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A STUDY OF TROPONIN T LEVELS IN HOSPITALISED ICU PATIENTS OF COVID 19 AND ITS RELATION WITH IN HOSPITAL MORTALITY.

NAVIDA BABBAR[(1),] RAJEEV BAGARHATTA[(2)] , SANJEEV KUMAR[(1),] SUSHANT BABBAR[(3)] , PRATEEK BAGARHATTA[(4)] , PRASHANK AJMERA[(1)]

1. **SENIOR RESIDENT, DEPARTMENT OF CARDIOLOGY, SMS MEDICAL COLLEGE, JAIPUR, RAJASTHAN, INDIA.**
2. **PRINCIPAL AND PROFESSOR, DEPARTMENT OF CARDIOLOGY, SMS MEDICAL COLLEGE, JAIPUR,RAJASTHAN, INDIA.**
3. **ASSISTANT PROFESSOR, DEPARTMENT OF RADIOLOGY, DAYANAND MEDICAL COLLEGE, LUDHIANA.**
4. **PRATEEK BAGARHATTA: JUNIOR RESISDENT, DEPARTMENT OF PULMONARY MEDICINE, D Y PATIL, NAVI MUMBAI.**

ABSTRACT

BACKGROUND : Coronavirus disease 2019 (covid-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV2) was a pandemic, with considerable mortality and morbidity exerting pressure on global health-care systems. We have studied the relationship of raised troponin levels in covid 19 affected patients with in hospital mortality.

RESULTS: Most people who died belonged to age group of more than 60 years age with males having high incidence of mortality. 36% of those who died had Type II diabetes. Out of 20 patients who died has strongly positive troponin T levels without any evidence of Acute Myocardial infarction on electrocardiography(ECG).

CONCLUSIONS: A positive correlation was found between mortality and rise in troponin T levels irrespective of any previous known cardiovascular disease in patients and the rise of troponin T levels had no correlation with Computed Tomography severity score.

KEYWORDS: COVID-19, TROPONIN, MORTALITY

BACKGROUND

Coronavirus disease 2019 (covid-19) a pandemic, caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV2), had a massive mortality and morbidity rate which pressurised the global health-care systems due to high burden of disease by highlighting the limited resource availability, scarcity of intensive care units available . Despite being primarily a respiratory infection, covid-19 had important impacts on many vital organs, including the heart [1,2] which was reflected by release of cardiac biomarkers such as troponins due to myocardial injury.[3-6] Cardiac troponin T levels predicts myocardial injury which is associated with significant morbidity and mortality in this disease. The presence of troponin elevation, or its dynamic increase during hospitalization, confers up to 5 times the risk of requiring ventilation, increases in arrhythmias such as ventricular tachycardia/ventricular fibrillation, and 5 times the risk for mortality.

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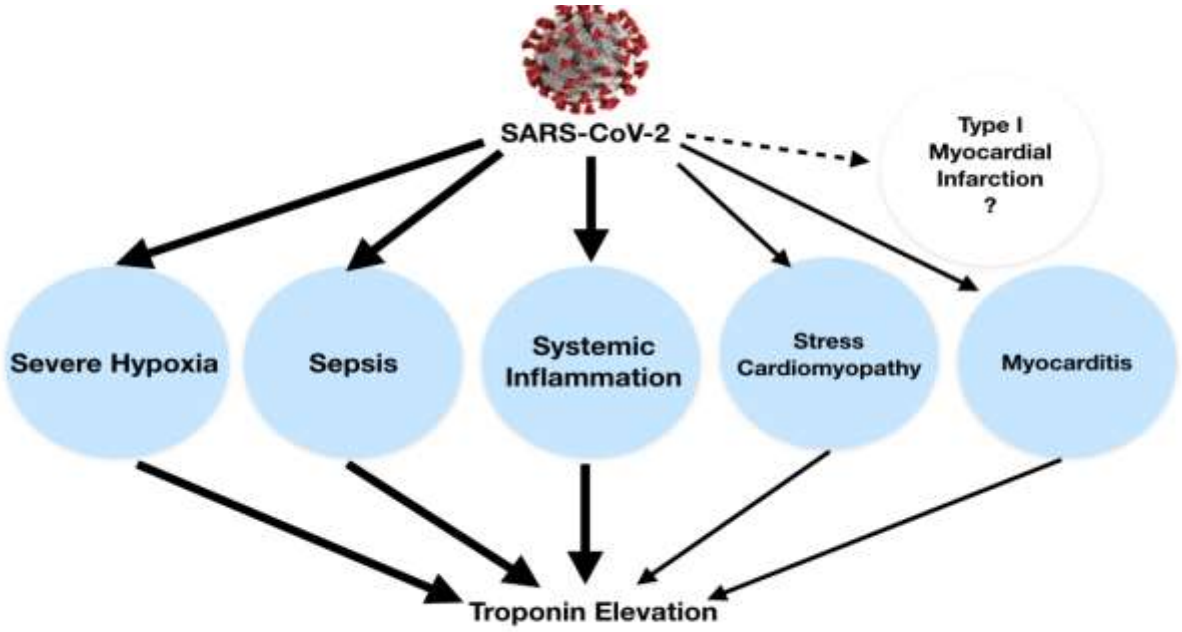
Troponin elevation in the setting of COVID-19 can be explained by different causes: (1) non-ischemic myocardial injury (more commonly) related to different possible mechanisms (e.g., severe hypoxia, sepsis, systemic inflammation, pulmonary thromboembolism, cytokine storm, stress cardiomyopathy) rather than a typical viral lymphocytic myocarditis, (2) ischemic myocardial injury with also different potential mechanisms (e.g., plaque rupture, coronary spasm, microthrombi, or direct endothelial or vascular injury). The various mechanisms leading to troponin rise are shown in figure 1.[7]

Myocardial injury occurs as cardiomyocytes inhabit ACE2 receptord in abundance which is the binding site for the SARS-CoV-2, direct ("non-coronary") myocardial damage is almost

Figure 1: Pathogenesis of myocardial injury



certainly the most common cause, also their is hypothesis due to rise in hs-cTn that myocarditis might be the reason in some cases, particularly as acute left ventricular failure has been described in some cases. Lastly, due to plaque rupture acute myocardial infarction (MI) Type 1 is possible.

REVIEW OF LITERATURE

Baner AL Abbasi et al [8]did a cohort study of cohort of 257 patients and found that Patients with an elevated troponin-I level were more likely to be older (77 ± 13 vs. 58 ± 16 years, P < 0.0001), had a history of hypertension (P < 0.0001), diabetes mellitus (P = 0.0019), atrial fibrillation or flutter (P = 0.0009), coronary artery disease (P < 0.0001), and chronic heart failure (P = 0.0011). Patients with an elevated troponin-I level in the first 24 h of admission were more likely to have higher in-hospital mortality (52% vs. 10%, P < 0.0001) and

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Troponin-I level in the first 24 h of admission had a negative predictive value of 89.7% and a positive predictive value of 51.9% for all-cause in-hospital mortality.
David T majure et al [9] studied the Usefulness of Elevated Troponin to Predict Death in Patients With COVID-19 and Myocardial Injury and found that Patients with COVID-19 with elevated troponin have markedly increased risk of death and also that Risk with elevated troponin is independent of acute phase and inflammatory markers. 11,159 patients hospitilisedwith COVID-19, 6,247 had a troponin assessment within 48 hours. Of these, 4,426 (71%) patients had normal, 919 (15%) had mildly elevated, and 902 (14%) had severely elevated troponin. Acute phase and inflammatory markers were significantly elevated in patients with mildly and severely elevated troponin compared with normal troponin. Patients with elevated troponin had significantly increased odds of death for mildly elevated compared with normal troponin (adjusted OR, 2.06; 95% confidence interval, 1.68 to 2.53; $p < 0.001$) and for severely elevated compared with normal troponin (OR, 4.51; 95% confidence interval, 3.66 to 5.54; $p < 0.001$) independently of elevation in inflammatory markers.

Zhao BC et al [10] included Fifty-one studies. Elevated troponins were found in 20.8% (95% confidence interval [CI] 16.8–25.0 %) of patients who received troponin test on hospital admission. Elevated troponins on admission were associated with a higher risk of subsequent death (risk ratio 2.68, 95% CI 2.08–3.46) after adjusting for confounders in multivariable analysis. The pooled sensitivity of elevated admission troponins for predicting death was 0.60 (95% CI 0.54–0.65), and the specificity was 0.83 (0.77–0.88). The post-test probability of death was about 42% for patients with elevated admission troponins and was about 9% for those with non-elevated troponins on admission. There was significant heterogeneity in the analyses, and many included studies were at risk of bias due to the lack of systematic troponin measurement and inadequate follow-up.

Aims and objectives:

- To determine the correlation of trop T levels and mortality in patients hospitalised with covid 19 pneumonia and it's comparison with non trop t elevated patients.
- Correlation of trop T levels with CT severity score.
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- **Methods:**

  1 Study design: Cross sectional retrospective observational descriptive study conducted at SMS MEDICAL COLLEGE: A tertiary care centre in north India.

  2.Sample size: 98 sample size was found to be sufficient for outcome of this study(5% alpha error and 80 % power)

  3. selection criteria:

  Inclusion criteria:

- All patients with covid 19 pneumonia admitted in hospital icu with drop in spo2 levels.

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Exclusion criteria

- Chronic kidney disease
- Patients with acute MI
- Valvular heart disease
- Chronic liver disease
- Sepsis

4. Data collection: It was done from medical records department of the college

5. Statistical analysis:

It was done using computer software (SPSS Trial version 23 and primer).

The qualitative data was expressed in proportion and percentages and the quantitative data expressed as mean and standard deviations.

The difference in proportion was analysed by using chi square test and where data will be less fisher test will be used.

The difference in means among the groups was analyzed using the student T Test.

probability level was considered as statistically significant i.e., $p<0.05$.

6. **Ethical considerations:** Approved by ethical committee board of sms medical college. Approval number:914/MC/EC/2023

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Results

Table No. 1

Association of age groups and mortality

AGE	**Death**		**Survival**		**Grand Total**		
	No	%	No	%	No	%	p-values
≤20	1	5	2	2.86	3	3.33	
21-30	3	15	2	2.86	5	5.56	
31-40	2	10	10	14.29	12	13.33	
41-50	2	10	17	24.29	19	21.11	
51-60	4	20	14	20.00	18	20.00	
>60	8	40	25	35.71	33	36.67	0.326NS
Grand Total	**20**	100	**70**	100.00	**90**	100.00	
Mean±SD	51.60±19.64		52.46±14.62		52.27±15.75		
Min./max.	19/85		20/89		19/89		0.831NS

Chi-square = 6.139 with 5 degrees of freedom; P = 0.326

Graph no 1 **Association of age groups and mortality**

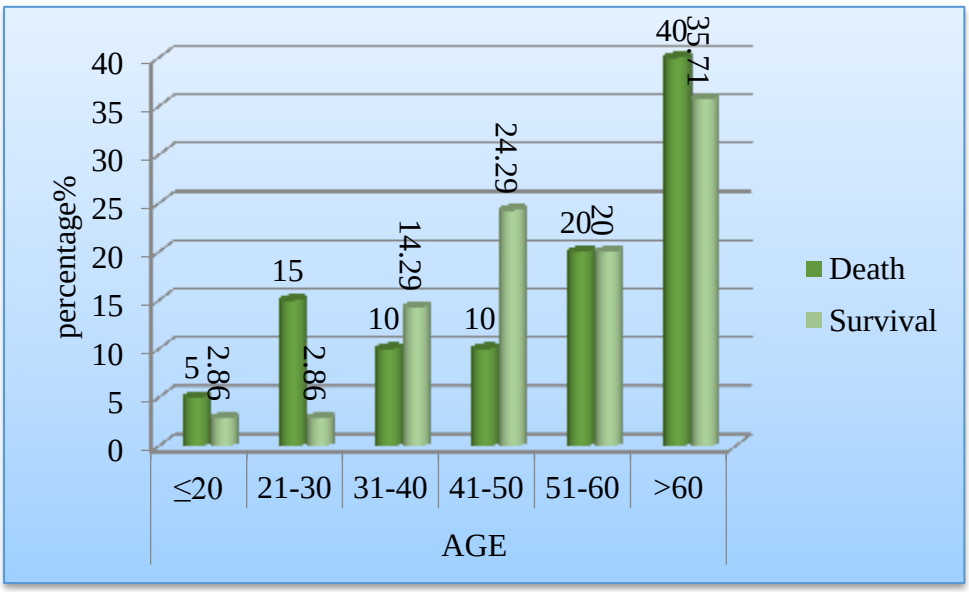

TABLE 1/GRAPH 1: SHOWS AGE RELATED MORTALITY IN DIFFERENT AGE GROUPS DUE TO COVID -19. MAXIMUM MORTALITY IS SEEN IN AGE GROUP>60YEARS.(P VALUE: NON SIGNIFICANT)

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Table No. 2
Association of sex according to death and survival

Sex	**Death**		**Survival**		**Grand Total**		
	No	%	No	%	No	%	p-values
Male	9	45	42	60.00	51	56.67	
Female	11	55	28	40.00	39	43.33	0.348NS
Grand Total	**20**	100	**70**	100.00	**90**	100.00	

Graph no 2 Association of sex according to death and survival

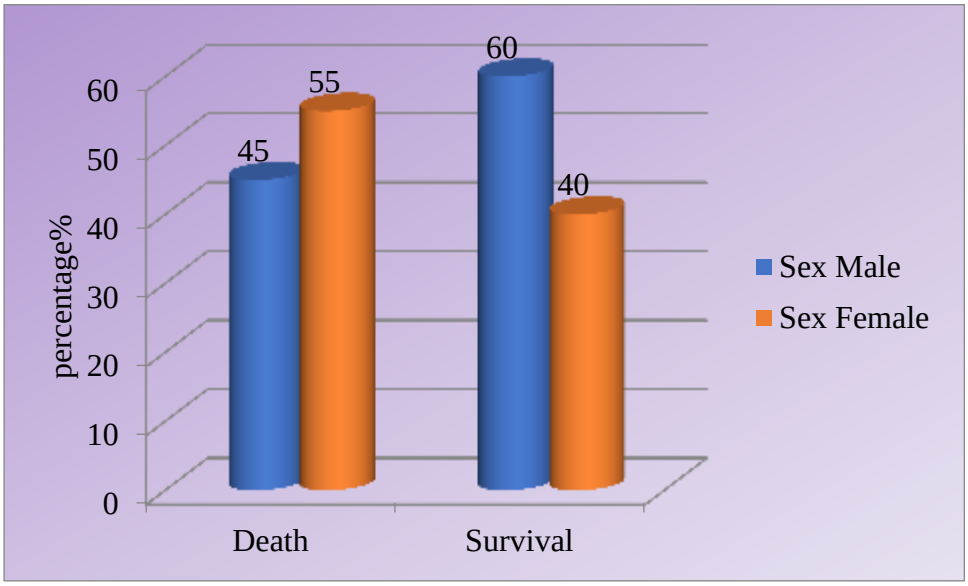

TABLE 2/GRAPH 2: SHOWS SEX RELATED MORTALITY AMONF FEMALES AND MALES.

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Table No. 3
Association of diseases and mortality

	Death		Survival		Grand Total		
	No	%	No	%	No	%	p-values
DIABETES MELLITUS	9	45	24	34.29	33	36.67	0.539NS
HYPERTENSION	5	25	18	25.71	23	25.56	0.821NS
CORONARY ARTERY DISEASE	6	30	17	24.29	23	25.56	0.821NS
CHRONIC OBSTRUCTIVE PULMONARY DISEASE	5	25	14	20.00	19	21.11	0.863NS

Graph no 3 Association of diseases and mortality

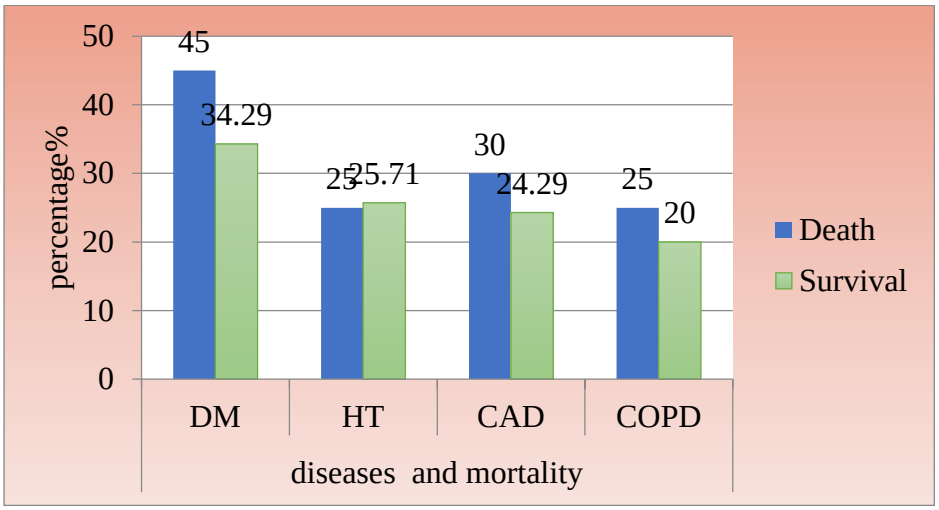

TABLE 3/GRAPH 3: IT SHOWS DEATH RATE IN PATIENTS WITH DIFFERENT COMORBID CONDITIONS WITH HIGHEST MORTALITY SEEN IN DIABETIC PATIENTS.

DM: DIABETES MELLITUS, HT: HYPERTENSION, CAD: CORONARY ARTERY DISEASE, COPD: CHRONIC OBSTRUCTIVE PILMONARY DISEASE

Table No. 4
Association of hypercholestrolemia and Personal history and mortality

	Death		**Survival**		**Grand Total**		
	No	%	No	%	No	%	p-values
Hypercholestrolemia	3	15	7	10.00	10	11.11	0.823NS
Smoking	5	25	19	27.14	24	26.67	0.924NS

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Graph no 4Association of hypercholestrolemia and Personal history and mortality

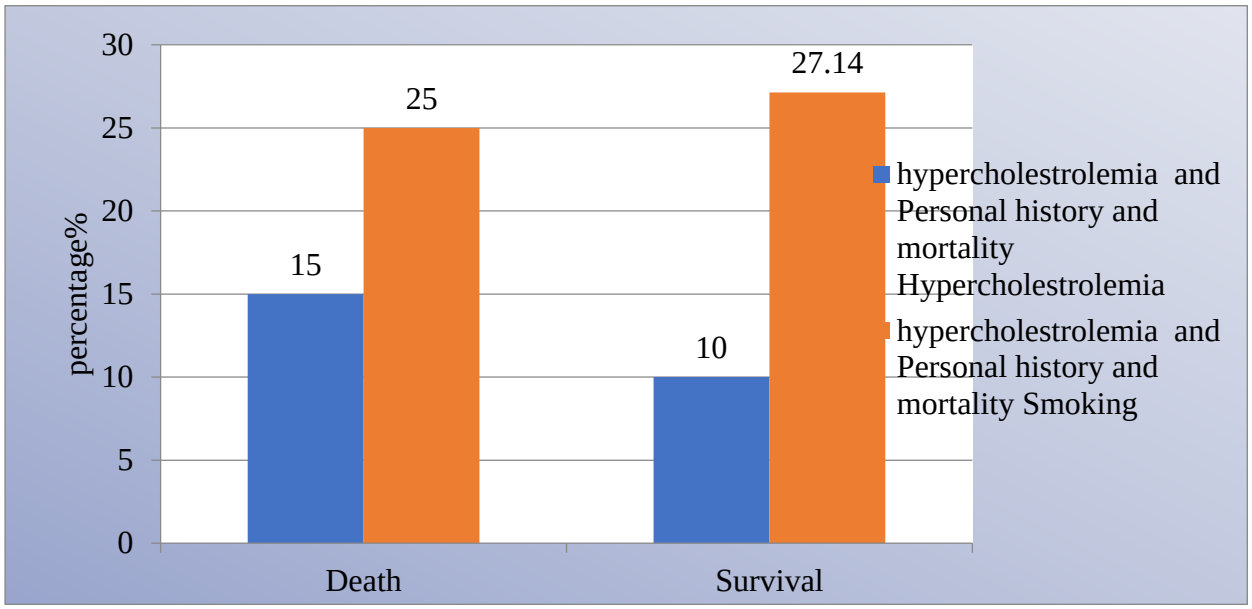

Table No. 5
Association of trop T levels and mortality

	Death		Survival		Grand Total		
	No	%	No	%	No	%	p-values
Negative	7	35	45	64.29	52	57.78	<0.001S
mildly positive	0	0	10	14.29	10	11.11	
strongly positive	13	65	15	21.43	28	31.11	
Grand Total	**20**	100	**70**	100	**90**	100	

Chi-square = 14.659 with 2 degrees of freedom; P = 0.000

Graph no 5
Association of trop T levels and mortality

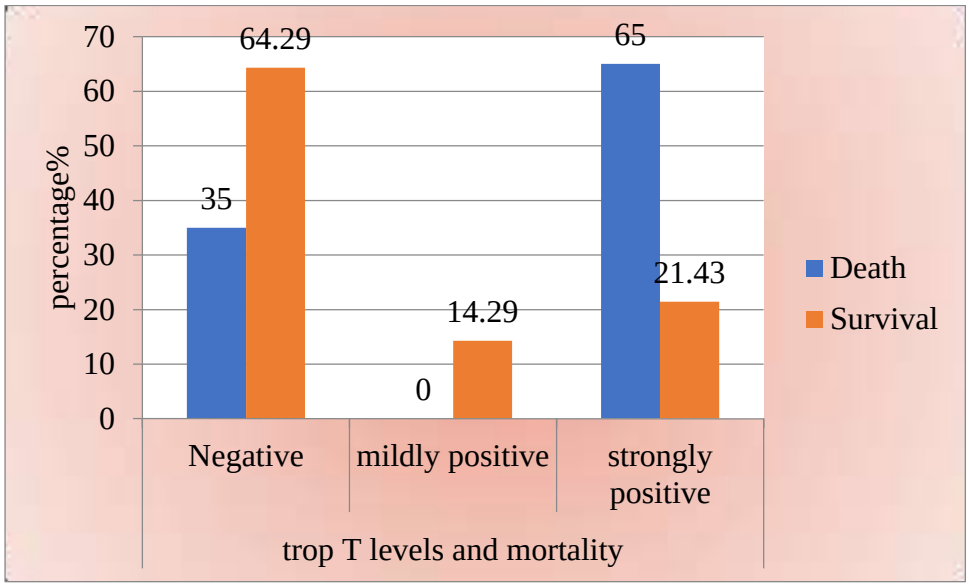

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TABLE5/GRAPH 5: IT SHOWS HIGHEST MORTALITY AMONG PATIENTS WITH RISE IN TROPININ LEVELS MORE THAN 3 TIMES AND RELATIVELY HALF OF THAT IN PATIENTS WITH NEGATIVE TROPONIN T LEVELS WITH A SIGNIFICANT P VALUE (<0.001)

Table No. 6
Correlation of trop T levels with CT severity score.

	N	Mean	SD	P value LS
Negative	32	10.44	5.74	
positive	58	16.09	26.38	0.236NS
Total	90	14.08	21.55	

Graph no 6
Correlation of trop T levels with CT severity score.

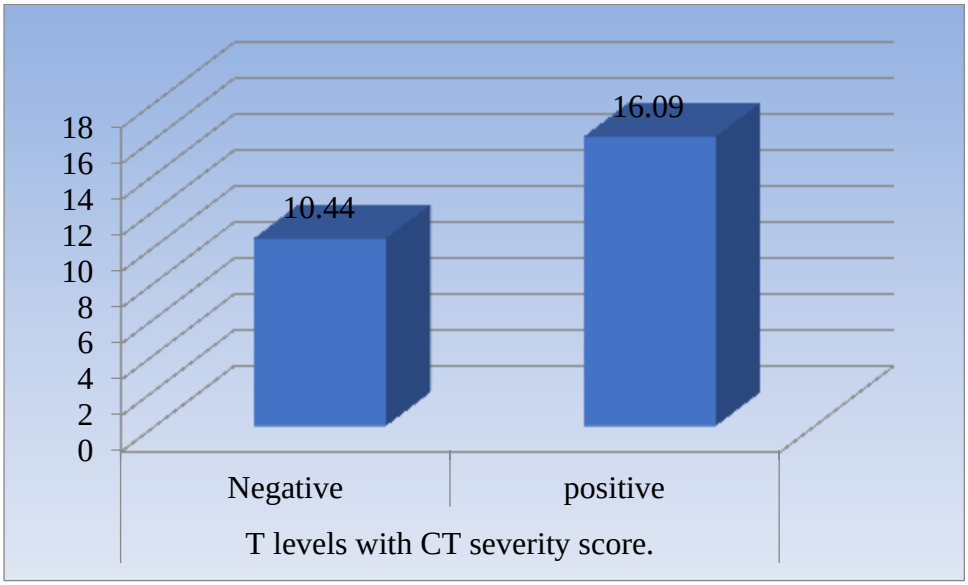

TABLE6/GRAPH 6 : CT SEVERITY SCORE AND RISE IN TROPONIN LEVELS. MEAN CT SCORE IN TROP T POSITIVE GROUP WAS 16.09 VS 10.44 IN TROP T NEGATIVE GROUP.

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Table No. 7
Correlation of MORTALITY WITH CT SEVERITY SCORE, D-DIMER(D), NT PRO BNP LEVELS

		CTSCORE	D-DIMER	NT PRO BNP
Death	N	20	20	20
	Mean	14.70	9974.95	4683.80
	SD	6.47	18436.02	3886.04
	Minimum	4	1030	72
	Maximum	24	87100	15897
Survival	N	70	70	69
	Mean	13.90	2341.62	5111.25
	SD	24.24	3075.22	24301.43
	Minimum	4	232	46
	Maximum	156	19500	198300
Total	N	90	90	89
	Mean	14.08	4037.92	5015.19
	SD	21.55	9490.84	21439.08
	Minimum	4	232	46
	Maximum	156	87100	198300
P value LS		0.885NS	0.001S	0.938NS

Graph no 7
Correlation of trop T levels with CT severity score.

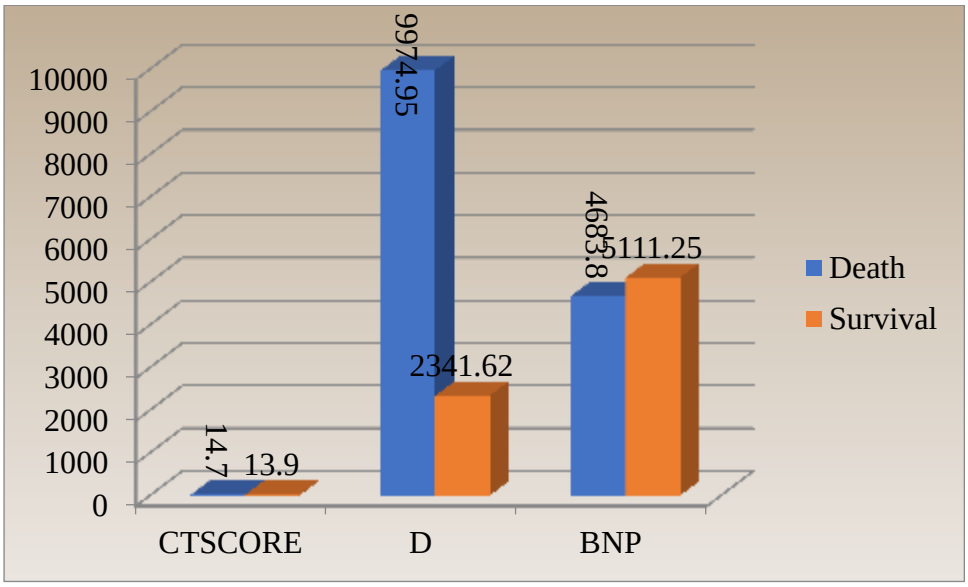

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Table7/graph 7: shows that patients who dies had significantly high levels of d-dimer levels 9974.95 v/s 2341.62 in survival group. However other parameters were not significantly related to mortality.

DISCUSSION

Our study demonstrates a positive correlation of mortality in covid 19 patients and the rise in cardiac biomarkers. Myocardial injury in covid 19 patients with already compromised lung functions due to pneumonia was associated with more complication leading to hypoxia, and unmet oxygen demands .
Its elevation during COVID-19 infection is likely to be multi-factorial, and it is not only attributable to athero-thrombotic coronary occlusion and might be related with an increase of the prevalence of non-ischaemic myocardial injury and type 2 myocardial infarction in SARS-CoV-2-infected patients with a significant respiratory compromise.
In our study, we included 45 patients with raised troponin levels and compared them with those who didn't have raised troponin levels despite rise in D-Dimer and NT pro BNP levels. We found that raised troponin levels were independently associated with high mortality. With increasing age, the risk of complications including death was more with maximum mortality in age group of more than 60 years in both study groups(40% vs 36.6%) however the difference was statistically insignificant. Amongst those who died 15% had underlying dyslipedemia as compared to patients who survived (10% had dyslipedemia), however the difference was not significant. Out of all patients 36.67% were diabetic and 45% of those died while only 33% survived (p value 0.539). Mortlality rate in those with positive troponin levels was found to be 65 % as compared to 35% with patients without myocardial injury as suggested by trop t levels (p value < 0.001). Also we studied any correlation between troponin levels and CT severity score in covid pneumonia and its further relation to mortality but no significant association found.

Our study results are in accordance with the study conducted by manocha et al (11) which also shows that severe troponin elevation defined as ≥0.34 ng/mL were independently associated with 30-day in-hospital mortality. Shi *et al.* (12) also reported that approximately 20% of COVID-19 patients had evidence of a cardiac injury manifested by a significantly elevation of hs-TnI and this finding was associated with a significantly higher in-hospital mortality [51.2% vs. 4.5% respectively; p<.001] as in our study.

Elevation of multiple biomarkers has been shown to correlate with severe COVID-19. Troponin level elevation has been reported in 7.2% to 36% of patients hospitalized with COVID-19.(13)
In the settings of COVID infection it has been suggested that troponemia can be due to microvascular damage occurring in the heart with perfusion defects, vessel hyperpermeability, vasospasm and high cytokine levels may represent the key player of myocardial injury (14). The imbalance between oxygen supply and demand in an acute setting, hypoxaemia, the infectious states often accompanied by fever, tachycardia, endocrine dysregulation, as well as a direct viral vascular infection and inflammation, typically observed in COVID-19 patients, could cause a MI (15). Nevertheless, up to now no substantial higher numbers of AMI have been described with COVID-19.

Our study has few limitations that its a single centre study with a small sample size. Moreover, unfortunately, we could not evaluate whether there was a pre-existing cardiovascular disease. Concluding, COVID-19 can cause a viral pneumonia with additional

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extra-pulmonary manifestations and complications. Cardiac injury, is commonly observed in severe cases, and is strongly associated with mortality. Further studies on large scale are neccessory to establish the correlation of mortality with cardiac biomarkers.

CONCLUSIONS:

A positive correlation was found between mortality and rise in troponin t levels irrespective of any previous known cardiovascular disease in patients and irrespective of the CT severity score. Troponin levels can predict high risk covid 19 pneumonia patients and can help triage the patients for further management.

LIST OF ABBREVIATIONS:

1. ACE- angiotensin converting enzyme
2. SARS-CoV2- severe acute respiratory syndrome coronavirus-2
3. ECG- electrocardiography
4. MI- myocardial infarction

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