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The Association Between Covid19 and Cardiovascular Diseases in COVID Patients Without Previous History of Cardiovascular Diseases

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Abstract

Context: COVID-19 is linked to substantial increases in morbidity and mortality around the globe. Cardiovascular disease (CVD), diabetes, hypertension, and obesity are all risk factors for a more severe case of COVID-19 and an increased risk of death. The purpose of this research was to demonstrate a link with covid19 and the development of cardiovascular disease in previously healthy covid patients. From June 2021 to June 2022, a cross-sectional observational research was carried out at the National Heart Institute in Egypt. Patients with covid-19 linked to cardiovascular disorders made about 20% of the sample, which comprised 200 hospital inpatients. The outcomes were as follows: 79 patients (39.5% of the total) experienced bleeding, 65 patients (32.5% of the total) experienced HF, 21 patients (10.5% of the total) experienced stroke, 10 patients (5%) experienced TIA, 21 patients (10.5% of the total) experienced tachycardia, 14 patients (7% of the total) experienced VA, 12 patients (6% of the total) experienced bradycardia, 11 patients (5.5%) experienced AF, 25 patients (12.5% of Of the 121 patients diagnosed with MI, 121 (or 60.5%) died before receiving PCI. Our research shows that Covid-19 is linked to preexisting cardiovascular illness. Among COVID-19 patients with cardiovascular problems, age, smoking, high blood pressure, diabetes, chronic obstructive pulmonary disease, and chronic kidney disease are all strong independent predictors of death. Patients with covid -19 who develop MACE or HF have an increased risk of dying.

Covid-19, Association, and Cardiovascular Diseases are the Keywords.

Introduction

The large family of single-stranded RNA viruses known as coronaviruses (CoVs) wasn't given much attention until the outbreaks of severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002 and Middle Eastern respiratory syndrome coronavirus (MERS-CoV) in 2012 brought to light their clinical significance and epidemic potential. SARS has a 10% fatality rate while MERS has a 37% mortality rate; both may induce symptoms ranging from the common cold to serious respiratory infections (1).

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE04, 2023

It has been observed that as many as 50% of individuals with severe COVID-19 symptoms also have coagulopathy. The most noticeable shift in coagulation markers in patients with severe COVID-19 is a rise in d-dimer, and rising levels may be utilised as a predictive indicator for a poorer result (2).

It has also been suggested that pulmonary microvascular thrombosis contributes to progressive lung failure. The International Society on Thrombosis and Haemostasis (ISTH) and the American Society of Hematology (ASH) both support LMWH for prophylaxis, however they don't agree on the optimal dose. Given the low frequency of bleeding in COVID-19, it is possible to examine dosages larger than those used in the standard treatment. The complicated picture of coagulopathy in patients with COVID-19 is improved by LMWH not only because of its anticoagulant impact, but also because of its non-anticoagulant features, such as the decrease in interleukin 6 release.

Globally, COVID-19 is linked to substantial increases in mortality and illness. Cardiovascular disease, diabetes, hypertension, and obesity are all risk factors for a more severe case of COVID-19 and an increased risk of death. COVID-19 causes a cascade of cardiovascular complications that culminate in heart failure (HF), including cardiac arrest, myocarditis, acute myocardial damage, stress-induced cardiomyopathy, cardiogenic shock, arrhythmias, and HF.

The purpose of this research was to demonstrate a link with covid19 and the development of cardiovascular disease in previously healthy covid patients.

Cases and Procedures

From June 2021 to June 2022, researchers from Egypt's National Heart Institute gathered data in a cross-sectional observational study. Patients with covid-19 linked to cardiovascular disorders made about 20% of the sample, which comprised 200 hospital inpatients.

The research was conducted with the blessing of Benha University's Medical School's Ethics Committee. All individuals who took part voluntarily provided their informed permission.

Individuals with COVID who developed a cardiovascular disease for the first time were considered for inclusion.

Patients with COVID who developed cardiovascular illness for the first time were not eligible for inclusion since they had a preexisting condition. Newly diagnosed COVID patients with cardiovascular disease often need mechanical breathing owing to imaging challenges and a poor outlook for recovery. Patients with COVID who have recently developed cardiovascular disease also often suffer from chronic kidney disease or chronic liver disease.

Whole patient histories were taken [including age, sex, weight, height, BMI, and any other complaints such as weariness (loss of energy and inability to exert more effort than previously)]. Risk factors such as high blood pressure, diabetes, high cholesterol, heart

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE04, 2023

disease, irregular heartbeat, previous myocardial infarction (MI), COPD, CKD, and smoking.

Indices of health [heart rate. systolic blood pressure, diastolic blood pressure, oxygen saturation, and temperature] sinus tachycardia (heart rate more than 100 bpm and seen by patient who reports sensing of his heart beats that he has not sensed before).

Hemoglobin, leukocytes, thrombocytes, cholesterol, triglycerides, potassium, sodium, creatinine, urea, troponin I, C-reactive protein, and D-dimer are some of the tests that may be run in the lab.

We also performed a PCR experiment.

All individuals who were suspected had a CT chest performed to rule out any lung affection caused by the corona virus.

The appearance of ground-glass opacities, consolidations, a crazy-paving pattern, or linear opacities in the lungs is among the CT criteria for diagnosing COVID-19 in patients. These symptoms may also include the involvement of numerous lobes, as well as a bilateral and peripheral spread of the lesions.

All patients had an echocardiogram while their electrocardiograms were being recorded. During end-expiratory apnea, the conventional parasternal long-axis view and three apical views were used to capture digital routine grayscale 2D cine loops of three consecutive heartbeats at depths of 12-14 cm with mean frame rates of 67 8 frames/sec. The frame rate was maximised while still allowing for full sector visibility of the myocardium. Current recommendations from the American Society of Echocardiography and the European Association of Cardiovascular Imaging were used to get standard LV values (3). Using apical 2- and 4-chamber views at ventricular end-systole, the left ventricular (LV) volumes and LVEF were determined using the modified biplane Simpson's approach, which was also used to determine the left atrial (LA) volume.

In order to account for the impact of obesity on the LV mass, it was indexed to both body surface area and height. The velocity-time integral was used to evaluate left ventricular (LV) stroke volume using pulsed-wave Doppler placed at the LV outflow tract.

Using pulsed-wave Doppler recording in the apical four-chamber view, we determined the velocities of the early diastolic (E) and atrial waves and the E-wave deceleration time. The septal mitral annulus early diastolic velocity (E') was measured using spectral pulsed-wave Doppler, and the E/E' ratio was used to determine left ventricular (LV) filling pressure (4).

Patients in need of percutaneous coronary intervention for acute coronary syndrome had their procedures performed through the femoral and radial arteries utilising the seldinger method (5).

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE04, 2023

Number crunching

SPSS v26 was used for the statistical analysis (IBM Inc., Armonk, NY, USA). The average and standard deviation of numerical variables were provided (SD). The percentage and frequency distributions of the qualitative variables were shown. Diagnostic performance was measured by sensitivity, specificity, PPV, and NPV. Analysis of the receiver operating characteristic (ROC) curve was used to compare the overall diagnostic performance of each test; a perfect test would have a curve that went from the bottom left to the top left to the top right. The area under the curve (AUC) measures how well a test does as a whole (where an AUC of 50% or higher indicates satisfactory performance and an AUC of 90% or higher indicates optimal performance). Independent predictive factors influencing mortality were assessed by multiple regression analysis. The cutoff for statistical significance was a two-tailed P value of less than 0.05.

Results

Patients' ages varied from 25 to 60, with a mean of 43.0510.64 years old, according to the study's demographic data. Of the total, 88 were male (44%), while 112 were female (56%). The average was 72.65 4.66 kg (65 to 80 lb). The average height was 1.63 m 0.06 m, while the range was from 1.5 m to 1.7 m. The average body mass index was 27.512.45 kg/m2, with a range of 22.76-34.22 kg/m2. All of the patients had a positive PCR. Table 1

The risk variables among the individuals evaluated were as follows: 68 (34%), hyperlipidemia; 62%, smoking; 61%, hypertension; 56%, diabetes; 10%, chronic kidney disease; 5%, chronic obstructive pulmonary disease; and 0%, coronary artery disease, cardiac arrhythmia, or prior MI. Clinical manifestations within the sample included: tiredness in 78 (39%) patients, dyspnea in 65 (32.5%) patients, swelling in 64 (32%) patients, swelling in 59 (29.5%) patients' upper limbs, fever in 35 (17.5%), chest discomfort in 33 (16.5%), headache in 31 (15.5%), and sore throat in 8 (4%) patients. Table 2

Patients' systolic blood pressure (SBP) was between 110 and 150 mmHg, with a mean of 130.1 mmHg (12.15). The average DBP was 84.35 mmHg, with a range of 70-100 mmHg. Heart rates varied from 70 to 125 bpm, with a mean of 87.19 bpm 13.5. The average RR was 25.496.2 beats per minute, with a range of 15-35 beats per minute. The average oxygen content was 91.311.93%, with a range of 88-94%. The average temperature was 37.520.32 degrees Celsius. Example 1 (A)

Patients' Hb levels on lab tests varied between 10 and 12 g/dL, with a mean of 10.96 g/dL 0.65 g/dL. WBCs were on average 5.211.26 *103/ l, with a range of 3.0–7.5 *103/ l. The platelet count varied from 151 to 400 per microliter of blood, with a mean of 279.05 72.8. The average cholesterol level was 185.02 14.5 mg/dL, with a range of 160-210 mg/dL. The average TG level was 131.23 11.49 mg/dL, with a range of 110-150 mg/dL. The average concentration of K+ was 3.72 0.73 mEq/L, with a range of 2.5-4.99 mEq/L. Average N+ concentration was 123.01 7.72 mEq/L, with a range of 110-135 mEq/L. The median creatinine level was 1.32 0.79 mg/dL, while the range was 0.74 4.4 mg/dL. The

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE04, 2023

average uric acid level was 13.24 8.97 mg/dL, with a range of 6-44 mg/dL. Mean and standard deviation for troponin I were 0.75 and 0.28 ng/mL, respectively. The average CKMB level was 1.86 2.23 IU/L, and the range was 0.5-11.5 IU/L. The average CRP level was 124.5 22.64 mg/L, with a range of 85-160 mg/L. The normal range of D-dimer was 0.5-10.2 ng/mL, and the median was 1.51.49 ng/mL. Example 1 (B)

A total of 79 (39.5%) patients experienced bleeding, 65 (32.5%) experienced heart failure, 21 (10.5%) experienced stroke, 10 (5.0%) experienced transient ischemic attack, 21 (10.5%) experienced tachycardia, 21 (10.5%), experienced ventricular arrhythmia (VA), 14 (7.0%) experienced bradyarrhythmia, 11 (5.5%) experienced atrial fibrillation (AF), 25 (12.5%) experienced pulmonary embolism, 25 (12.5%) Of the 121 patients diagnosed with MI, 121 (or 60.5%) died before receiving PCI. Example 2

With an area under the curve (AUC) of 0.594, sensitivity (S) of 68.60, specificity (S) of 43.04, PPV (P) of 664.8, and NPV (P) of 47.4(P value =0.021), troponin-I is a highly predictive biomarker for mortality. Model No. 3 (A)

With an AUC of 0.588, sensitivity of 69.42, specificity of 45.57, PPV of 64.23, and NPV of 44.8 (P value =0.029), CKMB is an excellent predictor of mortality. Image 3 (B)

Independent of one another, age, smoking, hypertension, diabetes, chronic obstructive pulmonary disease, and chronic kidney disease are all strong predictors of death. The risk of dying from hyperlipidemia or sex is not very high. Listing 3v

Significant independent mortality predictors are MACE and HF. In terms of predicting mortality, strokes, haemorrhages, MIs, and PCIs have just a little role. Table 4

Discussion

The risk variables among the individuals evaluated were as follows: 68 (34%), hyperlipidemia; 62%, smoking; 61%, hypertension; 56%, diabetes; 10%, chronic kidney disease; 5%, chronic obstructive pulmonary disease; and 0%, coronary artery disease, cardiac arrhythmia, or prior MI.

Kong et al. (2021) found similar numbers: 684 (12.9%) with diabetes, 55 (1.0%) with chronic kidney disease, 1,197 (22.6%) with hypertension, and 38 (0.7%) with chronic obstructive pulmonary disease.

The incidence of CVD was 36.7% in a Yale University prospective cohort study of 586 COVID-19 individuals. Hypertension was recorded at a rate of 60.2%, with diabetes at 39.8% and hyperlipidemia at 38.6% following closely behind. All-cause mortality was linked with advanced age (OR = 1.28), a history of ventricular arrhythmia (OR = 18.97), treatment with P2Y12-inhibitors (OR = 7.91), elevated C-reactive protein (CRP; OR = 1.81), elevated homocysteine (hs-cTnT; OR = 1.84) and low albumin (OR = 0.64) in this population (6).

Evidence from many research links CKD to an increase in COVID-19 mortality (7). CKD patients had an increased risk of death compared to healthy controls, and this increased

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE04, 2023

risk was inversely proportionate to the patients' glomerular filtration rate in studies conducted in Europe and the United States (8, 9). Renal failure exacerbates COVID-19 for several reasons. Uremic individuals, for one, have compromised immune systems (10).

Natural killer cell counts and ratios have been shown to be different between COVID-19 patients on hemodialysis and those who do not need the treatment. Second, cardiovascular disease is more common in those with CKD compared to those with normal renal function (11). In patients with CKD, cardiovascular disease is a leading cause of death and is a major contributor to the high COVID-19 mortality rate.

Those who already suffer from a respiratory condition seem to have a less favourable prognosis for any subsequent respiratory illnesses (12). The prognosis of COVID-19 pneumonia has been demonstrated to be significantly affected by chronic obstructive pulmonary disease. There has been no established evidence of this link among asthma sufferers. Previous meta-analyses indicated that compared to those without COPD, individuals with COPD had an odds ratio of 4.38 for developing severe COVID-19 and a relative risk of 1.88. (13). The aforementioned studies were meta-analyses; the present research differs in its methodology.

According to research conducted in China (14), patients with COVID-19 who had an elevated level of the cardiac biomarker troponin T had a higher risk of death regardless of preexisting cardiovascular disease. Furthermore, nearly 12% of patients without known cardiovascular disease had elevated troponin levels or experienced cardiac arrest while in the hospital (15). Indirectly explaining the mechanism of illness severity and death in our study, previous research has linked higher troponin levels to mortality.

Prior research has shown an independent association between high cardiac troponin and pro-brain natriuretic peptide and poor outcomes in individuals with COVID-19 (14, 16). Unfortunately, there is a dearth of data indicating which individuals have increased cardiac biomarkers. Virus mutations are still driving the COVID-19 pandemic, and other respiratory viruses are likely candidates for causing future worldwide pandemics. Hence, to better patients' outcomes, we need to keep studying COVID-19 and the cardiovascular system. Patients with numerous CV risk factors were shown to have a higher chance of severe COVID-19 by this investigation. The proportional increase of cardiac troponin or pro-brain natriuretic peptide or new-onset atrial fibrillation, reflecting cardiac complications and poor outcome of COVID-19 patients, should be investigated in future follow-up studies to determine whether the risk score model/multiple CV risk factors in this study is associated with this.

With an area under the curve (AUC) of 0.594, sensitivity (S) of 69.42%, specificity (S) of 45.57%, PPV (NPV) of 64.23%), and P value (P value =0.029), CKMB was shown to be a significant predictor of mortality in the current investigation.

Intensive care unit patients with COVID-19 were found to have significantly higher levels of cardiac damage markers (CK-MB and hs-cTnI) compared to those who did not

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE04, 2023

require intensive care, and they were also significantly more likely to exhibit arrhythmia (44.4% vs. 6.9%) than those who did not require intensive care .[6]

Moreover, some authors conducted a retrospective cohort research on 191 patients to investigate patient risk factors for mortality while hospitalised and to characterise the clinical course of symptoms, viral shedding, and temporal changes in laboratory data. Creatine kinase myocardial isoform (CK-MB) concentrations were found to be significantly higher in the deceased compared to the living (17).

Mortality was shown to be significantly predicted by age, smoking status, high blood pressure, diabetes, chronic obstructive pulmonary disease, and chronic kidney disease in the present investigation. The risk of dying from hyperlipidemia or sex is not very high.

According to a multivariate analysis, the following were all significant predictors of critical illness: age 60, male sex, diabetes mellitus, hypertension, heart failure, chronic renal disease, cancer, and dementia. Individuals over the age of 60, male gender, high blood pressure, and diabetes mellitus had a risk of severe COVID-19 that was almost 100 times greater than that of patients without these risk factors (OR; 95% confidence interval, 104; 45.6-240.6 for critical, 136.2; 52.3-3547.9). (18).

Around 130,000 people were infected with COVID-19 in Bergamo, Italy. Pediatric vascular inflammatory syndrome Kawasaki-like illness has increased 30-fold in this region. The average age of the afflicted individuals was significantly higher than the general population's ((7.5 3.5) vs. (3.0 2.5), P = 0.00035) and there was greater cardiovascular involvement in this group (19, 20).

Obesity classes I through III are risk factors for in-hospital death or mechanical ventilation (OR = 1.28, 1.57, and 1.80, respectively), and obesity class III is associated with the risk of in-hospital death (HR = 1.26), according to an analysis of 7606 patients from the AHA COVID-19 registry through July 22, 2020. Class I to III obesity and being overweight are also associated with an increased likelihood of needing mechanical ventilation (OR = 1.28, 1.54, 1.88, and 2.08, respectively) (21).

The French and the Chinese made parallel discoveries. After controlling for age, sex, and comorbidities like diabetes, hypertension, and dyslipidemia, the authors of a retrospective cohort study from the University Hospital in Lille, France found an OR of 7.36 for the need for invasive mechanical ventilation among obese COVID-19 patients (BMI 35 kg/m2) compared to those with a BMI 25 kg/m2 (22).

The present research finds that age, smoking, high blood pressure, diabetes, chronic obstructive pulmonary disease, and chronic kidney disease are all strong independent predictors of death. The risk of dying from hyperlipidemia or sex is not very high. Independent of one another, MACE and HF are strong predictors of death. The risk of dying from a stroke, haemorrhage, or heart attack is quite low.

These results are in line with previous research showing that older age and co-morbidities such hypertension, diabetes, and COPD are significant risk factors for death in COVID-

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE04, 2023

19 patients (23, 24). In addition, smoking has been linked in many studies to an increased risk of death from COVID-19 (25).

Patients with COVID-19 who had no history of cardiovascular disease were shown to have an increased risk of death if they developed MACE or HF. Consistent with previous reports, this study found that COVID-19 patients, especially those with preexisting cardiovascular disorders, had a significant rate of cardiovascular problems (26). Stroke, haemorrhage, MI, and PCI were not shown to be significant predictors of death in this study's sample of participants. Consistent with these data, a meta-analysis indicated that COVID-19 patients had a reduced risk of stroke and bleeding (27).

Conclusion

According on our findings, Covid-19 is linked to preexisting cardiovascular disease. Among COVID-19 patients with cardiovascular problems, age, smoking, high blood pressure, diabetes, chronic obstructive pulmonary disease, and chronic kidney disease are all strong independent predictors of death. Patients with covid -19 who develop MACE or HF have an increased risk of dying.

Funding Origins

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Authorship Responsibility

All authors made significant contributions to the work.

Interest discrepancies

No potential biases

References

Table 1: Baseline characteristic data of the studied patients

		N=200
Age (years)	**Mean ± SD**	43.05±10.64
	Range	25-60
Sex	**Male**	88 (44%)
	Female	112 (56%)
Weight (Kg)	**Mean ± SD**	72.65±4.66
	Range	65-80
Height (m)	**Mean ± SD**	1.63±0.06
	Range	1.5-1.7

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE04, 2023

BMI (kg/m^2)	**Mean ± SD**	27.51±2.45
	Range	22.76-34.22
PCR		200 (100%)

BMI: body mass index, PCR: polymerase chain reaction

Table 2: Risk factors and Clinical presentation of the studied patients

	N=200
Hyperlipidemia	68 (34%)
Smoking	62 (31%)
Hypertension	61 (30.5%)
Diabetes mellitus	56 (28%)
CKD	21 (10.5%)
COPD	10 (5%)
Coronary artery disease	0 (0%)
Cardiac arrhythmia	0 (0%)
Previous MI	0 (0%)
	N=200
Fatigue	78 (39%)
Dyspnea	65 (32.5%)
Lower limb swelling	64 (32%)
Upper limb swelling	59 (29.5%)
Fever	35 (17.5%)
Chest pain	33 (16.5%)
Headache	31 (15.5%)
Sore throat	8 (4%)

CKD: chronic kidney disease, COPD: chronic obstructive pulmonary disease, MI: myocardial infarction

Table 3: Multivariate logistic regression for independent predictors of mortality

Variable	Coefficient	Std. Error	Wald	P
Age	0.040483	0.018319	4.8837	**0.0271**
Sex	0.16840	0.38414	0.1922	0.6611
Smoking	-2.50162	0.36782	46.2571	**<0.0001**
CKD	2.42886	0.83301	8.5018	**0.0035**
HTN	-2.50527	0.67397	13.8175	**0.0002**
DM	-1.52016	0.70571	4.6401	**0.0312**
Hyperlipidemia	-0.31102	0.39440	0.6219	0.4303
COPD	-2.51405	1.12365	5.0059	**0.0253**

Odds Ratios and 95% Confidence Intervals		
Variable	Odds ratio	95% CI
Age	1.0413	1.0046 to 1.0794
Sex	1.1834	0.5574 to 2.5126
Smoking	11.3459	2.2170 to 58.0642
HTN	0.0817	0.0218 to 0.3060
DM	0.2187	0.0548 to 0.8720
Hyperlipidemia	0.7327	0.3382 to 1.5872

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE04, 2023

COPD	0.0809	0.0089 to 0.7322
CKD	2.4289	1.0382 to 5.6829

CI: confidence interval, CKD: Chronic kidney disease, HTN: Hypertension

Table 4: Multivariate logistic regression for independent predictors of mortality

Variable	Coefficient	Std. Error	Wald	P
MACE	0.99462	0.48572	4.1932	**0.0406**
HF	-2.42610	0.35568	46.5269	**<0.0001**
Stroke	0.29698	0.48736	0.3713	0.5423
Bleeding	-0.069506	0.29549	0.05533	0.8140
MI	-0.021414	0.92455	0.0005365	0.9815
PCI	0.27073	1.23338	0.04818	0.8263
Odds Ratios and 95% Confidence Intervals				
Variable	Odds ratio	95% CI		
MACE	2.7037	1.0435 to 7.0050		
HF	0.0884	0.0440 to 0.1775		
Stroke	1.3458	0.5178 to 3.4981		
Bleeding	0.9329	0.5227 to 1.6647		
MI	0.9788	0.1598 to 5.9937		
PCI	1.3109	0.1169 to 14.7045		

MACE: Major adverse cardiovascular events HF: heart failure, MI: myocardial infraction

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE04, 2023

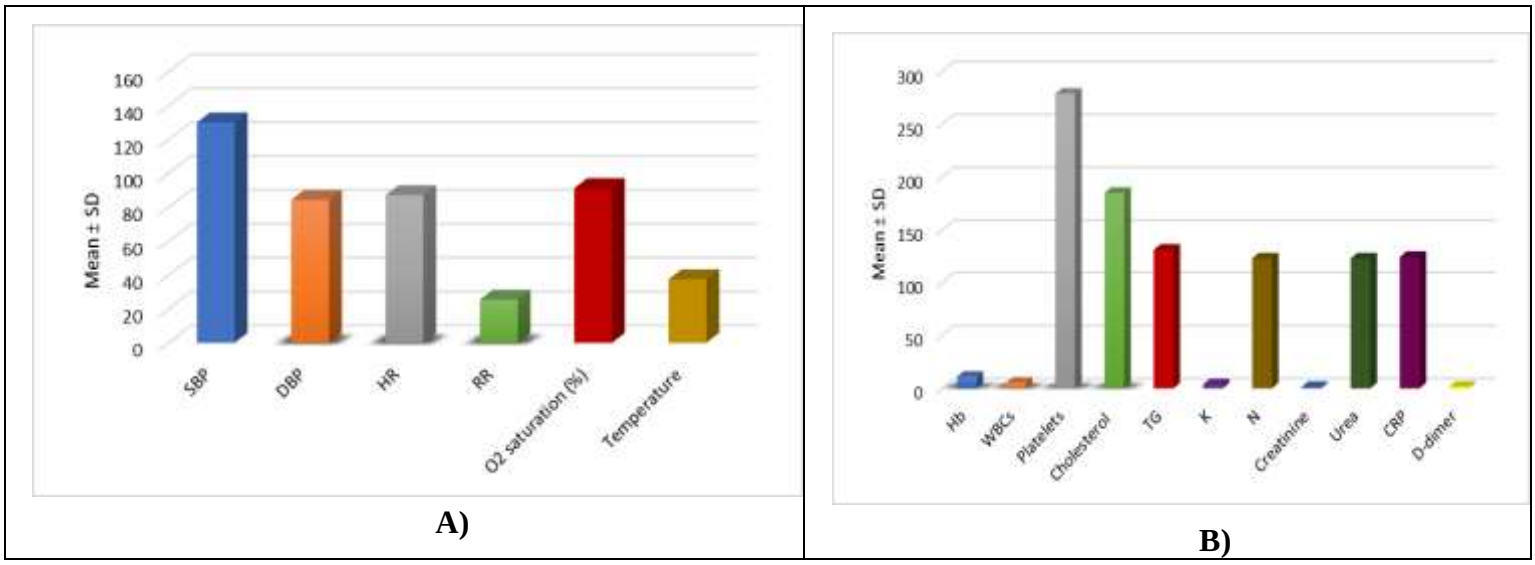

Figure 1: A) Vital signs of the studied patients and B) Laboratory investigations of the studied patients

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE04, 2023

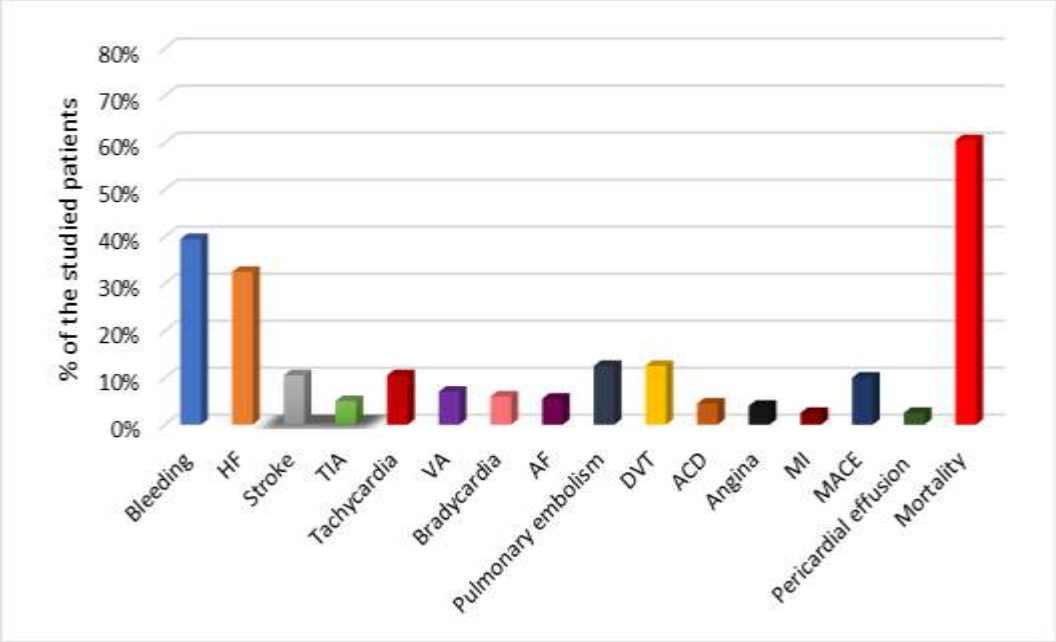

Figure 2: The outcome among the studied patients

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE04, 2023

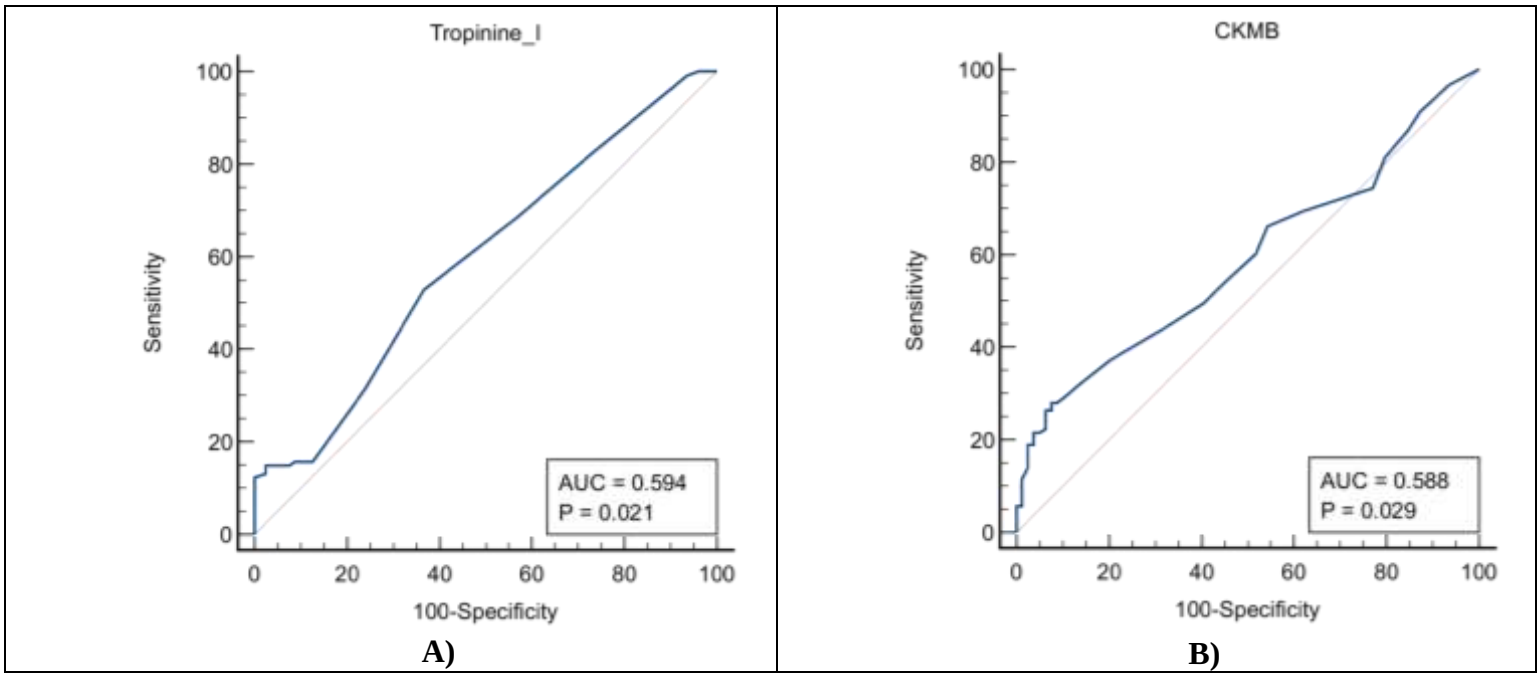

Figure 3: A) ROC curve of troponin-I for prediction of mortality and B) ROC curve of CKMB for prediction of mortality