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Early Determinants of Length of Hospital Stay: A Case Control Survival Analysis among COVID-19 Patients admitted in a Tertiary Healthcare Facility of East India

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Abstract

Background: Length of hospital stay (LOS) for a disease is a vital estimate for healthcare logistics planning. The study aimed to illustrate the effect of factors elicited on arrival on LOS of the COVID-19 patients. **Materials and Methods:** It was a retrospective, record based, unmatched, case control study using hospital records of 334 COVID-19 patients admitted in an East Indian tertiary healthcare facility during May to October 2020. Discharge from the hospital (cases/ survivors) was considered as an event while death (control/non-survivors) as right censoring in the case-control survival analysis using cox proportional hazard model. **Results:** Overall, we found the median LOS for the survivors to be 8 days [interquartile range (IQR): 7-10 days] while the same for the non-survivors was 6 days [IQR: 2-11 days]. In the multivariable cox-proportional hazard model; travel distance (>16 km) [adjusted hazard ratio (aHR): 0.69, 95% CI: (0.50-0.95)], mode of transport to the hospital (ambulance) [aHR: 0.62, 95% CI: (0.45-0.85)], breathlessness (yes) [aHR: 0.56, 95% CI: (0.40-0.77)], number of co-morbidities (1-2) [aHR: 0.66, 95% CI: (0.47-0.93)] (≥3) [aHR: 0.16, 95% CI: (0.04-0.65)], COPD/asthma (yes) [[aHR: 0.11, 95% CI: (0.01-0.79)], DBP (<60/≥90) [aHR: 0.55, 95% CI: (0.35-0.86)] and qSOFA score (≥2) [aHR: 0.33, 95% CI: (0.12-0.92)] were the significant attributes affecting LOS of the COVID-19 patients. **Conclusion:** Factors elicited on arrival were found to be significantly associated with LOS. A scoring system inculcating these factors may be developed to predict LOS of the COVID-19 patients.

Keywords
length of stay, COVID-19, association, dyspnea, comorbidity

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Introduction

It's being more than a year since the first case of COVID-19 reported in Wuhan, China.[1] Since then, the pandemic has affected millions of lives around the globe.[2] It has interrupted routine healthcare delivery and challenged healthcare infrastructure of even developed countries.[3-8] India reported first ever COVID-19 case in January 2020.[9] Since then, the country has reported over 30 million COVID-19 cases and 4 00 000 deaths associated with the disease.[2]

Length of hospital stay (LOS) for a disease is a vital estimate for healthcare logistics planning.[10] Decreased LOS is reported to be associated with lowered risk of hospital acquired infection, reduction in financial burden for treatment among the patients, higher bed turnover rate of the hospitals (increases bed availability for the other patients) and vice versa can be told for increased LOS.[11,12] For COVID-19 the reported associates of LOS are age, gender, nutritional status, presenting symptoms (ie, fever, breathlessness, fatigue, anorexia etc.), co-morbidities (ie, hypertension, heart disease, diabetes etc.), vitals (ie, respiratory rate, blood pressure etc.) laboratory parameters [ie, d-dimer,

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C-reactive protein (CRP), leucocyte count, lactate dehydrogenase (LDH), aspartate aminotransferase (AST) etc.], radio graphical parameters (ie, chest X-ray, CT scan findings etc.), and medications (ie, tocilizumab, ACEI, ARB, metformin etc.).[13-22] Although in terms of healthcare logistic planning the factors that could predict LOS of COVID-19 patients early bears additional importance. Patient characteristics and vital signs at the time of admission are being already linked with the level of care requirement, disease progression and mortality among COVID-19 patients by some prior studies.[23-25] Although considering specifically for LOS, no such prior attempts have been made in Indian context.

Early identification of factors influencing LOS of COVID-19 patients may help policymakers to plan healthcare logistics (man, money, and material) for the disease accordingly. On extensive literature search we could only retrieve 2 prior Indian studies which have explored LOS among COVID-19 patients.[13,14] Although these 2 studies had their own limitations. The study conducted by Thiruvengadam et al[13] did not report median survival time for the found associated variables. By contrast, Mishra et al[14] analyzed data extracted from media bulletin and elicited very few variables. Moreover, both these studies were conducted in Karnataka (a southern state of India). Therefore, the current retrospective case-control study was planned to illustrate the effect of factors elicited on arrival on LOS of the COVID-19 patients admitted in a tertiary care hospital of East India.

Materials and Methods

Study Setting and Period

It was a retrospective, record based, unmatched, case control study using hospital records of COVID-19 patients admitted in an East Indian tertiary healthcare facility situated in Patna city beside holy river Ganges during May to October 2020. Our institute have pioneered COVID-19 care in the region since its emergence with over 400 general and 60 intensive care unit (ICU) beds and over 3000 dedicated healthcare workforces. During July to December, 2020 the institute have also functioned as COVID-19 dedicated tertiary healthcare facility to meet increasing tertiary COVID-19 care needs of the region. Those who were discharged as per medical advice were the cases, while those who died were deemed as controls for the study. Notably those who were admitted in non-COVID-19 wards of the hospital before ultimately being diagnosed as a COVID-19 patient and left against medical advice (LAMA) during the study period were not considered for inclusion.

Sample Size Determination

Considering 1.75 relative hazard (median LOS in hospital for discharged and died cases were reported to be 14 and 8 days subsequently by Rees et al[26]), equal number of cases and controls, 99% precision and 85% power the minimum sample size for each group was calculated to be 167 using an online sample size calculator.[27] The said online sample size calculator uses following formula for sample size estimation in case of survival analysis: $n = (Z\alpha + Z\beta)^2/(\log(RH))^2 q_0 q_1$ where RH = relative hazard, q_1 = proportion of subjects that are in group 1 (exposed) and q_0 = proportion of subjects that are in group 0 (unexposed); 1-q_1.

Sampling Technique

During the study period in total 2981 COVID-19 patients (tested positive by RTPCR/rapid antigen test) were admitted in the selected healthcare facility. Out of these 297 (9.9%) were LAMA and 234 (7.8%) were admitted in non-COVID-19 wards before being diagnosed as COVID-19 positive. So, these were excluded. Out of the rest, 2450 patients 303 eventually died. Separate line list of these 2147 (87.6%) discharged cases and 303 (12.4%) death cases were prepared. The required number of cases and controls were selected from these line lists using simple random sampling. Microsoft excel 2016 was used to generate random numbers.

Data Collection Procedure

The variables extracted from the records of the selected COVID-19 patients were age (in completed years), sex (male/female), travel distance (distance of the current healthcare facility from his/her native place) (in kilometers), mode of seeking healthcare (contact tracing/self-reported) and mode of transport to the hospital (self-owned/rented vehicle/ambulance). Presenting complaints like fever (yes/no), cough (yes/no), breathlessness (yes/no), sore throat (yes/no), diarrhea (yes/no), nausea/ vomiting (yes/no) and fatigue (yes/no) were documented. Presence of co-morbidities like ischemic heart disease (IHD) (yes/no), hypertension (HTN) (yes/no), diabetes (DM) (yes/no), cancer (yes/no), chronic obstructive pulmonary disease (COPD)/asthma (yes/no) and chronic kidney disease (CKD) (yes/no) were elicited. Vitals documented at the time of admission like respiratory rate (RR) (in breaths per minute), temperature (in degree Fahrenheit), oxygen saturation (SpO_2) (in percentage), pulse rate (PR) (in beats per minute), systolic blood pressure (SBP) (in mmHg), diastolic blood pressure (DBP) (in mmHg), Glasgow coma scale (GCS) score and quick sequential organ failure assessment (qSOFA) score were also documented for the study.

Statistical Analysis

The data were first entered in Microsoft excel 2016. Then imported on Statistical Package for Social Sciences (SPSS) (Chicago, USA) (version 22.0) for analysis. We presented

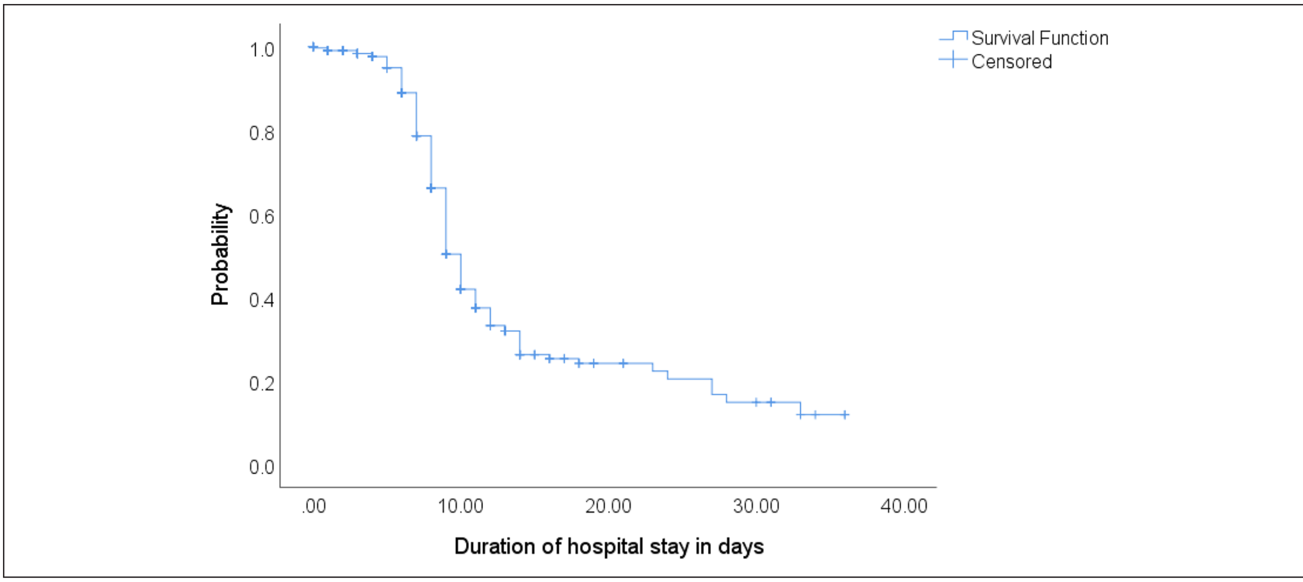

Figure 1. Kaplan Meier curve showing overall survival of the COVID-19 patients (n = 334).

categorical variables as frequency (percentage) while median [interquartile range (IQR)] were used to report continuous variables. We considered discharge from the hospital as an event (cases/survivors) while death was deemed as right censoring (control/non-survivors). Overall survival of the study subjects was depicted using Kaplan-Meier curve. To report survival time median [95% confidence interval (CI)] was used. To elicit association between LOS and its associates at first univariate cox proportional hazard regression was done. Attributes which were significant in univariate analysis ($P \leq .05$) were entered to multivariable cox proportional hazard model using backward likelihood ratio (LR) method. The multivariable model with highest −2 log likelihood value was finally reported. The strength of association was measured in terms of hazard ratios (HRs) at 95% confidence limits.

Results

The median age of the studied COVID-19 patients was 55 years with interquartile range (IQR) of 40 to 65 years. Overall, we found the median LOS for the survivors to be 8 days [interquartile range (IQR): 7-10 days] while the same for the non-survivors was 6 days [IQR: 2-11 days]. Survivors had more probability of higher LOS compared to non-survivors. In univariate cox-proportional hazard model; higher age, number of co-morbidities and travelling distance to seek healthcare, self-reporting to the healthcare facility, complaint of breathlessness, deranged RR, SpO_2, PR, SBP, DBP, GCS, and qSOFA score on admission increased LOS while complaint of sore throat on admission decreased the same. Similarly, among the reported co-morbidities, COPD/asthma was found be associated with slowest recovery followed by CKD, diabetes, hypertension and ischemic heart disease. The median days since symptomatic prior to admission was 6 days with IQR of 4 to 8 days. The duration of symptoms prior to admission was not found to be associated with LOS [HR: 0.85, 95% CI: (0.63-1.16)] (Figure 1 and Table 1).

In the multivariable cox-proportional hazard model; travel distance (>16 km) [adjusted hazard ratio (aHR): 0.69, 95% CI: (0.50-0.95)], mode of transport to the hospital (ambulance) [aHR: 0.62, 95% CI: (0.45-0.85)], breathlessness (yes) [aHR: 0.56, 95% CI: (0.40-0.77)], number of co-morbidities (1-2) [aHR: 0.66, 95% CI: (0.47-0.93)] (≥3) [aHR: 0.16, 95% CI: (0.04-0.65)], COPD/asthma (yes) [aHR: 0.11, 95% CI: (0.01-0.79)], DBP (<60/≥90) [aHR: 0.55, 95% CI: (0.35-0.86)] and qSOFA score (≥2) [aHR: 0.33, 95% CI: (0.12-0.92)] were the significant attributes affecting LOS of the COVID-19 patients. Thus, those who resided within 16 km from the health facility, used self-owned/rented vehicle on way to the hospital, did not have breathlessness, COPD/asthma and had no/less number of co-morbidities, normal DBP (between 60 to 89 mmHg) and lower qSOFA score at the time of admission recovered earlier compared to others (Table 2).

The multivariable cox-proportional hazard model can be presented as $h(t) = h_0(t) \exp[-0.37 \times (\text{travel distance}>_{16}) - 0.48 \times (\text{mode of transport to the hospital}_{\text{ambulance}}) - 0.59 \times (\text{breathlessness at admission}_{\text{yes}}) - 0.42 \times (\text{co-morbidity}_{1\text{-}2}) - 1.87 \times (\text{co-morbidity}\geq_{3}) - 2.25 \times (\text{COPD/asthma}_{\text{yes}}) - 0.60 \times (\text{DBP}<_{60/}\geq_{90}) - 1.11 \times (\text{qSOFA score}\geq_{2})]$

Discussion

In this retrospective case-control study we found that higher travelling distance, use of an ambulance as mode of transport,

Table 1. Univariate Cox Proportional Hazard Model Showing Factors Associated With Length of Hospital Stay Among COVID-19 Patients (n = 334).

Variables	Total N (%)	LOS Median (95% CI)	β	HR (95% CI)	*P*-value
Age: (in years)					
<40 (ref.)	76 (22.8)	9.0 (8.4-9.6)			
40-65	183 (54.8)	10.0 (8.4-11.6)	−0.71	0.49 (0.36-0.68)	.000
>65	75 (22.5)	24.0 (11.6*-36.4)	−0.99	0.37 (0.22-0.62)	.000
Sex					
Female (ref.)	66 (19.8)	9.0 (8.4-9.6)			
Male	268 (80.2)	10.0 (9.4-10.6)	−0.05	0.96 (0.66-1.38)	.811
Travel distance: (in kilometers)					
≤16 (ref.)	164 (49.1)	9.0 (8.4-9.6)			
>16	170 (50.9)	10.0 (8.6-11.4)	−0.55	0.58 (0.43-0.79)	.001
Mode of seeking healthcare:					
Contact Tracing (ref.)	49 (14.7)	9.0 (8.0-9.9)			
Self-reported	285 (85.3)	10.0 (9.4-10.6)	−0.44	0.64 (0.45-0.92)	.017
Mode of transport to hospital					
Self-owned/ rented vehicle (ref.)	111 (33.2)	9.0 (8.6-9.4)			
Ambulance	223 (66.8)	11.0 (9.1-12.8)	−0.76	0.47 (0.34-0.63)	.000
Fever					
No (ref.)	94 (28.1)	10.0 (8.7-11.3)			
Yes	240 (71.9)	9.0 (8.4-9.6)	0.22	1.29 (0.90-1.87)	.162
Cough:					
No (ref.)	142 (42.5)	9.0 (8.3-9.6)			
Yes	192 (57.5)	10.0 (9.0-10.9)	−0.30	0.74 (0.54-1.01)	.055
Breathlessness					
No (ref.)	123 (36.8)	9.0 (8.6-9.4)			
Yes	211 (63.5)	13.0 (10.8-15.2)	−0.78	0.46 (0.34-0.63)	.000
Sore throat:					
No (ref.)	313 (93.7)	10.0 (9.4-10.6)			
Yes	21 (6.3)	8.0 (6.7-9.3)	0.74	2.09 (1.32-3.31)	.002
Diarrhea					
No (ref.)	323 (96.7)	10.0 (9.4-10.6)			
Yes	11 (3.3)	9.0 (8.4-9.6)	0.45	1.57 (0.80-3.08)	.190
Nausea/vomiting					
No (ref.)	328 (98.2)	10.0 (9.4-10.5)			
Yes	6 (1.8)	*	−0.61	0.54 (0.13-2.20)	.394
Fatigue:					
No (ref.)	315 (94.3)	10.0 (9.4-10.6)			
Yes	19 (5.7)	9.0 (8.1-9.9)	0.15	1.16 (0.63-2.14)	.632
Co-morbidity					
None (ref.)	145 (43.4)	9.0 (8.6-9.4)			
1-2	146 (43.7)	10.0 (7.9-12.1)	−0.71	0.49 (0.36-0.69)	.000
≥3	43 (12.9)	*	−2.98	0.05 (0.01-0.21)	.000
Ischemic heart disease					
No (ref.)	315 (94.3)	9.0 (8.5-9.5)			
Yes	19 (5.7)	16.0 (4.8-27.2)	−1.26	0.28 (0.09-0.89)	.031
Hypertension					
No (ref.)	220 (65.9)	9.0 (8.6-9.4)			
Yes	114 (34.1)	14.0 (3.9-24.1)	−0.73	0.48 (0.33-0.70)	.000
Diabetes					
No (ref.)	211 (63.2)	9.0 (8.6-9.4)			
Yes	123 (36.8)	14.0 (4.9-23.1)	−0.79	0.45 (0.31-0.65)	.000

(continued)

Table 1. (continued)

Variables	Total N (%)	LOS Median (95% CI)	β	HR (95% CI)	*P*-value
Cancer					
No (ref.)	326 (97.6)	10.0 (9.5-10.5)			
Yes	8 (2.4)	*	−0.70	0.49 (0.12-1.99)	.265
COPD/asthma					
No (ref.)	292 (87.4)	9.0 (8.5-9.5)			
Yes	42 (12.6)	*	−3.49	0.03 (0.00-0.22)	.001
Chronic kidney disease					
No (ref.)	320 (95.8)	9.0 (8.4-9.5)			
Yes	14 (4.2)	*	−2.01	0.13 (0.02-0.95)	.045
Respiratory rate: (in breaths per minute)					
12-20 (ref.)	104 (31.1)	9.0 (8.5-9.5)			
<12/>20	230 (68.9)	10.0 (8.7-11.3)	−0.36	0.70 (0.52-0.95)	.024
Temperature: (in degree Fahrenheit)					
95-99.4 (ref.)	297 (88.9)	10.0 (9.4-10.6)			
<95/≥99.5	37 (11.1)	9.0 (8.2-9.8)	0.38	1.46 (0.89-2.38)	.133
SpO_2: (in percentage)					
≥95 (ref.)	219 (65.6)	9.0 (8.6-9.4)			
<95	115 (34.4)	24.0 (9.3-38.7)	−1.11	0.32 (0.21-0.49)	.000
Pulse rate: (in beats per minute)					
60-100 (ref.)	213 (63.8)	9.0 (8.6-9.4)			
<60/>100	121 (36.2)	11.0 (8.3-13.7)	−0.54	0.58 (0.40-0.84)	.004
SBP: (in mmHg)					
90-139 (ref.)	232 (69.5)	9.0 (8.5-9.5)			
<90/≥140	102 (30.5)	27.0 (8.2-45.8)	−0.86	0.42 (0.28-0.63)	.000
DBP: (in mmHg)					
60-89 (ref.)	265 (79.3)	9.0 (8.4-9.6)			
<60/≥90	69 (20.7)	12.0 (4.9-19.0)	−0.70	0.49 (0.32-0.76)	.001
GCS score					
15 (ref.)	293 (87.7)	9.0 (8.5-9.5)			
<15	41 (12.3)	*	−1.61	0.20 (0.06-0.63)	.006
qSOFA score					
0 (ref.)	97 (29.0)	9.0 (8.5-9.5)			
1	198 (59.3)	10.0 (8.9-11.0)	−0.33	0.72 (0.53-0.98)	.039
≥2	39 (11.7)	*	−1.63	0.19 (0.07-0.54)	.002

Abbreviations: CI: confidence interval; COPD: chronic obstructive pulmonary disease; DBP: diastolic blood pressure; GCS: Glasgow coma scale; HR: hazard ratio; LOS: length of hospital stay (in days); qSOFA: quick sequential organ failure assessment; ref.: reference; SBP: systolic blood pressure.
*Due to right censoring in these groups median survival time could not be calculated; HR < 1 indicates higher LOS.

presence of breathlessness at admission, co-morbidities, COPD/asthma, deranged DBP, and higher qSOFA score at admission were associated with greater duration of hospitalization. Demised COVID-19 patients had shorter LOS compared to those who were discharged. Development of a scoring system inculcating found significant attributes of LOS, giving each due weightage as per their adjusted strength of association might be useful in early prediction of LOS of COVID-19 patients. Moreover, linking this scoring system with the logistic management system of the hospital might help in optimal use of the available resources. This might also help in optimizing patient care and alleviate various logistical barriers associated with it (ie, shortage of staff, beds, medicines, equipment's etc.).

We found that patients who required to travel higher distance from their native place to seek healthcare from the present healthcare facility had longer LOS. It might be because our institute is the highest referral institute for most of the healthcare facilities in the state of Bihar. Therefore, usually critically ill patients from the peripheral institutes are used to be referred to our institute. Critically ill COVID-19 patients do usually have a longer LOS, as reported by a systematic review by Rees et al[26] Similarly, we found that those who used ambulance as mode of transport to the present healthcare facility had longer LOS. It was previously known that seriously ill and/or patients needing oxygen support during transportation use ambulance as a mode of transport.[28] Thus, distance from hospital and mode of transport to

Table 2. Multivariable Cox Proportional Hazard Model Showing Factors Associated with Length of Hospital Stay Among COVID-19 Patients: n = 334.

Variables	B	aHR (95% CI)	*P*-value
Travel distance: (in kilometers)			
≤16 (ref.)			
>16	−0.37	0.69 (0.50-0.95)	.023
Mode of transport to hospital:			
Self-owned vehicle (ref.)			
Ambulance	−0.48	0.62 (0.45–0.85)	.003
Breathlessness:			
No (ref.)			
Yes	−0.59	0.56 (0.40–0.77)	.000
Co-morbidity:			
None (ref.)			
1-2	−0.42	0.66 (0.47–0.93)	.018
≥3	−1.87	0.16 (0.04–0.65)	.011
COPD/asthma:			
No (ref.)			
Yes	−2.25	0.11 (0.01–0.79)	.029
DBP: (in mmHg)			
60-89 (ref.)			
<60/≥90	−0.60	0.55 (0.35–0.86)	.009
qSOFA score:			
0 (ref.)			
1	−0.00	0.99 (0.72–1.38)	.997
≥2	−1.11	0.33 (0.12–0.92)	.034

Abbreviations: aHR, adjusted hazard ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; GCS, Glasgow coma scale; qSOFA, quick sequential organ failure assessment; ref., reference.
aHR <1 indicates higher LOS.

the hospital might serve as a reliable proxy indicator of illness severity and LOS.

In the current study, those who had breathlessness at the time of admission had longer LOS. This was analogous with the findings of Thiruvengadam et al[13] and Liu et al[18] but unlike the findings of Wu et al[17] who did not find this association. A systematic review and meta-analysis by Jain and Yuan[29] reported that dyspnea was the sole symptom which strongly predicted both intensive care unit (ICU) admission and serious disease. The said study also recommended using dyspnea as a measure of risk assessment and clinical management. Thus, breathlessness may be used as a prognostic indicator of LOS as well. With higher number of co-morbidities, LOS increased in the present study. This was identical with the finding of Thiruvengadam et al[13] which revealed similar opinion. This may be because with increased in the number of co-morbidities chances of developing a severe form of COVID-19 and mortality also reported to be increased.[30] Similarly, we observed that patients with COPD/asthma had slower recovery compared to others. A study in Mexico by Lee et al[31] reported that individuals with COPD are at higher risk of hospitalization and death owing to COVID-19. This might be because persons with chronic respiratory diseases like COPD and asthma have prevailing compromised lung function. COVID-19 infection might have further detorieted the lung function among them. This might have compelled them to hospitalize early. Unfortunately, most of them die. Those who survive recover gradually.[32,33] Patients with deranged DBP at admission had longer LOS in our study. This was in line with the findings of a study in China by Ran et al[22] which reported that with elevation of DBP hazard of mortality among COVID-19 patients also increases. We observed significant association between higher qSOFA score and LOS in the present study. qSOFA score is a previously established prognostic indicator for COVID-19.[34-36] An investigation in US by Wilfong et al[36] reported that on admission qSOFA score might predict ICU admission and fatality among COVID-19 patients.

Limitations

Despite adaptation of case-control design, we could not match background characteristics of the cases and controls. It could not be accomplished owing to restricted availability of controls for the study. However, use of simple random sampling might have alleviated chances of bias arising out of non-matching to some extent. There may be various other possible attributes (ie, nutritional status, insurance coverage, etc.) which might influence LOS of COVID patients.[20,37] Effect of these factors on LOS could not be elicited due to non-documentation of those data in our hospital records.

Conclusion

Factors elicited on arrival was found to be significantly associated with LOS. Travel distance, mode of transport to the hospital, breathlessness, number of co-morbidities, presence of COPD/ asthma, DBP and qSOFA score which are easily elicitable at the time of admission found to be significantly associated with LOS. Further research is warranted to gain more knowledge on this issue. These future studies should elicit effect of nutritional status and insurance coverage on LOS of COVID-19 patients which we could not do due lack of those data. A scoring system inculcating these factors may be developed to predict LOS of the COVID-19 patients.

Author Contributions

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity. Concept or design: N Agarwal, B Biswas, CM Singh. Acquisition of data: B Biswas, R Nair, H Haripriya, G Mounica, KM Das, AR Jha. Analysis or interpretation of data: B Biswas, N Agarwal, CM Singh. Drafting of the manuscript: B Biswas, R Nair, H Haripriya, G Mounica, KM Das, AR Jha. Critical revision of the manuscript for important intellectual content: N Agarwal, B Biswas, CM Singh, R Nair, H Haripriya, G Mounica, KM Das, AR Jha.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Issues

Ethical clearance of the Institutional Ethical Committee (IEC) of All India Institute of Medical Sciences (AIIMS), Patna (Ref. No.-AIIMS/Pat/IEC/2020/491, dated June 25, 2020) was taken before conduction of this research. Informed written consent of the study participants could not be collected because it was a retrospective analysis of regularly gathered information. Throughout the analysis and drafting of the article, confidentiality of the study participants was affirmed.

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Data Availability

All data generated or analyzed during this study are included in this published article.

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