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Study Of Clinical Prolife And Outcomes Of Patients With Severe Covid-19 With Diabetes Mellitus

[1]Prabhu S, [2]Varsha V
[1]Associate Professor, [2]Postgraduate,
Department of Medicine, BMCRI

***Corresponding Author:**
Prabhu S
Associate Professor, Department of Medicine, BMCRI

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Abstract

Background: High prevalence of diabetes, makes it important to understand the special aspects of COVID-19 infection in them. The abnormalities in cell-mediated immunity and phagocyte function associated with hyperglycaemia, leads to increased severity of infection in diabetics.

Objective: To study the clinical profile of patients with type 2 diabetes with severe COVID-19 and compare with glycaemic control, survival duration, mode of ventilation and mortality.

Methods: This retrospective study included consenting type 2 diabetics who presented with Severe COVID 19 infection (>30 RR, <90%SPO2 on RA, PaO_2/FiO_2 <300 mmHg, or lung infiltrates >50%) based on WHO COVID 19 severity staging and confirmed by real time RT-PCR, conducted at the hospital attached to Bangalore Medical College and Research Institute involving 90 subjects admitted to ICU in September.Clinical outcome of the patients was measured based on survival duration, mode of ventilation and mortality. The blood investigations included were complete blood count, N/L ratio, HbA1c, CRP, ferritin, D-Dimer and LDH levels.

Results: The mean age of the subjects was 60.74 with 64 males (71.1%), 26 females (28.9%) Among 90 patients 30(33.3%) had requirement of mechanical ventilation, 46(51.1%) were on NIV remaining 14(15.5%) 0n HFNO and FM. Patients with mortality had poor glycemic control median HbA1c(10.3) , maximum (14) minimum (8.6) and recovered cases had lower median HbA1c (7.1) ,minimum (6.6) maximum(7.5) . Patients with mortality even had elevated levels of inflammatory markers LDH (592), D-Dimer (2.1), Ferritin (1137) , N/L ratio (20.8) and shorter duration of survival(5days). Among 90 a total of 60(66.7%) patients had mortality with most common complication being ARDS (88.3%), followed by sepsis with septic shock (10%), and others (1.6%)

Conclusion: The results of this study revealed significant correlation between the clinical severity of COVID 19 illness with poor glycaemic control, increased N/L ratio, ferritin, D-Dimer, shorter survival duration and mortality in type 2 diabetes patients.

Keywords: NIL

Introduction

The disease burden of coronavirus infectious disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS CoV-2) has been increasing continuously with more than 110 million confirmed cases worldwide with 2.4 million death as of February 21 2021.

With a high prevalence of diabetes, it is important to understand the special aspects of COVID-19 infection in people with diabetes.

The abnormalities in cell-mediated immunity and phagocyte function associated with hyperglycaemia, as well as diminished vascularization leads to increased frequency and severity of infection in

diabetics. Pneumonia is more common in diabetic population. [1]

Past viral pandemics have witnessed the association of diabetes to increased morbidity and mortality. Diabetes was considered as independent risk factor for complications and death during 2002–2003 outbreak of Severe Acute Respiratory Syndrome (SARS-CoV-1).

Diabetes is associated with an increase in furin, which is a type-1 membrane-bound protease, belonging to the proprotein convertase subtilisin/kexin family (PCSK). It is involved in the entry of coronaviruses into the cell and increased Furin has been reported in diabetes, which might facilitate viral replication [2].

Several cytokines are increased in COVID-19 infection. Amongst these, IL-6 is increased in diabetes and may play a more deleterious role in Covid-19 infection.

Increased expression of ACE2 may favour more efficient cell binding and entry into cells. Early recruitment and function of neutrophils and macrophages are impaired in DM. Delay in the initiation of adaptive immunity and dysregulation of the cytokine response in DM may lead to the initiation of cytokine storm.

Potential mechanisms that may increase the susceptibility for COVID-19 in patients with DM include: 1) higher affinity cellular binding and efficient virus entry, 2) decreased viral clearance, 3) diminished T cell function, 4) increased susceptibility to hyperinflammation and cytokine storm syndrome, and 5) presence of CVD [3]

Diabetes might be one of the important risk factors in COVID-19 patients. Our study aims at analysing the clinical characteristics and outcome in diabetics with severe COVID-19.

Study design and population: A Retrospective observational study carried out in hospitals attached to Bangalore medical college in September 2020. All patients admitted with type 2 diabetes with severe covid19 pneumonia based on WHO clinical staging were studied. Inclusion criteria: (1) Adults more than 18 years old. (2) Laboratory confirmation of covid-19 by real-time PCR. (3) Chest CT findings meeting the standard for diagnosis of covid-19. (4) previously known type 2 diabetes. Exclusion criteria: 1) Missing data on clinical characteristics. (2) Missing data on laboratory characteristics. (3) Secondary diabetes. (4) Type 1 diabetes.

Methodology: After obtaining approval and clearance from the institutional ethics committee, the patients fulfilling the inclusion criteria when rolled for the study after obtaining informed consent.

In patients with self-reported medical history of diabetes or newly diagnosed with type 2 diabetes will be studied. Newly diagnosed patients will be considered to have type 2 diabetes mellitus according to American Diabetic Association (ADA) guidelines [4]

Severe COVID-19 Illness: Individuals who have respiratory frequency >30 breaths per minute, SpO_2 <94% on room air at sea level, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) <300 mmHg, or lung infiltrates >50% will be considered based on 'National Institute of Health COVID 19 Treatment Guidelines' [5]

Detailed assessment of history with information on chronic medical history, clinical symptoms, laboratory data such as blood routine, liver and renal function, random blood glucose, glycated haemoglobin, CRP, ferritin, d dimer, PT INR, LDH and radiological investigation like chest x-ray or CT thorax.

Statistical Analysis: SPSS (Statistical Package For Social Sciences) version 20. (IBM SPASS statistics [IBM corp. released 2011] was used to perform the statistical analysis Descriptive statistics of the explanatory and outcome variables were calculated by median and IQR (based on normalcy test- shapiro wilk test - data was not normally distributed, hence non-parametric tests are applied) for quantitative variables, frequency and proportions for qualitative variables. Inferential statistics like Chi-square test will be applied for qualitative variables. Mann-whitney test was applied to check the statistical difference of quantitative variables between the groups. The level of significance is set at 5%.

Results: Among 90 patients, the mean age of the subjects was 60.74 years, majority belonged with 56-65 years and mortality rate increased with age (Fig 1). There were 64 males (71.1%), 26 females

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(28.9%). Mortality rate in males-65%, and in females-67% (Fig 2).

Fig 1

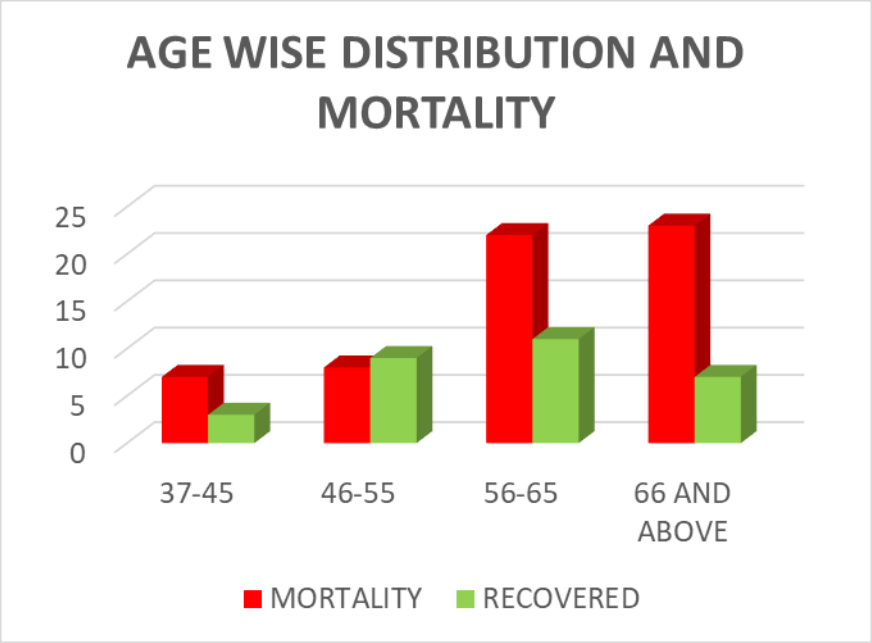
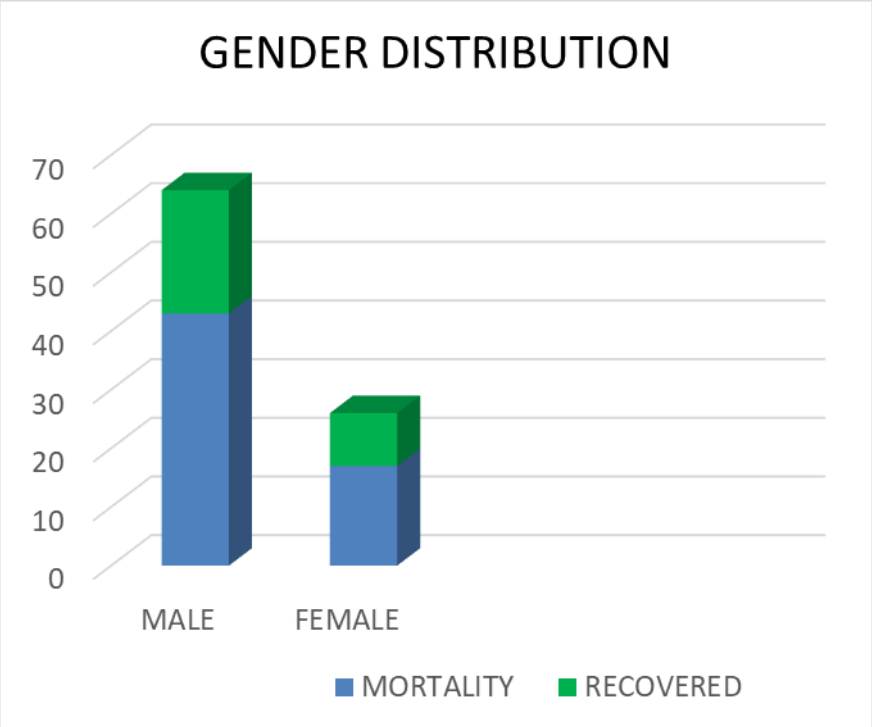


Fig 2



Among 90 patients 23 patient had only diabetes as comorbidity whereas 67 had other comorbidities like cardiovascular disease, hypertension, hypothyroid and chronic kidney disease. Among 90 patients 30(33.3%) had requirement of mechanical ventilation, 46(51.1%) were on NIV remaining 14(15.5%) 0n HFNO and FM. (fig 3).

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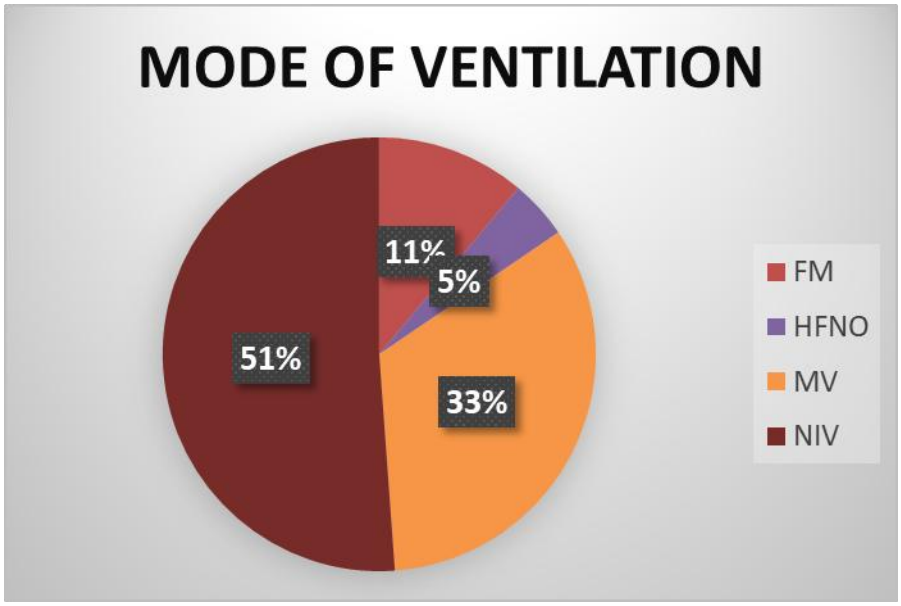
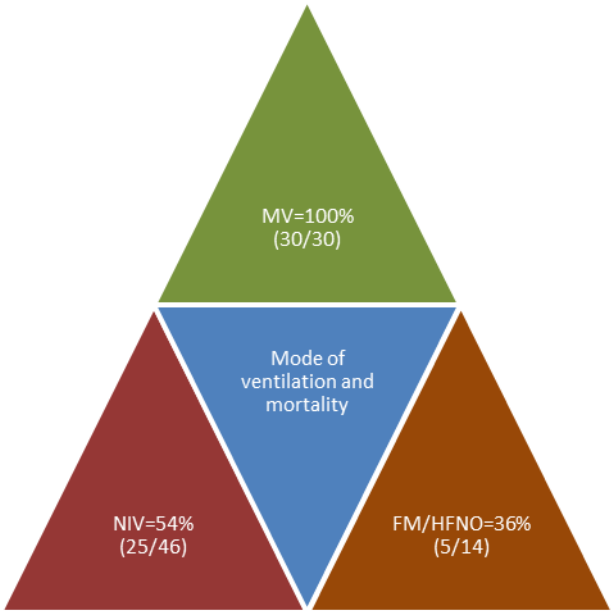
Fig 3



Mortality with Mechanical ventilation was 100%, NIV- 54%, HFNO and FM -36% (fig 4)

Fig 4



Patients with mortality median HbA1c (10.3), maximum (14) minimum (8.6). Patients with mortality inflammatory markers LDH (592), D-Dimer (2.1), Ferritin (1137), N/L ratio (20.8), CRP (120) and duration of survival(5days). Recovered group median HbA1c (7.1), minimum (6.6) maximum (7.5), inflammatory markers LDH (465), Ferritin (582), N/L ratio (13.2) ,CRP (98) and duration of hospital stay (12 days). (Table 1 and Fig 5)

Table 1: Comparison Of The Clinical Parameters Based On Mortality Using Mann Whitney Test

	Mortality	N	Minimum	Maximum	Median	IQR	p value

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Age	No	30	42	84	59.50	13.000	0.207
	Yes	60	37	84	65.00	17.000	
Length of stay	No	30	8	31	12.00	8.000	0.00*
	Yes	60	1	16	5.00	5.000	
HbA1C	No	30	6.6	7.5	7.1	1.15	0.00*
	Yes	60	8.6	14.00	10.30	2.70	
Hb	No	30	9.20	15.30	12.95	2.50	0.89
	Yes	60	7.60	17.20	13.10	2.30	
TC	No	30	6000.00	22400.00	11200.00	5100.00	0.32
	Yes	60	3000.00	31500.00	13500.00	875.00	
Platelet count	No	30	1.84	6.35	3.09	1.24	0.05*
	Yes	60	.48	44.00	2.80	1.41	
N\L	No	30	3.75	49.00	13.20	15.07	0.01*
	Yes	60	1.25	49.00	20.87	32.91	
D-Dimer	No	30	.05	5.40	0.92	1.64	0.00*
	Yes	60	.23	6.37	2.08	1.80	
LDH	No	30	204.00	747.00	465.00	246.00	0.00*
	Yes	60	283.00	2847.00	592.00	318.75	
CRP	No	30	9.59	335.03	98.00	97.13	0.00*
	Yes	60	12.62	336.00	120.96	124.88	
Ferritin	No	30	90.00	2000.00	514.50	582.65	0.00*
	Yes	60	154.00	2000.00	1291.50	1137.50	

*significant

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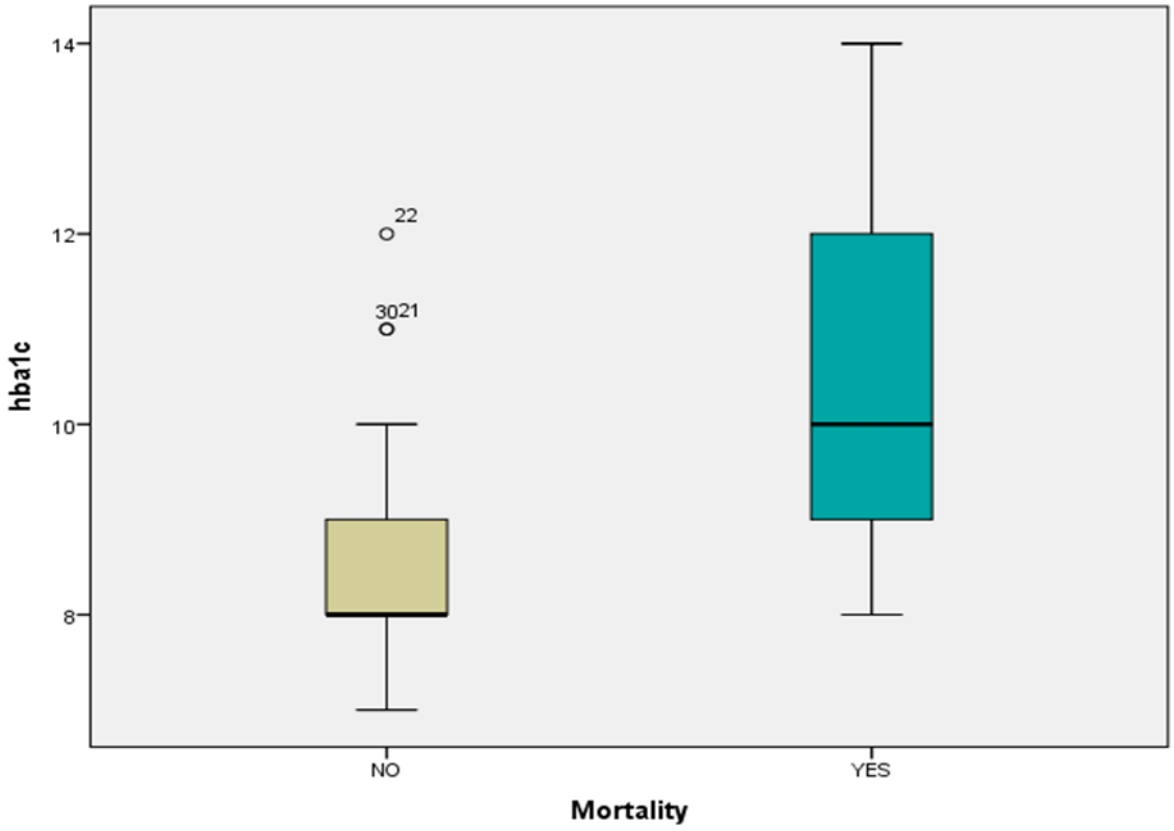
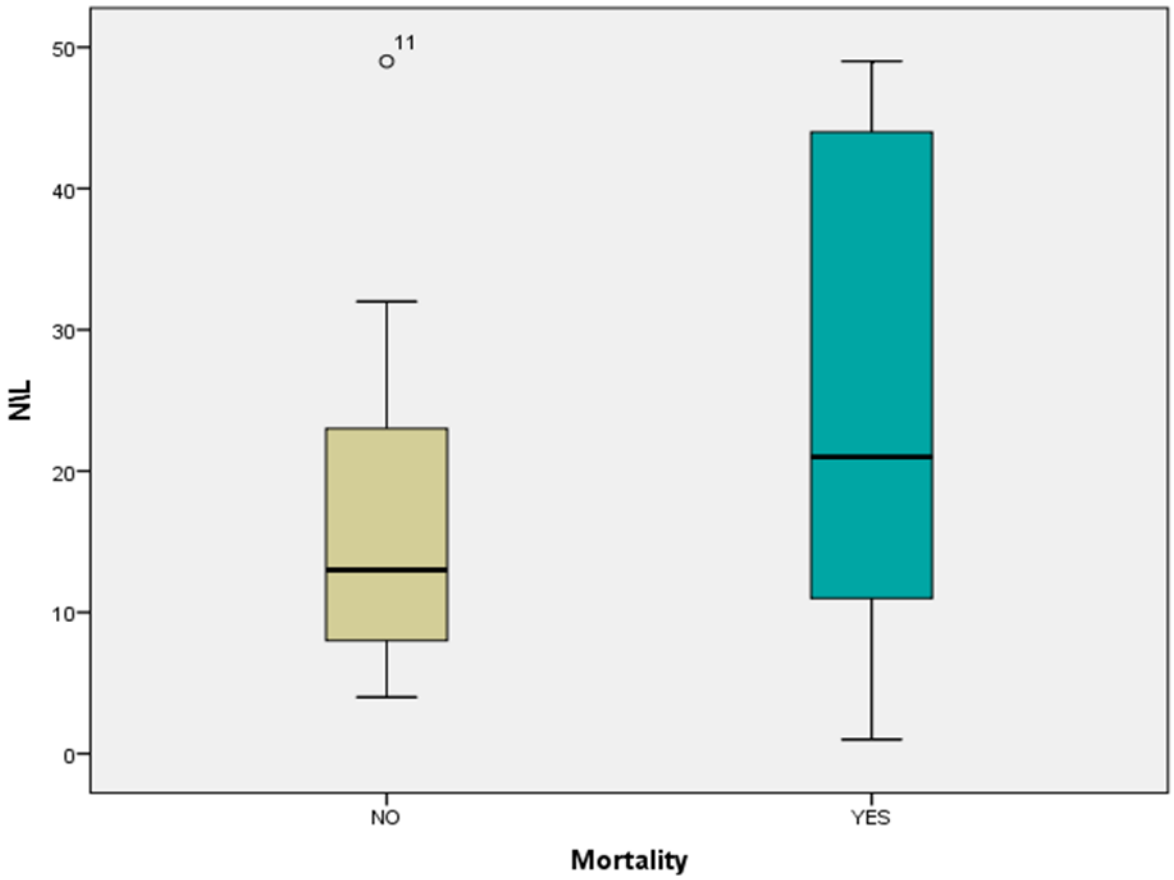
Fig 5





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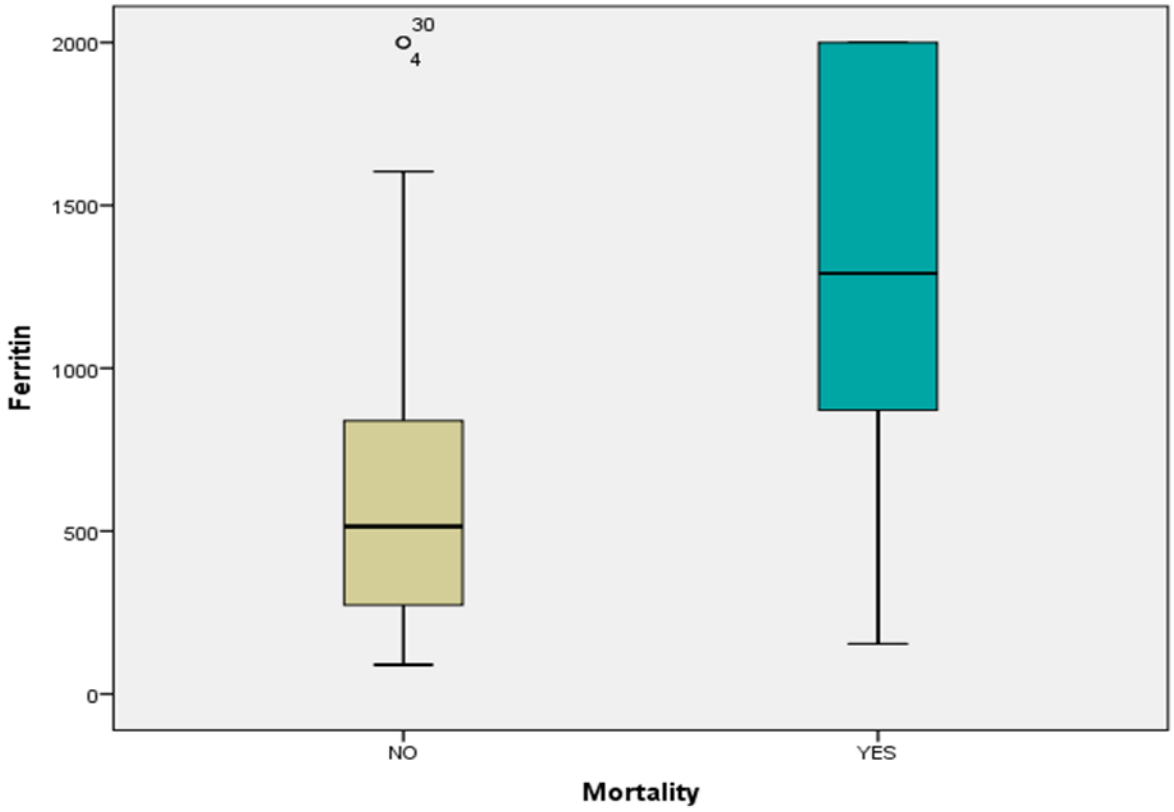

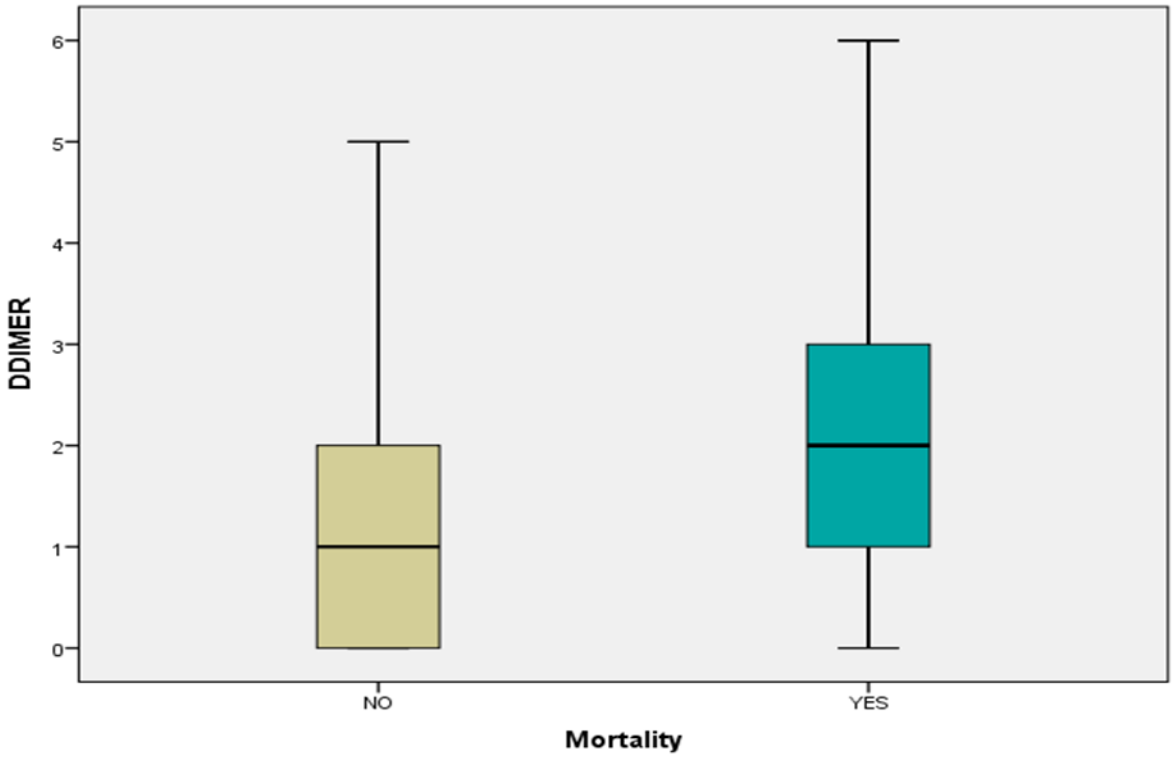

Among 90 a total of 60(66.7%) patients had mortality with most common complication being ARDS (88.3%), followed by sepsis with septic shock (10%), and others (1.6%) (FIG 6).

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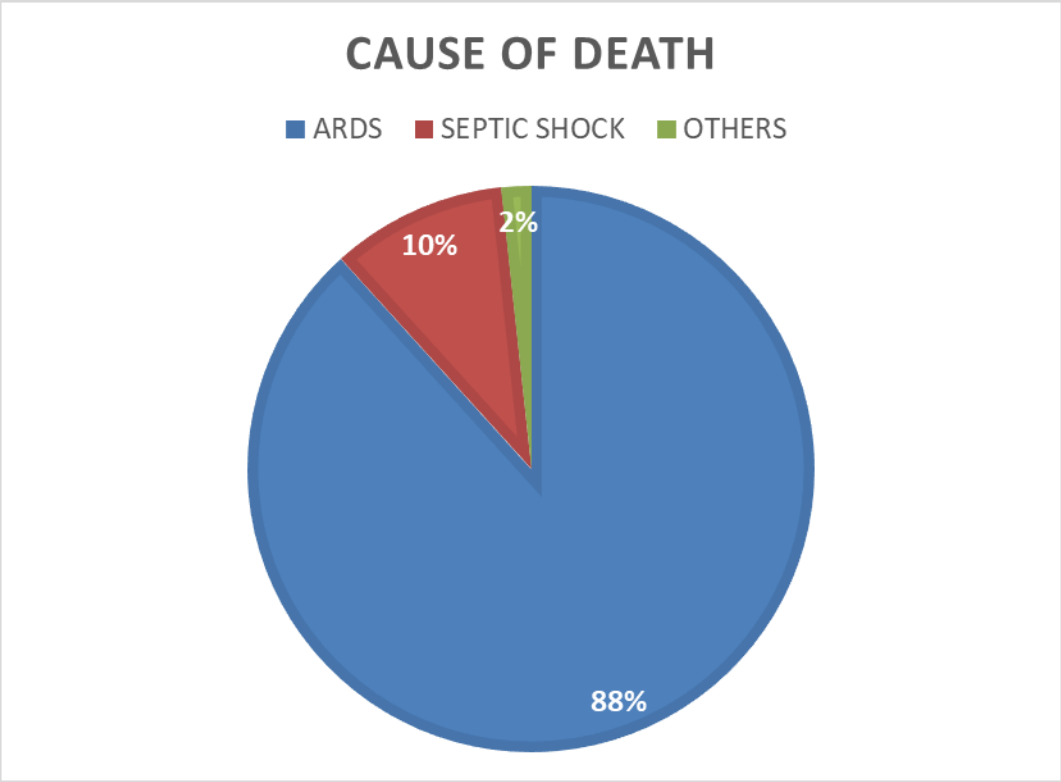
Fig 6



Discussion

This study was conducted to see the clinical profile and outcomes of patients with type 2 diabetes and severe covid 19. Diabetes mellitus is well known comorbidity, which if uncontrolled, causes immune dysfunction and susceptibility to infection. Hence we compared glycemic control of severe covid 19 patients with clinical profile, inflammatory markers, duration of survival, mode of ventilation and mortality.

COVID-19 and diabetes mellitus: An unholy interaction of two pandemics explained by Rimesh et al from data on various studies showed Compromised innate immunity, pro-inflammatory cytokine, reduced expression of ACE2 inhibitors in people with diabetes mellitus contribute to poor prognosis in COVID-19. Direct B-cell damage, cytokine-induced insulin resistance and drugs used in the treatment of COVID-19 (like corticosteroids), can lead to worsening of glucose control in people with diabetes mellitus. The interaction between COVID-19 and diabetes mellitus sets leads to worsening of dysglycemia and diabetes mellitus, in turn, exacerbates the severity of COVID-19 [(6)]

Study done by guan et al. Compared with patients with severe covid-19 without diabetes, patients with diabetes were older, susceptible to receiving mechanical ventilation and admission to ICU, and had higher mortality and higher levels of inflammatory markers line leukocyte count, neutrophil count, high-sensitivity C reaction protein, D-dimer, lactic dehydrogenase[(7)] and A study done by Zhu et al. large retrospective study of 810 patients with diabetes, reported a significant increase in septic shock , ARDS ,acute kidney injury and acute heart injury in patients with poorly-controlled diabetes[(8)].

In our study among 90, gender distribution 64 were male and 26 female. No significant difference in mortality rate 67% in males and 65% in females. Diabetes was the only comorbidity in 23 patients, whereas 67 had other comorbidities most commonly hypertension. No significant difference in mortality rate between the two groups (67% vs 65%). Age distribution majority belonged between 56-65 years (36.7%), mortality rate was maximum between 66-75 years (75%). Patient with mortality had poor glycaemic control median hba1c 10.3 (IQR 2.7) while recovered had median hba1c 7.1 (IQR 1.15).

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Patient with mortality had poor glycaemic control and hence had elevated inflammatory markers compared to recovered group. Inflammatory markers among patient with mortality- N/L ratio 20.8 (IQR 32.9), Ddimer 2.08 (IQR 1.8), LDH 592 (IQR 318), Ferritin 1291 (IQR 1137), CRP 120 (IQR 129.8) and duration of survival 5days (IQR 5). While recovered patients had N/L ratio 13 (IQR 15), Ddimer 0.9 (IQR 1.6), LDH 465 (IQR 246), Ferritin 514 (IQR 528), CRP 98 (IQR 98) and duration of hospital stay 12days (IQR 8).

Mode of ventilation maximum patients were on non invasive ventilation (51.1%), followed by mechanical ventilation (33.3%), face mask (11.1%), HFNO (4.4%). Mortality was maximum among mechanically ventilated patients (100%), NIV (54%) FM and HFNO (36%). Higher the mode of ventilation more was mortality. Cause of death was ARDS in 88% , septic shock in 10% and other causes 2%.

Limitation of study

Smaller sample size, no comparison group with patients who did have diabetes, majority of patients had multiple comorbidities which acted as confounder and as our hospital is tertiary care centre majority patients were referred with severe pneumonia on admission which might have contributed to mortality.

Summary- In our study severe covid 19 patients with diabetes with poor glycemic control had increased mortality elevated inflammatory markers and shorter duration of survival. Hence poorly controlled diabetes acts as important risk factor contributing to mortality. This study emphasizes need for good glycaemic control in diabetics.

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