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Demographic Perspectives on Covid 19 Mortality in a Tertiary Care Hospital

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Abstract

Aim: To study the demographics, baseline comorbidities and clinical course of patients who succumbed due to COVID 19 infection.

Materials and Methods: A single-centre, cross-sectional, observational study was conducted among SARS-CoV-2 infected patients from March 2020 to Dec 2020.

Results: A total 704 patients who succumbed to COVID 19 were studied. The mean age was 59.38±10 years with the male preponderance of 68.9%. Diabetes mellitus and Hypertension almost had the similar prevalence i.e; 381 (54.1%) and 374 (53.1%) respectively. 614 (87.2%) patients required ICU admission and mean duration of stay among them was 96.08 ± 105.070 hrs. 571(81.1%) of them were intubated and required mechanical ventilation. The mean duration of mechanical ventilation was 27.51 ± 49.57 hrs. 282 (40.1%) patients received Remdesivir injection with the mean duration of 4.24 ± 1.426 days. Acute respiratory distress syndrome was the major cause of death. 420 (59.7%) had only ARDS whereas 106 (15.1%) had ARDS complicated by Sepsis and 105 (14.9%) had ARDS complicated by MODS and Sepsis.

Conclusion: During the first wave of COVID 19 pandemic in India, mortality seems to be higher in older individuals with male preponderance. Major comorbidities associated among those who succumbed to COVID 19 were diabetes and hypertension. Maximum number of deaths were in ICU who required mechanical ventilation. Acute respiratory distress syndrome was the major cause of death complicated by sepsis and MODS

Keywords: Covid 19 mortality, ARDS, Remdesivir, Mechanical ventilation

Introduction

COVID-19 infection, which first reported as a cluster of pneumonia from Wuhan, China, in December 2019, has rapidly emerged as a global pandemic and has endangered human lives[1].

By September 9 2021, more than 33 million confirmed cases of COVID-19 were reported in India, representing the second-highest total of any country after the USA[2].

Although India has reported 441749 COVID-19 deaths, this substantial burden nonetheless represents a lower overall fraction of fatal cases than other settings have shown[3,4]. Hypothesis addressing this apparent gap have surrounded both the younger age distribution of India's population[5]. and possible undercounting of deaths attributable to COVID-19, which has been reported in other low-income and middle-income countries[6,7].

However, large-scale studies of SARS-CoV-2 infection and mortality in India are scarce, hindering

efforts to compare COVID-19 epidemiology against observations in other settings.

This condition is associated with high morbidity, leading to significant burden on health care infrastructure and resources. The associated fatality rate is also higher than other respiratory viral infections.

The immune system plays an important role in disease severity. A combination of underlying comorbidities such as hypertension, diabetes, obesity, cardiovascular and chronic renal diseases contribute to disease severity by up-regulation of ACE 2 receptor, immune system dysfunction and also by causing alveolar and endothelial dysfunction[8]. The most common comorbidities reported till date includes hypertension, cardiovascular diseases and diabetes mellitus and these patients are most prone to develop ARDS, severe pneumonia and multi organ failure[9,10].

Patient's sex, age, and comorbidity may act as triggers for increased risk of either infection or mortality caused by COVID-19.

Hence studying the correlation of the factors with mortality is important to understand the disease well and thus establish robust evidence regarding associations.

Materials And Methods

This was a single-centre, cross-sectional, observational study, conducted among patients admitted under General Medicine department at Victoria Hospital, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India. The study included all deceased patients between March 2020 and December 2020 during the first wave of COVID 19 who were diagnosed with SARS-CoV-2 infection by RT-PCR technique.

Sample size estimation:

Where, n = no of sample size

$Z_{(1-\alpha)}$=1.96 at 95% Confidence interval

p= proportion = 18.6%

q= 100-p = 100-18.6 = 81.4 %

d= absolute precision = 3%

on substitution,

$$n = \frac{4 \times 18.6 \times 81.4}{3^2}$$

n = 672

Therefore, the sample size is rounded up to 700 approx

Data was obtained from patient records available at Hospital Medical Records Department. Patients data such as age, sex, previous hospitalization history, ICU admission, duration of hospital stay from admission till death, duration of mechanical ventilation, usage of novel therapy and the cause of death and complications associated were recorded and analyzed.

Statistical Analysis:

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Continuous data was represented as mean and standard deviation. **Graphical representation of data:** MS Excel and MS word was used to obtain various types of graphs such as bar diagram and Pie diagram.

p value(Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

Results:

Age And Sex Distribution: Table 1 And Table 2

A total of 6748 COVID 19 cases were admitted from March 2020 to December 2020, out of which, there were 704 deaths. Among these deceased patients, 485 (68.9%) were males and 219 (31.1%) were females. The mean age in years was 59.38± 10 years, of which the older population aged >60 years constituted 48.2% (339) of the total deaths. Maximum deaths were in the age group of 50-70 years.

Associated Conditions And Comorbidities (Table 3 and Table 4)

Among comorbidities majorly contributing to mortality were, Diabetes mellitus and Hypertension which almost had the similar prevalence i.e.381 (54.1%) and 374 (53.1%) respectively. Other major comorbidities were chronic kidney disease 155

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(22%), ischemic heart disease 115 (16.3%), Cerebrovascular accidents 54 (7.7%), Chronic airway disease including Bronchial Asthma and COPD 34 (4.8%), Hypothyroidism 29 (4.1%), Various malignancies 26 (3.7%) and Pulmonary tuberculosis 11 (1.6%). Other minor conditions that directly or indirectly contributed to mortality were Chronic liver disease 11 (1.7%) epilepsy 9 (1.3%), Alzheimer's 8 (1.1%), Obesity 5 (0.7%), OSA 2 (0.3%), OSA with obesity 4 (0.6%), Mucormycosis 2 (0.3%), Parkinson's disease 5 (0.7%), SLE 1 (0.1%). Out of the deceased, 2 were pregnant.

Icu Admission And Mechanical Ventilation (Table 5)

614 (87.2%) patients required ICU admission and mean duration of stay among them was 96.08 ± 105.070 hrs. 571(81.1%) of them were intubated and required mechanical ventilation. The mean duration of mechanical ventilation was 27.51 ± 49.57 hrs. 18 (2.6%) patients were intubated at outside hospital.

Immunomodulators (Table 6)

282 (40.1%) patients received Remdesivir injection with the mean duration of 4.24 ± 1.426 days. 9 patients had received Plasma therapy, 8 had received Tocilizumab and 2 had received both Plasma therapy and Tocilizumab along with Remdesivir therapy.

Cause Of Death And Complications Associated (Table 7)

Acute respiratory distress syndrome was the major cause of death. 420 (59.7%) had only ARDS whereas 106 (15.1%) had ARDS complicated by Sepsis and 105 (14.9%) had ARDS complicated by MODS and Sepsis. Other causes that contributed to mortality were Acute coronary syndrome 31 (4.4%), Aspiration pneumonitis 12 (1.7%), Encephalopathy secondary to Hepatic, metabolic and uremic causes constituted 23(3.3%), Cardiogenic shock 3 (0.4%) and 1 patient died of Pulmonary embolism.

Discussion

Age And Sex Distribution

Our study showed patients aged more than 50 years were affected more with male preponderance. Similarly, a meta-analysis done by Mohitosh Biswas et al, also showed a male preponderance[11]. Some of the hypothesis proposed were that male patients have higher expression of ACE 2 which maybe partly because ACE 2 expression encoded by the ACE2 gene lies on the X Chromosome where men are homozygous allowing them to be potentially high ACE2 expressor[12]. It is also postulated that older patients aged more than 50 years have higher expression of ACE2 gene contributing to higher mortality in this age group. It also may be related to high prevalence of comorbidities among elderly.

Impact Of Comorbidities

Our study showed similar prevalence of Diabetes and Hypertension among those who succumbed. A meta-analysis by Pieshan Qiu et al; showed higher incidence of Hypertension[13]. Hypertension has been repeatedly reported as the highest pre-existing comorbidity in COVID-19 patients. However, whether hypertension itself or the use of hypertensive therapies are responsible for these statistics is currently unknown. Hypertensive patients are commonly treated with ACE inhibitors (ACEI) and angiotensin-receptor blockers (ARB) which can significantly increase ACE2 expression[13]. However there is a conflicting evidence and opinions among the scientific community, it remains unclear whether treatment with ACEI/ARB has a positive or negative impact on COVID-19 progression.

The potential mechanisms by which severity of Covid-19 might be increased in patients with DM include higher affinity cellular binding for more efficient virus entry, inhibition of viral clearance, impaired T-cell function. They are more susceptible for hyperinflammation and cytokine strom. Diabetics also have a greater risk of diabetic ketoacidosis, which inhibits the ability to mitigate sepsis[14]. It is also important to highlight the higher mortality among CKD patients in our study. A study done by Ron T Gansevoort demonstrated severe forms of CKD have a very high risk for COVID 19 mortality[15]. Efforts to be made to include CKD patients in clinical trials with disease modifying treatment and vaccination trials.

Interestingly, percentage of patients who had chronic airway disease was only 4.8%. Similarly a study done by Donato Lacedonia et al, showed no higher prevalence of COVID 19 infection among COPD and smokers but had high mortality[16].

Icu And Mechanical Ventilation

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Maximum mortality was among those who were admitted in ICU with majority being mechanically ventilated by invasive ventilation. A study published in the *Journal of the American Medical Association* on New York patients stated that the mortality for mechanically ventilated patients was 88%[17]. The concern for potentially harmful overuse of IMV has been raised, since IMV itself carries risks that may adversely affect survival. Additionally, inappropriate timing of intubation too early or too late, inadequately trained staff, as well as improper ventilation settings and IMV associated pneumonia can all potentially enhance mortality[18].

Remdesivir And Immunomodulators

The experimental antiviral drug remdesivir (manufactured by Gilead) was granted Emergency Use Authorization by the US Food and Drug Administration in May 2020 for patients hospitalized with severe COVID-19[19]. The report by Spinner et al provides important new data on the potential efficacy of remdesivir in patients with moderate COVID-19 and suggests modest clinical benefit for the 5-day course compared with standard care[20]. A study published in New England Journal of Medicine on Tocilizumb in patients hospitalised with COVID 19 pneumonia showed that patients who were not receiving mechanical ventilation, tocilizumab reduced the likelihood of progression to the composite outcome of mechanical ventilation or death, but it did not improve survival[21].

Death And Complications

In our study, the major cause of death was ARDS complicated by sepsis and MODS. A study conducted by Sefer Elezkurtaj on causes of death and comorbidities on hospitalised covid 19 patients where autopsy was performed found that sepsis caused by purulent lung infection was the most frequent cause of death, while, in some cases, it was observed deadly respiratory insufficiency due to diffuse alveolar damage[22].

An increased risk of acute coronary syndrome (ACS), including myocardial infarction (MI), Acute ischemic stroke and venous thromboembolism is found in COVID illness, with the greatest risk within the first week of infection due to systemic inflammation resulting in atherosclerotic plaque disruption Literature suggests acute MI may occur in 7–17% and in up to 5% of hospitalized patients with COVID-19[23]. Our study showed incidence of ACS and CVA to be about 4.4% and 7.7% respectively. It is unclear whether these thromboembolic events are due to direct complications of COVID 19 infection or due to pre-existing comorbidities.

Conclusion

During the first wave of COVID 19 pandemic in India, mortality seems to be higher in older individuals with male preponderance. Major comorbidities associated among those who succumbed to COVID 19 were diabetes and hypertension. Maximum number of deaths were in ICU who required mechanical ventilation. Acute respiratory distress syndrome was the major cause of death complicated by sepsis and MODS.

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Tables And Graphs

Table 1: Age distribution of subjects

		Count	%
Age	18 to 20 years	5	0.7%
	21 to 30 years	16	2.3%
	31 to 40 years	51	7.2%
	41 to 50 years	107	15.2%
	51 to 60 years	181	25.7%
	61 to 70 years	192	27.3%
	71 to 80 years	104	14.8%
	81 to 90 years	43	6.1%
	91 to 100 years	5	0.7%
	Total	704	100.0%

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FIGURE 1: Age Distribution

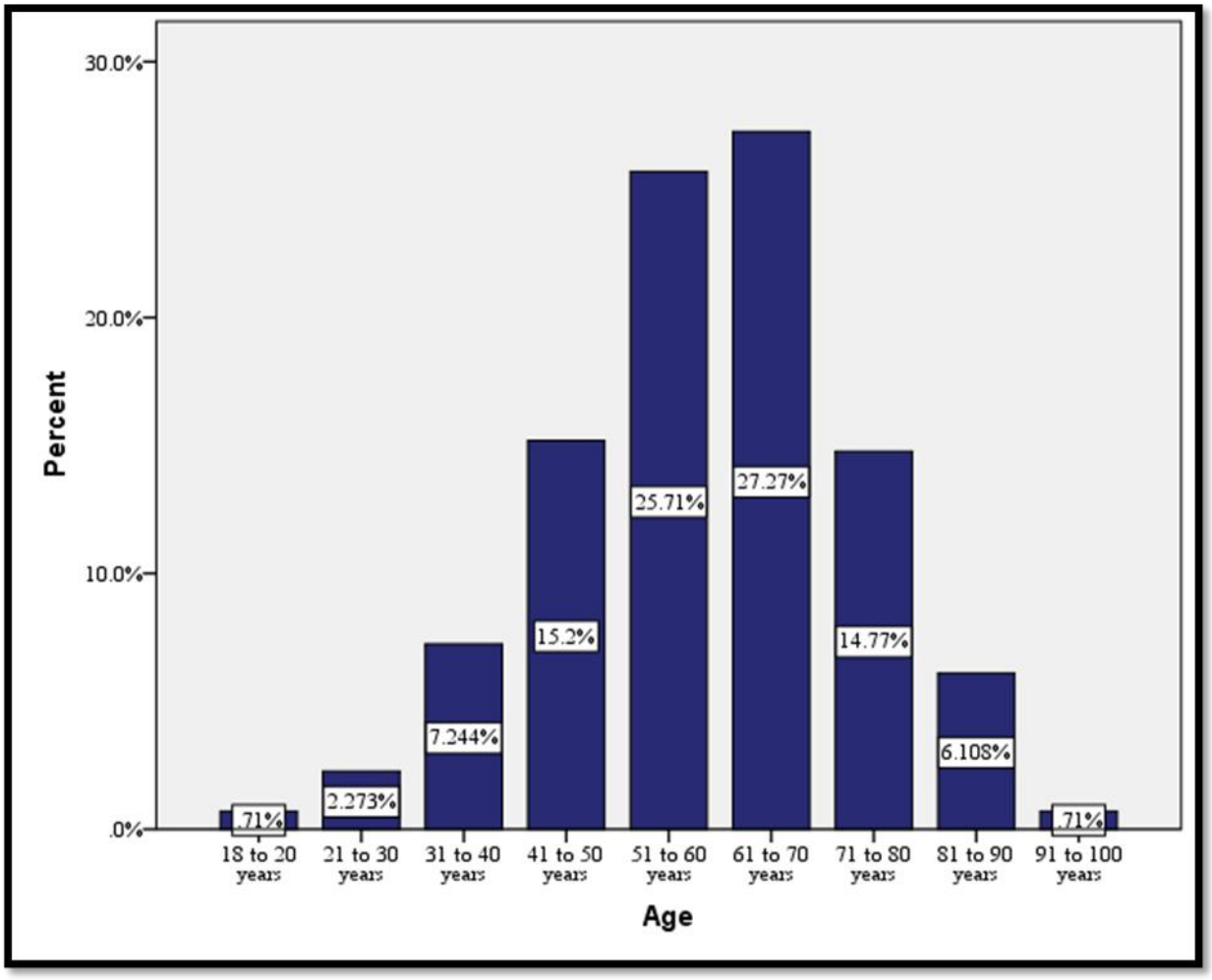

Table 2: Sex distribution

		Count	%
Sex	Female	219	31.1%
	Male	485	68.9%
	Total	704	100.0%

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Figure 2: Sex distribution

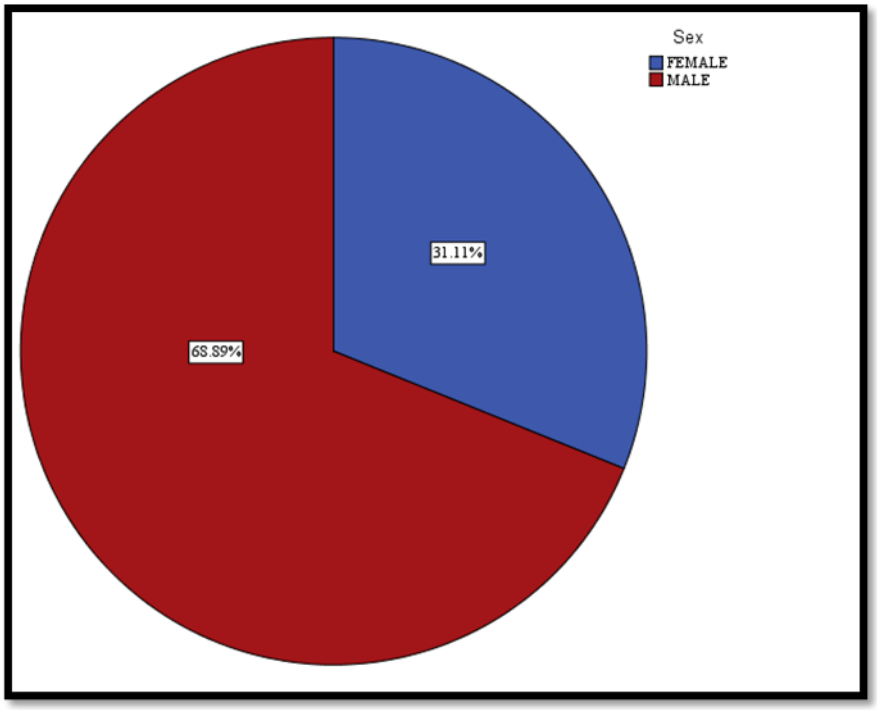

Table 3: Associated conditions or Comorbidities distribution

Associated conditions or Comorbidities	Yes	
	Count	%
Pregnant	2	0.3%
Hypertension	374	53.1%
Diabetes Mellitus	381	54.1%
IHD	115	16.3%
CKD	155	22.0%
Hypothyroidism	29	4.1%
BA/COPD	34	4.8%
PTB	11	1.6%
Cancer	26	3.7%
CVA	54	7.7%

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Figure 1: Bar diagram showing Associated conditions or Comorbidities distribution

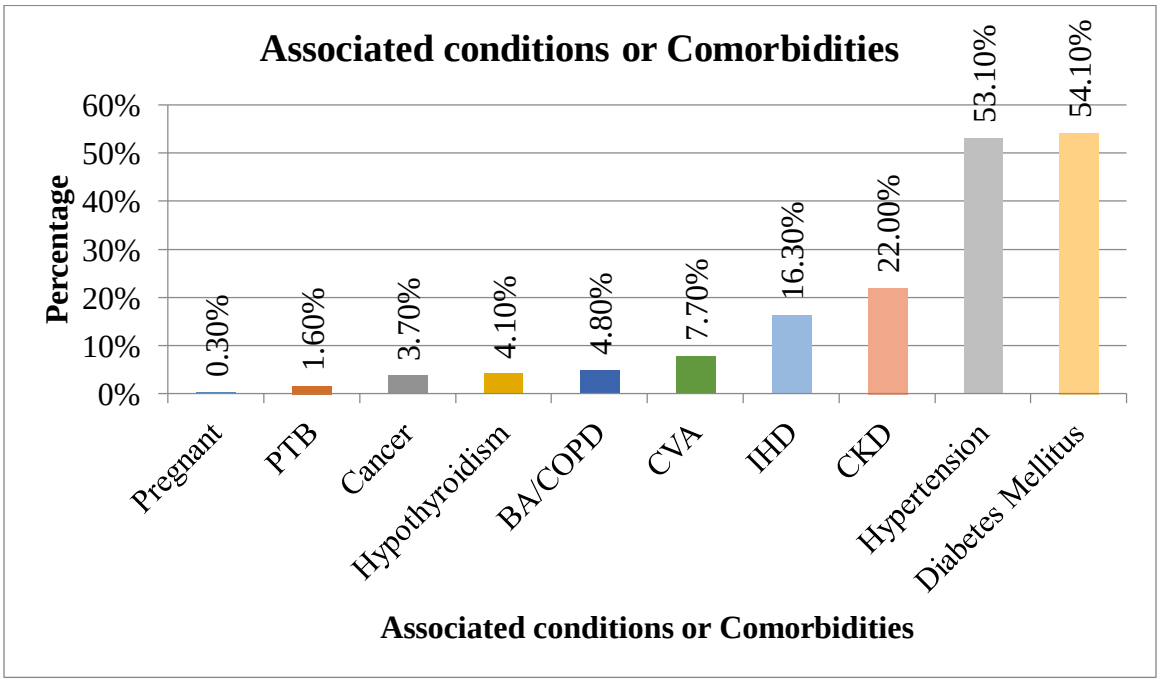

Table 4: Others Comorbidities distribution

		Count	%
Others	Alzheimer's Disease	8	1.1%
	CLD	12	1.7%
	Creutzfeldt Jacob	1	0.1%
	Epilepsy	9	1.3%
	Intestinal Obstruction	1	0.1%
	Mucormycosis	2	0.3%
	Obesity	5	0.7%
	OSA	2	0.3%
	OSA With Obesity	4	0.6%
	Parkinson's Disease	5	0.7%
	Post renal Transplant	2	0.3%
	RTA	2	0.3%
	RVD	1	0.1%
	Schizophrenia	3	0.4%
	SLE	1	0.1%

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Figure 2: Bar diagram showing Others Comorbidities distribution

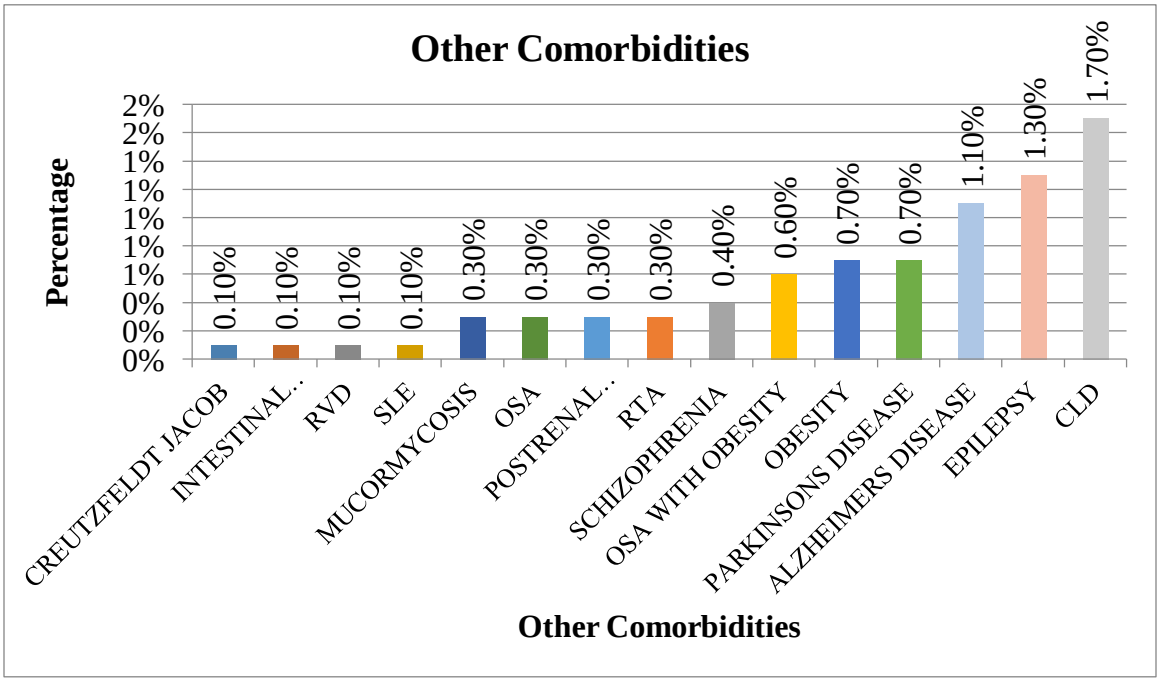

Table 5: ICU admission, intubation and treatment distribution

	Yes	
	Count	**Row N %**
ICU Stay	**614**	**87.2%**
Outside Intubation	**18**	**2.6%**
Ventilation	**571**	**81.1%**

Figure 5: ICU admission, intubation and treatment distribution

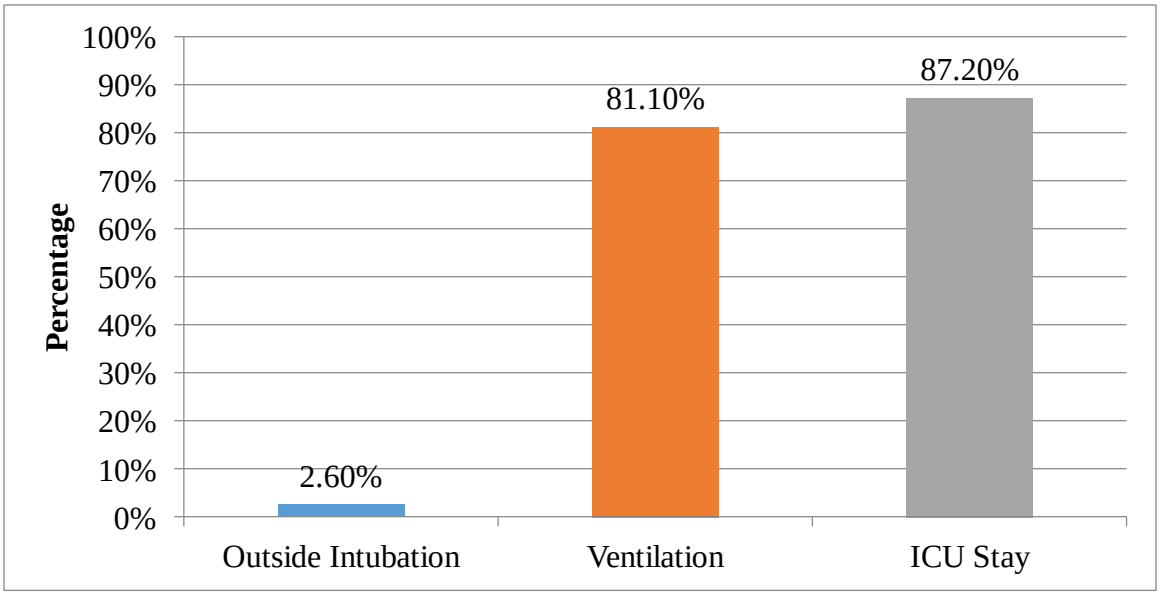

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Table 6: Immunomodulators distribution

		Count	%
	Nil	422	59.9%
Immunomodulators	Remdesivir	282	40.05%
	Plasma Therapy with Remdesivir	9	1.2%
	Tocilizumab with Remdesivir	8	1.1%
	Tocilizumab, Plasma Therapy and Remdesivir	2	0.2%

Figure 6: Immunomodulators distribution

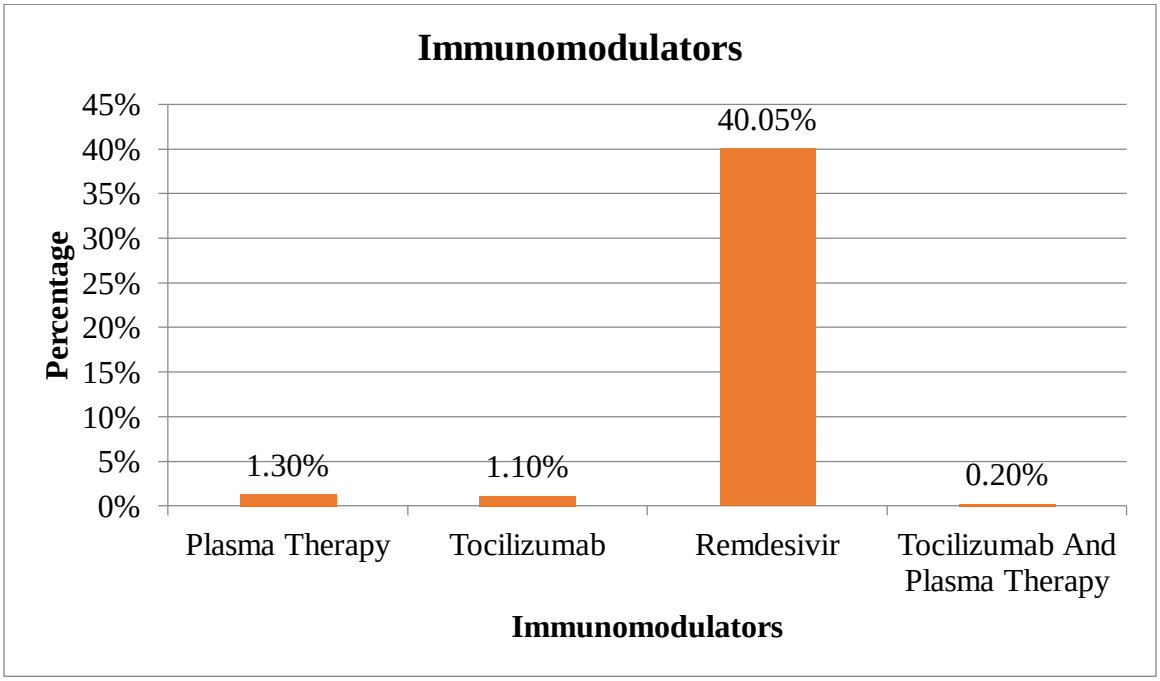

Table 7: Cause of Death distribution

		Count	%
Cause of Death	ACS	31	4.4%
	ARDS	420	59.7%
	ARDS With MODS With Sepsis	105	14.9%
	ARDS With Sepsis	106	15.1%
	Aspiration Pneumonia	12	1.7%
	Cardiogenic Shock	3	0.4%
	Hepatic Encephalopathy	7	1.0%
	Metabolic Encephalopathy	2	0.3%

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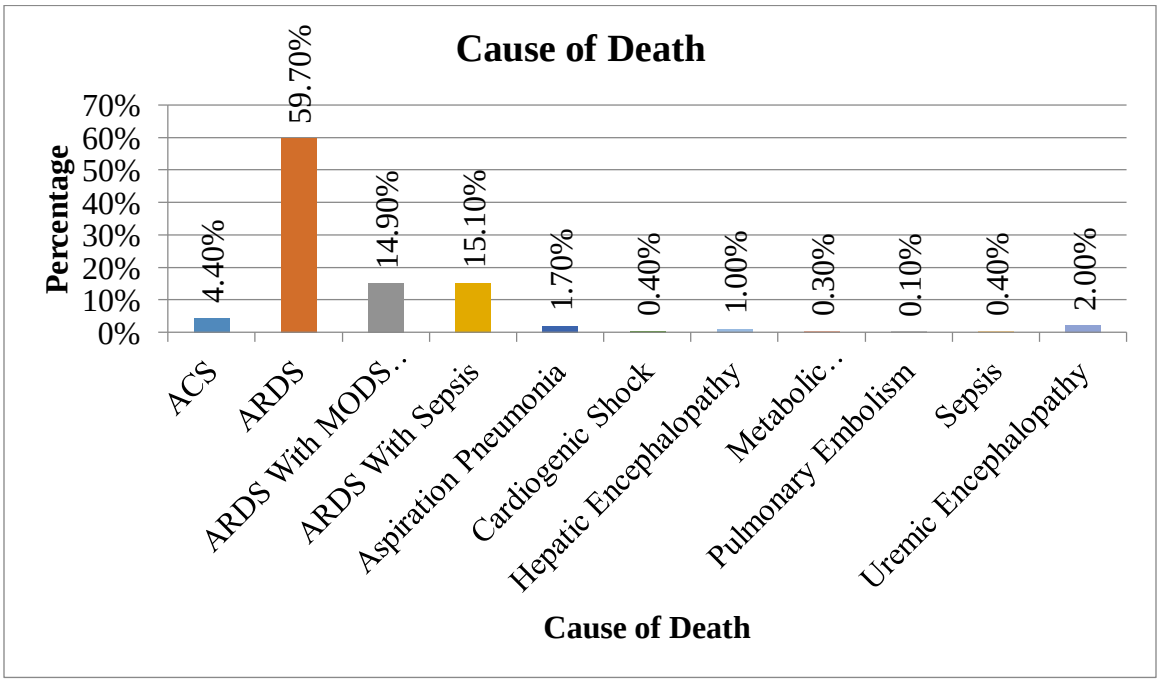
	Pulmonary Embolism	**1**	**0.1%**
	Sepsis	**3**	**0.4%**
	Uremic Encephalopathy	**14**	**2.0%**
	Total	**704**	**100.0%**

Figure 7: Cause of death distribution



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