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RESEARCH ARTICLE

DETERMINANTS OF MORTALITY IN PATIENTS OF COVID-19 BRONCHOPNEUMONIA: A PROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Background & objectives:COVID-19, an emerging viral disease affected more than 200 countries worldwide andnovel coronavirus pandemic has caused significant mortality throughout the world.The present study was undertaken to identify the determinants of mortality in COVID-19 bronchopneumonia patients.

Methods:A total of160 COVID RT-PCR and RAT positive patients with evidence of bronchopneumonia were admitted in medicine covid ward and ICU above the age of 12 years were included in the study during a period of 2.5 years from July 2020- August 2022.Patients were divided into two groups- Survivors (119 patients) and non-Survivors (41 patients). Various sociodemographic factors, clinical symptoms, NEWS-2 scores inflammatory markers,imaging modalities,oxygen levels,type and duration of oxygenation support given were compared between two groups.

Results: The sociodemographic data included age, gender and place of residence was not statistically significant with the outcome(mortality) whereas greater number of preexisting medical conditions, requirement of higher quantity of oxygen, various lab parameters (higher values of CRP, Ferritin, LDH, D-Dimer, N-L ratio) and a higher score in NEWS-2, HRCT and chest x-ray was statistically significant factor associated with mortality in our patients suffering from COVID-19 bronchopneumonia.

Interpretation & Conclusions: We thereby conclude that, patients in the mortality group had greater number of preexisting medical conditions higher requirement of oxygen at the time of admission, higher NEWS-2 score, N-L ratio, CRP, Ferritin, LDH, D-dimer, Chest x-ray score & HRCT severity score and hence these parameters may be used to predict disease severity, especially in resource-limited settings.

Introduction:-

A novel human coronavirus, SARS-CoV-2, that caused pneumonia and other complications named as COVID-19 was first reported in Wuhan, China, at the end of 2019. During the first trimester of 2020, it spread worldwide and on March 11, WHO considered COVID-19 as pandemic. As of 22 March 2020, a total of 307297 confirmed cases had been reported in at least 169 countries [1]. However, in India, the first cases of COVID-19 were reported in Kerala in January 2020, when three medical students returning from China were found to be positive. In India, the

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first wave began in March 2020 and lasted till nearly November 2020, while the second wave began in March 2021 lasting till the end of May 2021 [2].

The presentation of this disease varied widely in severity, and it mainly affected the respiratory system. It challenged the clinician with unique respiratory failure [3].At the onset ofdisease, there is apparently normal lung mechanics and no clinical clue of derangement in airway resistance or dead space ventilation. Various factors like impaired lung diffusion especially due toformation of intravascular microthrombi lead to an array of changes in gas exchange leading to adecrease in the partial pressure of oxygen in the blood [4]. Hence an unusual feature of COVID-19 pneumonitis is severe hypoxemia with normal lung mechanics [5]. This unique pathophysiology of disease thus tricks the respiratory center that fails to sense hypoxia-related dyspnea. Usually, there is a gross mismatch between extent of arterial hypoxemia and signs of respiratory distress in these patients [6]. Thus, the term "happy hypoxemia" (severe hypoxia without dyspnea) came to existence in the presentation of such pneumonia during the COVID-19 pandemic.

Knowledge on the association between demographic factors and different severity stages of COVID-19 such as infection, severe disease, ICU admission and death may provide insight into the underlying pathophysiological mechanisms (immunity, coagulopathy, and comorbidities) [7]. Moreover, severe, or critical COVID-19 is strongly linked with mortality [8] and the high mortality rate amongst these cases is linked with SARS-CoV-2 infection-induced hyperinflammation of the innate and adaptive immune systems and the resulting cytokine storm, a cytokine release syndrome (CRS)-like syndrome in severe/critical COVID-19 cases [9, 10]. Previous studies have reported that the inflammatory parameters are closely linked to the COVID-19 severity and mortality [11, 12]. In addition, two recent meta-analyses have also shown an association of inflammatory parameters with the COVID-19 severity [13, 14]. However, with an increase in the number of studies now published, it is important to carry out more comprehensive reviews and analyses of inflammatory parameters linked to COVID-19 severity. Therefore, the aim of this prospective observational study was to describe the association between demographic factors, clinical and radiological parameters affecting mortality in COVID-19 bronchopneumonia.

Material and Methods:-

The present prospective observational study was conducted in Medicine COVID ICU and medicine COVID positive wards at tertiary care centre in central India during a period of 2.5 yearsfrom July 2020 to August 2022. A total 160COVID RT-PCR and RAT positive patients with evidence of bronchopneumonia were admitted in medicine covid ward and ICU above the age of 12 years and consenting were included in the study.Non-consenting patients and patients with age less than 12 years were excluded from the study. Selected patients were divided into two groups- Survivors (119 patients) and non-Survivors (41 patients). Various sociodemographic factors, clinical symptoms, NEWS-2 scores inflammatory markers, imaging modalities, details about their blood sugar levels, oxygen levels, type and duration of oxygenation support given, and treatment modalities were compared between two groups.

Samples collected in Nasopharyngeal Oro-pharyngeal swabs in VTMs. VTMs was sent to the lab maintaining the cold chain and patient details was recorded.PCR result interpretation was done as per kit insert. Processed in Microbiology lab in our hospital in QUANTS and BIORAT machine.

Statistical analysis

For statistical analysis data were analyzed by SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and Graph Pad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. A chi-squared test ($\chi 2$ test) was any statistical hypothesis test wherein the sampling distribution of the test statistic was a chi-squared distribution when the null hypothesis is true. Without other qualification, 'chi-squared test' often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate.In each case, the formula for a test statistic that either exactly follows or closely approximates a t-distribution under the null hypothesis was given. Each of these statistics can be used to carry out either a one-tailed test or a two-tailed test. Once a t value was determined, a p-value can be found using a table of values from Student's t-distribution. If the calculated p-value was below the threshold chosen for statistical significance (usually the 0.10, the 0.05, or 0.01 level), then the null hypothesis was rejected in favor of the alternative hypothesis. p-value ≤ 0.05 was considered statistically significant.

Results:-

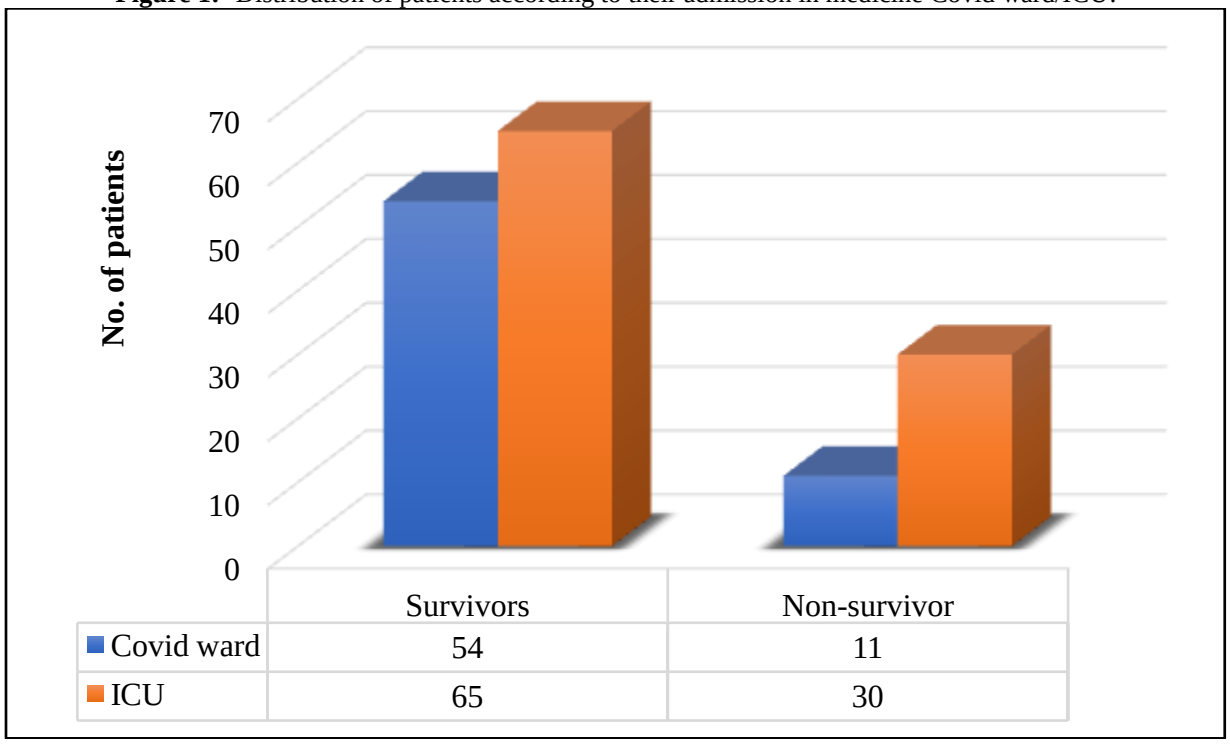
A total of 160 patients were included in this study and were divided into two groups i.e. Survivors (119 patients) and Non-Survivors groups (41 patients). Association of age (p=0.0551), gender (p=0.4259) and residence (p=0.3722) with mortality was not found to be statistically significant as shown in table 1.

Table 1:- Socio-demographics profile of patients.

Socio-demographics data		Survivors	Non-Survivors	P value
Age groups (years)	<20	7(5.9%)	8(19.5%)	0.0551
	21-30	16(13.4%)	6(14.6%)	
	31-40	24(20.2%)	3(7.3%)	
	41-50	23(19.3%)	2(12.2%)	
	51-60	17(14.3%)	2(4.9%)	
	61-70	10(8.4%)	7(17.1%)	
	71-80	7(5.9%)	6(14.6%)	
	81-90	15(12.6%)	4(9.7%)	
	Mean	48.30±20.55	51.95±24.43	0.3524
Gender	Female	52(43.7%)	15(36.6%)	0.4259
	Male	67(56.3%)	26(63.4%)	
Residence	Rural	75(63.0%)	29(70.7%)	0.3722
	Urban	44(37.0%)	12(29.3%)	

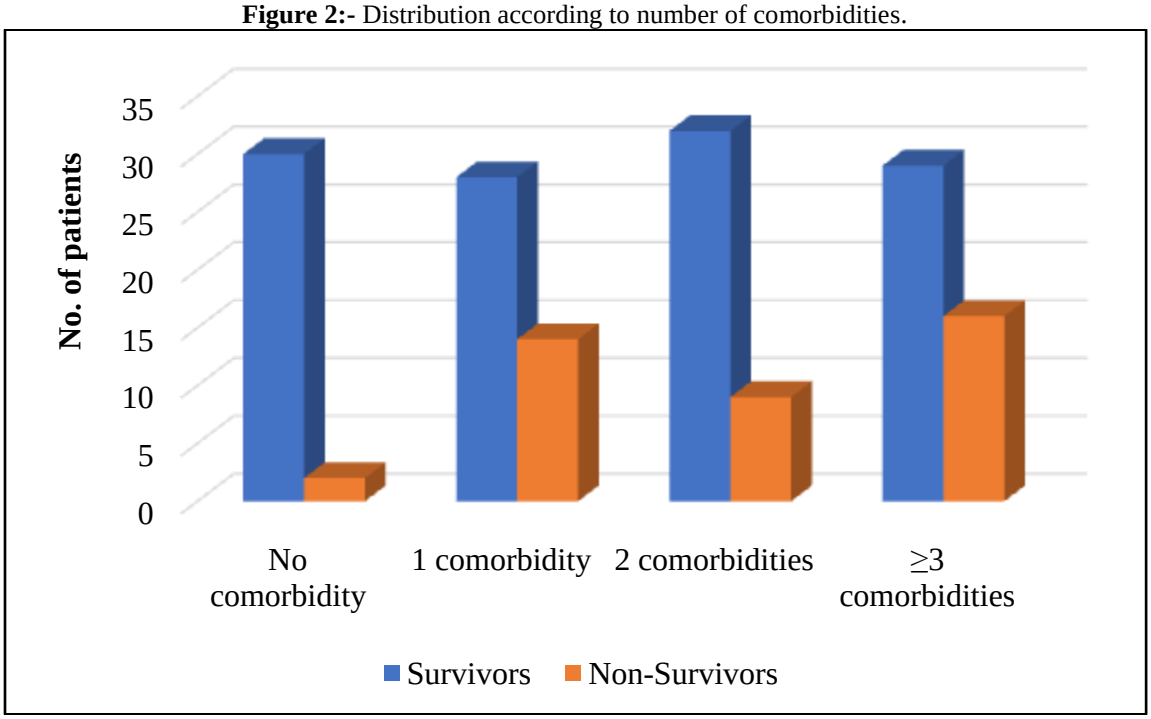
Out of 160 patients, 65 were admitted in COVID medicine wards and 95 patients were admitted in COVID ICU.The mortality was more in patients admitted in COVID ICU. Association with survival was statistically significant in patients admitted in medicine covid ward as compared covid ICU wards (p=0.0370), (figure 1).

Figure 1:- Distribution of patients according to their admission in medicine Covid ward/ICU.



Association of number of comorbidities with outcome was statistically significant (p=0.0167). Distribution of patients according to comorbidity is depicted in figure 2.

Figure 2:- Distribution according to number of comorbidities.



Association of O2 mask (4-8L), NRBM (8-15l), HFNO (15-60l), NIV and mechanical ventilation with outcome as mortality was statistically significant (p=0.4763) and distribution is shown in figure 3.

Figure 3:- Distribution according to type of oxygen support required at the time of admission.

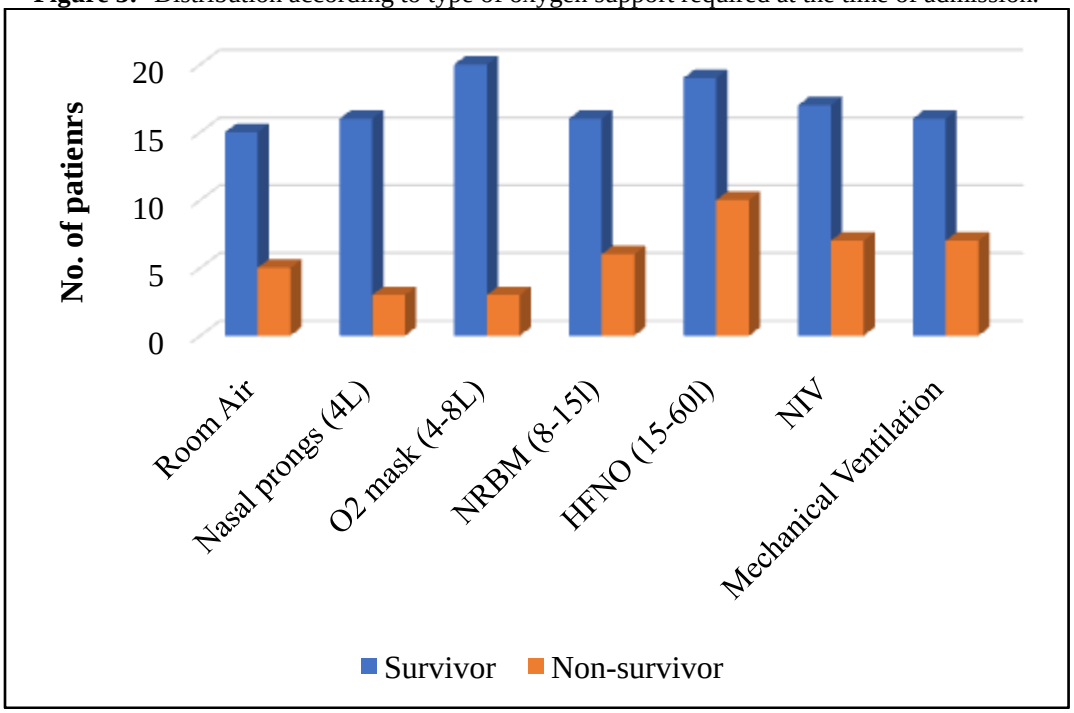


Table 2 showed that, higher values of CRP, Ferritin, LDH, D-Dimer and N-L ratio at the time of admission was significantly associated with mortality in our patients of COVID-19 Bronchopneumonia. Whereas mean CRP (p=0.0012) and mean N-L ratio (p=0.0002) when compared between the two groups was found to be statistically significant with mortality.

Table 2:- Lab parameters (CRP, Ferritin, LDH, D-Dimer, N-L ratio).

Lab parameters		Survivors	Non-survivors	P value
CRP (mg/l)	>25	19 (16%)	2 (4.9%)	0.0480*
	26 to 50	22 (18.5%)	3 (7.3%)	
	51 to 75	19 (16%)	8 (19.5%)	
	>76	59 (49.6%)	28 (68.3%)	
	Mean	84.8479±58.8224	124.0244±81.6308	0.0012*
Ferritin (µ/l)	<250	07 (5.9%)	00 (0.0%)	0.0120*
	251 to 500	09 (7.6%)	02 (4.9%)	
	501 to 750	27 (22.7%)	07 (17.1%)	
	751 to 1000	09 (7.6%)	08 (19.5%)	
	>1001	67 (56.3%)	24 (58.5%)	
	Mean	1090.0769±625.3558	1220.9024±586.4992	0.2434
LDH (IU/L)	<400	04 (3.4%)	00 (0.0%)	0.0131*
	401 to 600	22 (18.5%)	03 (7.3%)	
	601 to 800	29 (24.4%)	04 (9.8%)	
	801 to 1000	22 (18.5%)	08 (19.5%)	
	>1001	42 (35.3%)	26 (63.4%)	
	Mean	948.7815±432.1744	810.1951±436.2973	0.0792
D-Dimer (mg/l)	≤5	60 (66.7%)	05 (33.3%)	0.0138*
	>6	30 (33.3%)	10 (66.7%)	
	Mean	1419.6329±1016.4234	1801.1818±1142.5501	0.1329
N-L ratio	<3	86 (72.3%)	18 (43.9%)	0.0010*
	>3	33 (27.7%)	23 (56.1%)	
	Mean	2.4536±.6892	2.9425±.7798	0.0002*

A higher score in NEWS-2, HRCT and chest x-ray was statistically significant factor associated with mortality in our patients suffering from COVID-19 bronchopneumonia. Also, the association of mean of NEWS 2 score, CXR score and HRCT severity score with mortality was found to be statistically significant as shown in table 3.

Table 3:- NEWS-2 score and radiological parameters.

Variables		Survivors	Non-survivors	P value
NEWS 2 score	≤3	14 (11.8%)	01 (2.4%)	0.0004
	4 to 6	60 (50.4%)	10 (24.4%)	
	>7	45 (37.8%)	30 (73.2%)	
	Mean	6.1092±2.3607	11.0000±4.8734	<0.0001
Chest X Ray score	0 to 3	20 (16.8%)	01 (2.4%)	0.0159
	4 to 6	13 (10.9%)	07 (17.1%)	
	7 to 9	23 (19.3%)	06 (14.6%)	
	10 to 12	37 (31.1%)	09 (22.0%)	
	13 to 15	16 (13.4%)	08 (19.5%)	
	16 to 18	10 (8.4%)	10 (24.4%)	
	Mean	9.0672 ±4.6845	11.2195 ±4.6503	0.0120
HRCT severity score	5 to 10	27 (31.4%)	02 (5.9%)	0.0200
	11 to 15	21 (24.4%)	10 (29.4%)	
	16 to 20	16 (18.6%)	12 (35.3%)	
	21 to 25	22 (25.6%)	10 (29.4%)	
	Mean	15.1688±5.7271	12.1875±6.3166	0.0181

Discussion:-

In the present study, most of patients were from the age group of 41-50 years (28;17.5%) but it did not have any significant effect on mortality (p=0.0551). The mean age in non-survivors was 51.9512±24.4386 years and in survivors it was 48.3025±20.5507 years which was not statistically significant. These finding comparable with the study done by Yanez ND et al [15] and Ho FK et al [16]. Male population was higher [93 (58.1%)] than the female

population [67 (41.9%)]. Male: Female ratio was 1.4:1 but this was not statistically significant (p=0.4259) factor contributing to severity of the disease. The mortality was higher in our study subjects who hailed from rural areas [29 (70.7%)] as compared to those from urban areas [12(29.3%)] but was not a significant contributor (p=0.3722) towards severity of disease. A study conducted by Peters DJ et al in the United States, concluded that about 33% of rural countries are highly susceptible to COVID-19 [17]. Major vulnerabilities in rural counties include fewer physicians, lack of mental health services, higher disability, Poor Internet access limits telemedicine, Lack of social capital and social services may hinder local pandemic recovery.

After dividing study subjects into two groups –Survivors and Non survivors, we examined our subjects for various medical conditions they had and studied their effect on the mortality in covid-19 bronchopneumonia. Various comorbidities included Hypertension, diabetes,chronic kidney diseases, chronic liver disease, cerebrovascular accidents, ischemic heart disease, respiratory disease(COPD, asthma, TB),immunocompromised statuses were studied. We observed that the study subjects having higher the number of pre-existing medical conditions (≥3 comorbidities) in Non-survivors Group [16 (39.0%)] compared to Survivors Group [29 (24.4%)] being the highest) significantly increased the severity of Covid-19 bronchopneumonia leading to mortality of the patient (p=0.0167). Similar findings are reported in previous studies [18-20].

The present study showed that patients on room air at the time of admission had a higher chance of survival as compared to those requiring oxygen. While patients requiring oxygen at the time of admission, the higher the requirement of oxygen, the higher the association it had with mortality with maximum mortality in patients requiring HFNO, NIV and mechanical ventilation. These results are correlated with the study done by Zirpe KG et al [2].

In the maximum number of non survivors, we found higher values of inflammatory markers (CRP, Ferritin, LDH, D-Dimer) which were significantly associated with mortality in covid-19 bronchopneumonia (p<0.05). Other studies supportive of our findings [20, 21].

We found that, the mean NEWS 2 score was more in non-survivors [11.0000±4.8734] compared to Survivors [6.1092±2.3607] suggesting that higher NEWS-2 score was predictor or morbid outcome in our study patients (p<0.0001) which is comparable with the study conducted by Baker KF et al [22]. N-L ratio <3 in Survivors Group [86 (72.3%)] compared to Non-Survivors Group [18 (43.9%)] suggesting that lower N-L ratio had a fairer outcome for survival of our study subjects (p=0.0010). We found that, patients having N-L ratio >3 had higher mortality, suggestive of higher N-L ratio significantly associated to mortality. This is in accordance with the other studies [23, 24].

In the current study, patients who had a score Chest x-ray score of 10-12 had higher mortality. higher HRCT severity score was associated with higher mortality and highest mortality (12) occurred in the score group between 16-20. This finding is comparable with the study done by Sharma S et al [25]. Our study showed that, patients having a RALE (Radiographic Assessment of Lung Edema) score of >4 were having a higher association with mortality as an outcome which is correlated with Hoang-ThiTN et al [26] andCozzi D et al study [27].

There are some limitations of the study which includes- small sample size; the study has been done in a single tertiary care Centre, so hospital bias cannot be ruled out. The study subjects were selected only from those who were admitted in medicine covid wards, and ICU The lab parameter values considered in the study have been taken from the investigations done on the day of admission and serial investigations were not taken.

Conclusion:-

The present study concluded that, the patients in the mortality group had greater number of preexisting comorbidities, higher requirement of oxygen at the time of admission, higher NEWS-2 score, N-L ratio, CRP, Ferritin, LDH, D-dimer, Chest x-ray score & HRCT severity score and hence these parameters may be used to predict disease severity, especially in resource-limited settings.

Conflicts of Interest:
None.

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