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Initial oxygen saturation at presentation as a predictor of mortality in COVID19 positive cases in a tertiary care center in South India

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Abstract
Background: *The Rapid emergence of novel COVID 19 infections has resulted in infection to millions of people and hundreds of deaths around the world. India is ranking second in terms of the number of Covid19 cases. Although there is no specific treatment for COVID, early recognition and supportive treatment can help in reducing mortality.*
Materials and methods: *aim of this study is to describe the association between the initial oxygen saturation when the patient presented to the hospital and the risk of mortality.This is a retrospective study of all laboratory confirmed cases of covid-19 patients admitted in Government Hospital for Chest and Communicable diseases (GHCCD), tertiary hospital in Visakhapatnam from April to June month of 2021. Demographic, clinical history, initial oxygen saturation, comorbidities, and outcome data were collected from Government hospital for chest and communicable diseases and were entered in MS Excel. The data was analyzed using univariate binomial logistic regression, generalized linear model with poisson distribution.*
Results: *By using multiple Cox regression, oxygen saturation values of less than 90% on admission correlated with mortality, presenting 1.67(95% CI 1.02-3.36), 2.23(95% CI 1.89-5.63), 4.89(95%CI 3.02-8.09), 6.97(95% CI 4.63-11.07), 9.87(95%CI 5.23-13.53) times greater risk of death for spo2 of 89-80,79-70, 69-60, 59-50, 49-40 respectively, when compared to patients with spo2 >90%. We included 306 covid 19 positive patients with a median age of 46 years. Of these, 64.05% were males and 36.94% were females. Risk associated with worse outcome included males, old age, comorbidities like hypertension (47.38%), diabetes (37.58%), cardiac disease (4.9%), Hypothyroidism (3.26%), CKD(3.26%), malignancies (1.63%).*
Conclusions: *SPO2 below 90% on admission is a strong predictor of mortality in patients with COVID19. Risk factors for poor outcomes among covid-19 cases include old age, males, diabetic patients, hypertensive patients, cardiac patients, and chronic kidney disease patients.*
Keywords: *COVID-19, SARS CoV-2, risk factors, mortality, Spo2*

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I. Introduction:

The rapid emergence of the novel corona viruses has led to infection to millions of patients and death of hundreds of thousands of patients worldwide. In India, the total numbers of confirmed cases as of 30 June 2021 are 3.03 crore out of which 2.94 crore cases recovered and 3.98 Lakh cases died[1]. It is difficult to control the spread of covid 19 infection. Most of the COVID19 patients experience mild symptoms only, but some develop more severe disease requiring hospitalization. About, 14 to 30% of in-patients further need admission in ICU[2]. Mortality in hospitalized COVID-19 patient's ranges from 13.2% to 28.3% [2]. Efforts should focus on effective measures to minimize the disease impact on those who are prone to develop adverse outcomes. Healthcare services become compromised due to the rapid increase in infected patients[2]. Overwhelming of the healthcare system leads to an unexpected rise in mortality and morbidity[3]. Therefore, it is important to risk stratify COVID-19 patients on the basis of predicted outcomes and guide treatment accordingly[4].

Several countries have seen a two-wave pattern of reported cases. In India, the first wave of COVID-19 began in June 20, 2020 and lasted until August 2020, although some isolated cases had been reported in September 2020 to February 2021. As a consequence of the first outbreak, the Indian government introduced a series of strict prevention measures, which was followed by a period of progressively increasing social interaction, work and commercial activity. As of March 2021, life in the country has returned to relative normality, except for a facemask and safe social distancing. Unfortunately, the number of COVID 19 cases

began to increase towards the end of April and it once again presented numbers similar to 2020. This forced the government to introduce serious restrictive measures, including lockdowns, curfew after 12 noon until 6 AM.

The clinical manifestation of COVID-19 is broad and ranges from asymptomatic and mild upper respiratory tract symptoms to severe illness and death[5]. It is also very difficult to predict beforehand the clinical course and risk of deterioration in COVID-19 patients[6]. Previous studies have identified that older age and male gender are at risk for severity and higher mortality7. Some distinct symptoms and laboratory findings were correlated with poor outcomes[8]. Other comorbidities that were found to be associated with poor prognosis were cardiovascular disease, diabetes mellitus, chronic respiratory disease, and hypertension[9]. However, it is difficult to generalize these studies in countries like India with a lot of diversity, where the presentation of COVID is different among different states. Literature regarding the risk factors and prognostic factors for covid19 in hospital mortality is limited in India.

With this background, this study was conducted to investigate the severity and characteristics of hospitalized patients in GHCCD, Visakhapatnam. We have assessed the risk factors for death among COVID-19 patients. We have evaluated age, gender, comorbidities, mortality, and outcomes in COVID 19 patients.

II. Materials & Methods

The study type that we have conducted is a retrospective cohort study. It is conducted in GHCCD (Government hospital for chest and communicable diseases), which is a tertiary care Government hospital in Visakhapatnam. We have collected data from all laboratory confirmed cases located in GHCCD (government hospital for chest and communicable diseases) in the period between April 2021 and June 2021. GHCCD is a tertiary care institute equipped with around 300 beds. It was designated as Dedicated COVID health care centre (DCHC). Standard care is being provided free of cost to COVID patients seeing care at the hospital as per the Ministry of Health and Family Welfare, Government of Andhra Pradesh.

Study design: Restrospective observational cohort study.

Study Location: This was a tertiary care teaching hospital based study done in Department of pulmonary medicine, at government hospital for chest and communicable diseases, Pedda Waltair, Visakhapatnam, Andhra Pradesh.

Study Duration: April 2021 to June 2021

Study size: 1041 patients

The selection criteria for the study included all critically ill patients who tested RTPCR positive for COVID-19 on nasopharyngeal swab/ oropharyngeal swab, and got admitted in the hospital and died during treatment. In parallel with the WHO protocol, COVID-19 was diagnosed based on the results of qualitative RT-PCR testing from nasopharyngeal samples/oropharyngeal swabs taken from suspected patients who were admitted in the hospital. Case sheets of all COVID-19 positive patients who died during the treatment in the hospital were collected. The Demographic, clinical, laboratory, and comorbidity data of COVID 19 positive patients who died were collected and entered in MS excel. The variables that were collected from the case sheets included age, gender, personal history of smoking and alcohol intake, comorbidities like diabetes, hypertension, cardiac diseases, chronic kidney disease, hypothyroidism, malignancies. A total of 1041 patient's case sheets of COVID confirmed cases were collected. Out of which case sheets of COVID 19 patients who died were separated and analyzed. Age and gender distribution of mortality of COVID19 positive patients were calculated. The risk of mortality due to comorbidities was compared between the patients who died and patients who got discharged.

Statistical analysis:

Data were entered using Microsoft Excel and analysis was done using STATA statistical software version 14. 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 the data. The categorical variables are summarized as frequency and proportions. Categorical variables underwent a test of association using the chi-square test or Fisher exact test. The data was analyzed using univariate binomial logistic regression to analyze the risk factors associated with covid 19 mortality. The strength of association is expressed as relative risk with 95% confidence intervals. Survival curves were made using the Kaplan-meier method. Long-rank test was used to test the equality of survivor functions between the groups.

Ethical consideration: Ethical approval was taken from the Andhra Medical College ethics committee to which the hospital is affiliated before the study was conducted.

III. Results

Between April 1st 2021 and June 29, 2021, a total of 1041 COVID-19-positive cases were screened, 306 patients died, and 735 patients were discharged. The patients included in the study had a mean age of 46.9 years. The median duration of symptoms prior to hospital admission was 6 days (IQR: 4-9). In-hospital

mortality was 38.5%. By using multiple Cox regression, oxygen saturation values of less than 90% on admission correlated with mortality, presenting 1.67(95% CI 1.02-3.36), 2.23(95% CI 1.89-5.63), 4.89(95%CI 3.02-8.09), 6.97(95% CI 4.63-11.07), 9.87(95%CI 5.23-13.53) times greater risk of death for spo2 of 89-80,79-70, 69-60, 59-50, 49-40 respectively, when compared to patients with spo2 >90%. The distribution of gender in COVID mortality cases was males constituted 64.05% (n=196) and females constituted 35.94% (n=110) as shown in figure 1. The median survival time of male COVID19 patients (9days) was lesser than the female COVID19 patients (15 days) and the difference was statistically significant (p value < 0.023). The results (table.1) show that as the age increased, the risk of death due to COVID-19 also increased. when compared to the 31 – 40 years age group, patients with 41-50 years age had 1.6 (95%CI: 0.9-2.8) times increased risk of mortality. 51-60 year old had 2.7 (95% CI: 0.9 – 2.8) times increased risk of mortality. 61-70 -year-old patients had 2.8 (95% CI: 1.1 – 6.9) time increase risk of dying and 71-80 years age group had 3.8 (95% CI: 1.2-7.8) times increased risk of mortality.

Figure 1. Gender distribution among the COVID 19 patients who died.

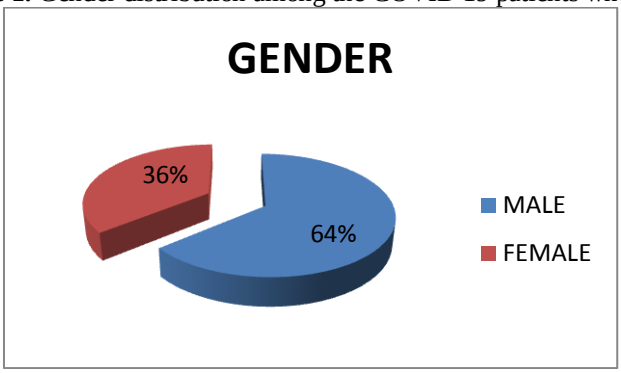

Figure2. Gender distribution among the COVID19 patients who got discharged.

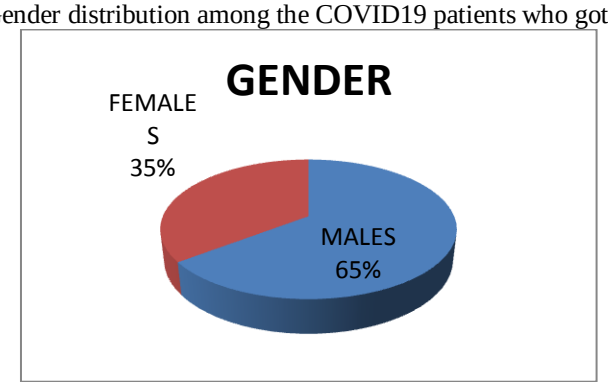

Figure 3. Median survival time among males and females

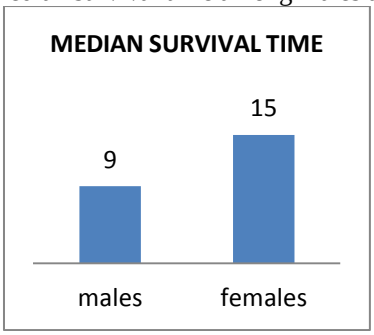

Table 1: Age distribution among COVID19 patients admitted to the tertiary care centre

Characteristics	Categories	Discharged N=1041	Died n=306	RR(95%CI)	aRR(95%CI)	P-value
Age	20-30	4	0	0.6(0.3-1.7)	0.4(0.2-1.4)	0.04
	31-40	84	21	1.3 (0.5-2.8)	1.0(0.6-1.9)	0.03
	41-50	195	59	1.6 (0.9-2.8)	1.8(0.9-2.1)	0.04
	51-60	165	78	2.7(0.9-5.1)	2.1(1.1-3.3)	0.002
	61-70	125	91	2.8(1.1-6.9)	2.4(1.3-4.5)	0.003

	71-80	162	56	3.8(1.2-7.8)	3.3(1.7-5.9)	0.001

Table 2: Gender distribution

Gender		Discharged	Died	RR(95%CI)	Arr(95%CI)	P-value
	Male	490	196	1.9(0.8-5.9)	0.7(0.4-3.4)	0.016
	Female	245	110	1.1(0.7-4.5)	0.5(0.3-3.2)	0.012

The comorbidities with which COVID19 patients most commonly presented were hypertension (47.38%), diabetes (37.58%). Other comorbidities were cardiac disease (4.9%), hypothyroidism (3.26%), CKD (3.26%),and malignancies (1.63%). COVID 19 patients with comorbidities had 3.4(95CI: 2.3-5.4) increased risk of death than patients with no comorbidities. Hypertension was the most common comorbidity followed by diabetes mellitus with which the COVID 19 patients presented to the hospital. Hypertensive patients had increased risk of mortality by 4.5(95% CI: 0.8 – 6.7). Diabetic patients had increased risk of mortality by 3.3 (95% CI: 0.9 – 7.8). Risk of mortality in COVID-19 patients with CKD was 3.2(95% CI: 0.7 – 4.9) and cardiac illness 2.9 (95% CI: 0.6 – 4.8) figure 3.

Table 3: Comorbidities

		Discharged	Died	RR(95%CI)	Arr(95%CI)	P-value
Diabetes		456	115	3.3(0.9-7.8)	1.8(1.1-2.9)	0.015
Hypertension		367	145	4.5(0.8-6.7)	1.7(0.7-3.2)	0.018
Cardiac		35	15	2.9(0.6-4.8)	1.8(0.9-4.9)	0.019
CKD		24	10	3.2(0.7-4.9)	2.3(0.8-5.2)	0.009
NEURO		9	4	3.3(0.9-5.7)	4.5(0.7-5.4)	0.008
Hypothyroid		14	2	2.1(0.8-3.7)	3.5(0.9-5.6)	0.015
Malignancy		4	1	1.0(0.4-2.7)	1.2(0.6-3.2)	0.016

Table 4. Oxygen saturation in adult hospitalized patients with COVID-19

Oxygen saturation	RR (95%CI)	Arr (95%CI)
>90%	Ref	Ref
89-80%	1.56(1.02-3.36)	1.43(1.0-2.34)
79-70%	2.23(1.89-5.63)	2.07(1.07-4.67)
69-60%	4.89(3.02-8.09)	3.34(2.45-6.89)
59-50%	6.97(4.63-11.07)	5.87(4.45-10.87)
49-40%	9.87(5.23-13.53)	8.76(6.73-12.45)

IV. Discussion

The most striking finding of our study is that the degree of hypoxemia on admission was independently associated with in-hospital mortality. The relationship between hypoxemia on admission and in-hospital mortality was previously described in China and USA. Petrilli et al. found spo2<88% on admission was associated with higher mortality. In these studies, the proportion of patients with hypoxemia was lower when compared to our study. These findings could suggest that a higher proportion of patients from our cohort were hospitalized too late after developing severe hypoxemia, which resulted in higher mortality. This suggests late presentation which may be due to lack of awareness of alarming signs, fear of going to hospital, and other limitations like lack of access to emergency care near the residence. Newer strategies are required to detect such patients early during the disease, like making available a pulse oxymeter to each family for monitoring hypoxia. Measuring tachypnea could be an alternative predictive factor for mortality which is simple and inexpensive.

The results of our study also show that increasing age, male gender, comorbidities such as diabetes mellitus, hypertension, CKD, cardiac disease, and malignancy were significantly associated with higher mortality in COVID 19 patients. In our study, male COVID19 patients they showed higher mortality and higher risk ratio. Meta analysis done by Hannah Peckham also showed higher mortality in male COVID19 patients[10]. Our study shows that increasing age has the higher risk of covid-19 mortality in Indian population. Metanalysis done by Clara Bonanad also shows that COVID19 patients have increased mortality with increasing age[11]. Immunisenescence (ageing causing decline in immune function), presence of comorbidities, mucosal barrier changes could be the reasons for the increased covid-19 mortality risk among older patients.

The presence of any comorbidity increased the risk of mortality by 4 times in our analysis, which is similar to other studies. Diabetes and hypertension are the most common comorbidities which were associated with increased COVID-19 mortality. Meta analysis done by Giovanni Corona showed higher mortality in COVID19 patients having diabetes mellitus[12]. This may be due to the altered immune response caused by diabetes and hypertension. Studys done by T. M. Cook showed higher mortality in COVID19 patients with associated hypertension as comorbidity[13]. Our study also showed that CKD patients are 5 times more at risk of COVID-19 mortality. Other comorbidities that were associated with higher mortality were cardiac disease, neurologic diseases, hypothyroidism, Malignancies.

Limitation of this study is that it is a record-based study done in a dedicated respiratory centre. Therefore patients with other comorbidities might be less, especially cardiac, renal, and pregnant women.

V. Conclusion

To conclude, we need a better and faster way to recognize hypoxemia in the community setting, which became challenging in the context of "silent hypoxemia" that many of the COVID-19 patients experience during illness. In our study, we found that increasing age, male gender, and presence of comorbidities are associated with significant risk factors for mortality due to COVID-19. Early identification of patients with these risk factors and appropriate treatment is important to prevent death among COVID-19 patients. COVID-19 patients with these risk factors should be given appropriate inpatient care than domiciliary management to prevent fatal outcomes among high risk patients.

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