptoms for COVID-19 disease, our study identified that the presence of fever, cough and breathlessness are significantly associated with COVID-19 mortality. Other studies done in China and Nigeria also showed that these symptoms are associated with severe disease and mortality due to COVID-19 [27-29]. In the study done in Nigeria, breathlessness increased the risk of mortality by 19 times (OR=19.26 95% CI 10.95-33.88) which is similar to our study [27]. The presence of any comorbidity increased the risk of death by 4 times in our study, which is similar to other studies [11,27,29]. With diabetes and hypertension are the most common co-morbidities among COVID-19 patients in India, ACE2 mediated pathway, abnormal blood glucose levels mediated disruption of immunity might be the reasons for increased mortality among COVID-19 patients [30]. The pres-

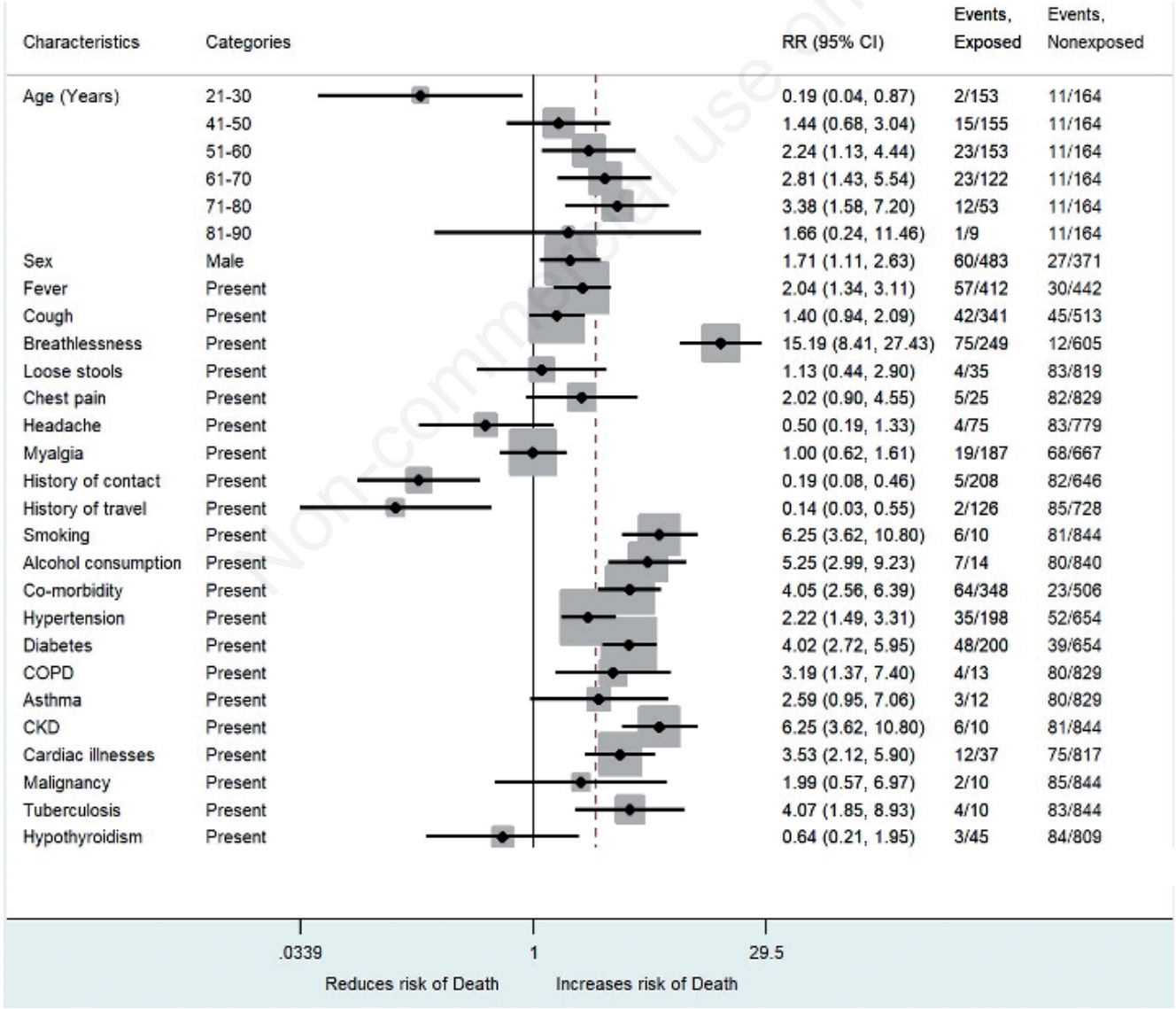

Figure 2. Forest plot of univariate analysis of risk factors associated with COVID-19 mortality.

ence of other co-morbidities like obesity in diabetes and hypertension might also be contributing to the mortality by altered immune responses due to low vitamin D levels and adiponectin levels and high leptin levels [30,31]. Our analysis also identified 6 times increased risk of COVID-19 mortality among CKD patients. SARS-CoV-2 might affect the kidney through the ACE2-dependent pathway, causing acute renal impairment and death [32].

Strengths and limitations

Our study analyzed the data from a large number of COVID-19 patients. The results of the study are comparable to the literature on risk factors for COVID-19 mortality from India and other countries. Since this is a record-based study from a tertiary health care center, the generalizability of the results needs to be done with caution. This study represents the findings from a dynamic and rapidly changing pandemic for which the evidence may change over time. Nevertheless, our study provides valuable evidence on the symptom profile and risk factors for COVID-19 mortality from India.

Conclusions

To conclude, increasing age, male gender, presenting symptoms like fever, cough, breathlessness, smoking, alcohol consumption, presence of comorbidities were identified as the significant risk factors for mortality due to COVID-19. Early identification of these risk factors and appropriate treatment is important to prevent death among COVID-19 patients. It is recommended that COVID-19 patients with these risk factors can be given appropriate inpatient care instead of domiciliary management to prevent fatal outcomes among high-risk patients. We also need to implement public health campaigns aimed at reducing the prevalence of risk factors like diabetes, hypertension, smoking and alcohol use and other comorbidities. Long term consequences of COVID-19 disease need to be assessed with longitudinal studies with longer follow up period.

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