Assiut University Registry for Acute Coronary Syndrome Patients during COVID-19 Pandemic: A Prospective Observational Study

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Abstract:

Background: The COVID-19 pandemic affected management protocols for acute coronary syndrome (ACS) patients worldwide, including Egypt, to provide optimal management for this critical group of patients while minimizing harm to patients and healthcare workers. We aimed to investigate the impact of the COVID-19 pandemic on the management strategies and outcomes of ACS patients in a university hospital. In this observational prospective longitudinal cohort study, all ACS patients admitted to a university hospital within 15 months during the COVID-19 pandemic were recruited. All patients were subjected to a full medical history, ECG, echocardiography, routine investigations, and follow-up for in-hospital major complications and 12-month adverse events. They were screened for COVID-19 symptoms, and CT chest and PCR tests were conducted for suspected cases.

Results: A total of 2252 patients were recruited. ACS was more prevalent among rural, elderly, male, and hypertensive patients. Among them, 1482 (65.9%) had STEMI, with 74.9% undergoing primary PCI and 15.4% receiving thrombolytic therapy. Regarding COVID status, 690 (30.6%) of patients were suspected based on symptoms. A multivariate logistic regression model showed that COVID-19 was associated with more in-hospital complications and more MACE on 12-month follow-up (OR=5.021, 95%CI= 1.995 – 8.661, P < 0.001). The number of ACS admissions and the percentage of primary PCI procedures performed during the pandemic both decreased in comparison to before and after the pandemic (P value=0.044).

Conclusion: COVID-19 strongly affected management strategies as STEMI patients with suspected COVID-19 infection received more thrombolytic therapy and underwent less PPCI, in addition to higher in-hospital and 12-month MACE.

Keywords: Acute coronary syndrome; COVID-19; Primary percutaneous; Intervention; MACE.

Background

During the rapidly evolving coronavirus disease 2019 (COVID-19) pandemic, many healthcare systems around the globe modified their routine management of patients presenting with acute cardiovascular emergencies, including those with acute coronary syndrome (ACS). A unifying theme in the new management strategies was the adoption of restrictive measures to mitigate the increased risk of infection among healthcare workers [1].

The developing countries already struggle to provide many services and support to their citizens; for the most vulnerable citizens in the most vulnerable countries, this crisis was particularly destructive. Already strained health systems were struggling to manage the effects of COVID-19[2].

Egypt, with an estimated population of 100 million, faced exceptional challenges during the COVID-19 crisis. The large-scale use of polymerase chain reaction (PCR) tests for SARS-CoV-2 in such a vast population was problematic, resulting in an unknown prevalence of COVID-19 infection in the country. Additionally, the supply of personal protective equipment (PPE) fell far short of demand, particularly in cardiac catheterization rooms where professional protection was lacking. As the pandemic progressed within this densely populated country, the care of COVID-19 patients overwhelmed hospital supplies, beds, and staff [1].

COVID-19 patients with cardiac issues are at higher risk of morbidity and mortality. They may experience exacerbations of pre-existing cardiac conditions, acute heart failure, acute myocarditis, acute coronary syndrome, acute stent thrombosis, venous thromboembolism, and various arrhythmia. Some may present with ACS-like ECG findings despite non-significant lesions, while others may exhibit severe cardiomyopathy with normal coronary arteries (resembling Takotsubo syndrome). Additionally, certain treatments for COVID-19, such as the hydroxychloroquine-azithromycin combination, can lead to potentially fatal prolonged QT intervals [3].

In this study, we aimed to investigate the change in management strategies and outcomes of ACS patients admitted to a University Heart Hospital during and after the control of the COVID-19 pandemic.

Methods

Study Group and Design: This is an observational, prospective, longitudinal cohort study that enrolled consecutive patients admitted with ACS to the Cardiovascular Medicine Department at Assiut University Heart Hospital. Enrollment of patients began on March 1st, 2020, and concluded on May 31st, 2021.

Inclusion and Exclusion Criteria: Patients with any type of ACS were included in the study (no patients were excluded).

Methodology:

All patients underwent Full history taking, including demographic data. Risk factors for CAD: Hypertension, diabetes, smoking status, family history. Co-morbidities: Stroke, chronic kidney disease, chronic liver disease, COPD. History of suspected or confirmed COVID-19 infections on admission. Full physical examination, including cardiac examination and twelve-lead ECG. ACS-related data: Type of ACS: STEMI or NST-ACS (high, moderate, or low risk). For STEMI patients: (Location of infarction. Reperfusion strategy: fibrinolysis, primary PCI, or medical treatment only; Time from onset of chest pain to ER; Time from door to device for those undergoing PPCI; Success of fibrinolysis and Reason for conservative management). For NST-ACS: (Risk category by GRACE score: High vs. intermediate vs. low; Definitive management: invasive or conservative strategy). Risk stratification according to the GRACE score [4] was calculated for NST-ACS patients. considering a GRACE score of ≤ 109 as low, 110 – 139 as moderate, and ≥ 140 as high. Variables included in the in-hospital GRACE risk score are Age, Heart rate, Systolic blood pressure, Serum creatinine level, KILLIP class, Cardiac arrest at admission, Elevated cardiac markers, and ST segment deviation.

Laboratory and Imaging data

1. All routine laboratory investigations were done. A single sample of troponin I, withdrawn on admission, was recorded.
2. Transthoracic echocardiography is used to assess regional wall motion abnormalities, valvular assessment, MI mechanical complications, and left ventricular ejection fraction on discharge.

COVID status: WHO criteria were used for diagnosis of COVID-19 infection and identification of suspected, probable, and confirmed cases [5]. Presence of COVID was checked by one or more of the following:

1. Symptoms: fever or respiratory distress.

2. CT chest with findings based on CORADS classification for COVID diagnosis [6].
3. Polymerase chain reaction (PCR) test.
4. Transfer to the isolation hospital.

Outcome ascertainment: All patients were followed up for 12 months in the hospital with major adverse cardiac events (MACE).

In-hospital MACE, including length of hospital stay, was documented. MACE included: Mortality; ACS-related Mechanical complications (e.g., mitral regorge, septal rupture); Cardiogenic shock; Arrhythmias (Heart block and ventricular arrhythmia); New congestive heart failure; Need for mechanical ventilation and Ischemic stroke and intracranial hemorrhage.

Hospital Follow-up data: All patients were followed up 30 days and 12 months after discharge (by phone calls) for reporting MACE, including: Hospital readmission for any cause; Unplanned Coronary revascularization; New MI, Stroke; All-cause mortality [7] including COVID-related mortality [8].

Impact of the COVID-19 pandemic on ACS admissions and PPCI: We compared the numbers of ACS admissions and the percentage of PPCI in our study with a similar period (15 months) before and after the pandemic.

Statistical Analysis:

Data was verified, coded by the researchers, and analyzed using IBM-SPSS (IBM-SPSS Inc., Chicago, IL, USA). Descriptive statistics: Means, standard deviations, medians, ranges, frequency, and percentages were calculated. Test of significance: The chi-square test was used to compare the difference in the distribution of frequencies among different groups. A t-test was used to compare the means of different groups.

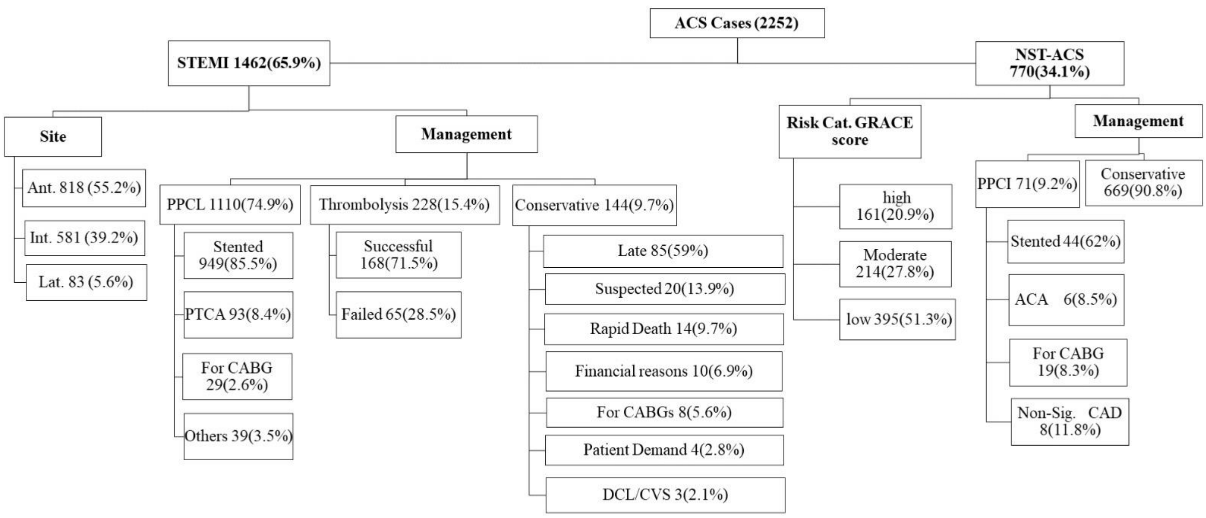
Univariate and multivariate logistic regression models were used to predict the relations between dependent and independent variables, and a backward stepwise regression model was used to eliminate insignificant variables. McNemar test was used to compare frequency on repeated analysis. The P-value of the two-way ANOVA for interaction between time and group was calculated to compare numbers during, before, and after the pandemic. A P-value of less than 0.05 was considered significant.

Ethical Considerations:

All patients gave informed consent immediately after admission to the Coronary Care Unit. If patients died before admission, consent was obtained from relatives. The study protocol, including patient information and consent forms, was reviewed and approved by the Ethics Committee of Medicine faculty, Assiut University, **IRB No.17101309. Assiut's Faculty of Medicine approved the study.**

Results

Figure 1: Flow chart shows the distribution and management of the total study group



Flow chart (1)

Abbreviations: Ant = anterior, CABG = coronary artery bypass graft, CAD = coronary artery disease, CVS = cerebrovascular stroke, DCL = disturbed conscious level, Inf = inferior, lat = lateral, NST-ACS = non-ST elevation acute coronary syndrome, post = posterior, PPCI = primary percutaneous intervention, PTCA = percutaneous trans=coronary angioplasty, STEMI = ST-elevation myocardial infarction.

Baseline Characteristics of the Studied Patients

The current study included 2252 adult patients presenting with acute coronary syndrome during the recruitment period admitted to Assiut University Hospitals, as shown in **Figure 1.**

Regarding the baseline characteristics of the studied group: Most of our patients came from rural areas (63.4 %), male gender was predominant (71.7 %) with a mean age of 60.65 ± 11.7 years; however, 3.8% were ≤ 35 years old, 2/3 of our patients were STEMI and 1/3 had NST- ACS. **(Table 1)**

Hypertension and previous history of dyslipidemia were the most frequent risk factors among the study population (44.9 % vs 37.5%), respectively. Smoking and chronic kidney disease (CKD) were more prevalent among COVID-suspected patients, with statistically significant differences. Regarding out-of-hospital COVID status, (2.3 %) of recruited patients had a history of confirmed infection before admission. **(Table 1)**

Table (1): Baseline characteristics and history of the studied sample:

	Total	**Non-Suspected**	**Suspected**	**P-value**
Number	2252	1562 (69.4%)	690 (30.6%)	
Age/years (Mean ± SD)	58.14 ± 11.9	58.13 ± 11.9	58.16 ± 11.9	= 0.962
Age category (years)				= 0.587
• ≤ 35	85 (3.8%)	56 (3.6%)	29 (4.2%)	
• 35 – 55	743 (33%)	524(33.5%)	219 (31.7%)	
• ≥ 55	1424 (63.2%)	982 (62.9%)	442 (64.1%)	
Male sex	1614 (71.7%)	1118 (71.6%)	496 (71.9%)	= 0.881
Smoking	375(16.7%)	274 (17.5%)	101 (14.6%)	= 0.049
Co-morbidities				
• Hypertension	1012 (44.9%)	703 (45.1%)	309 (44.8%)	= 0.902
• DM	834 (37.1%)	564 (36.2%)	270 (39.1%)	= 0.097
• CVS	83 (3.7%)	60 (3.8%)	23 (3.3%)	= 0.578
• COPD	57 (2.5 %)	37 (2.4%)	20 (2.9%)	= 0.461
• CKD	96 (4.3%)	57 (3.6%)	39 (5.7%)	= 0.041
• Liver disease	14 (0.6%)	11 (0.7%)	3 (0.4%)	= 0.681
History of IHD				
• Previous MI	583 (25.9%)	409 (26.2%)	174 (25.3%)	= 0.341
• Previous PCI /CABG	384 (17.1%)	277 (17.7%)	107 (15.5%)	= 0.108
• Statin therapy	805 (37.5%)	564 (36.2%)	241 (34.9%)	= 0.305
Out of hospital COVID status				
• Confirmed	52 (2.3%)	30 (3.2%)	22 (1.9%)	= 0.241

Abbreviations: COPD = chronic obstructive pulmonary disease, CKD = chronic kidney disease, CVS = cerebrovascular stroke, MI = myocardial infarction, PCI = percutaneous intervention, CABG = Coronary artery by bass graft, STEMI = ST-elevation myocardial infarction, NST-ACS = non-ST elevation acute coronary syndrome, IHD=ischemic heart disease.

The in-hospital COVID status of the total study population: Table (2) shows that out of the total study population, 30.6 % were suspected to have COVID-19 infection by either fever, respiratory distress, or both. CT chest was done for (13.9 %) of the total population, and it was highly suggestive of COVID-19 in (57.4 %) of them. PCR was done for (7.9%) of patients and was positive in (60.9 %) of them. Accordingly, (4.8%) confirmed COVID-19 infection by PCR, and (25.7 %) confirmed cases were transferred to isolation within our hospital.

Laboratory investigations and Echocardiographic assessment: In our study, 14.4 % of our patients were newly diagnosed diabetic during hospital admission with hemoglobin A1C ≥ 6.5 %. 22.5% of STEMI patients had negative Troponin on presentation. This can be explained by an early presentation from nearby residents, presenting within less than one hour from the onset of symptom, those whose ECG showed ST elevation and CA showed normal coronaries or had non-significant obstruction in addition to false negative results. As for NST-ACS patients (81.6%), they had positive Troponin, as shown in Table (2).

Table (2): In-hospital COVID-19 Status, laboratory investigations, and LV- EF of the studied sample

Symptoms	Total	STEMI	NST-ACS	P-value
Suspected by symptoms				
Fever only	444 (19.7%)	259(17.5%)	185(24%)	< 0.001
RD only	63 (2.8%)	41(2.8%)	22(2.9%)	= 0.681
Both Fever and RD	183(8.1%)	119(8%)	64(8.3%)	= 0.816
Total	690 (30.6%)	419(28.3%)	271(35.2%)	=0.045
Probable by suggestive CT chest	179/312(57.4%)	106/140(75.7%)	73/172(42.4%)	< 0.001
Confirmed by Positive PCR Result	109/179(60.9%)	71/102(69.7%)	38/77(49.4%)	= 0.006
Excluded	111 (4.9%)	69(4.7%)	42(5.5 %)	= 0.406
Transferred to isolation	28/109 (25.7%)	17/71(23.9%)	11/38(28.9%)	= 0.010
Positive Troponin by mg/ dl	1879 (83.4%)	1150 (77.5%)	628 (81.6%)	= 0.033
Hemoglobin by mg/dl	12.91 ± 2.1	12.08 ± 2.1	12.88 ± 1.9	< 0.001
TLC by 1000 cell /µl	10.53 ± 4.5	10.3 ± 4.5	10.52 ± 4.2	= 0.357
Lymphocytes ratio	25.72 ± 7.3	56.9 ± 7.6	59.95 ± 7.9	< 0.001
Neutrophil ratio	58.53 ± 7.2	25.36 ± 7.8	25.14 ± 8.2	= 0.533
Creatinine by mg/dl	1.19 ± 1.3	1.21 ± 1.1	1.13 ± 0.8	= 0.074
Hemoglobin A1C by mg/dl	6.40 ± 1.1	6.36 ± 1.1	6.47 ± 1.2	= 0.029
Newly diagnosed diabetic	324(14.4 %)	237 (15.9 %)	87 (11.3 %)	= 0.003
LDL-Cholesterol by mg /dl	1117 ± 42.4	116.55 ± 42.4	118.51 ± 43.2	= 0.301
Total Cholesterol by mg /dl	188 ± 52.9	187.60 ± 53.5	191.10 ± 51.9	= 0.137
LV-EF on discharge (ratio)	51.07±10.9	50.65 ± 10.9	51.66 ± 10.7	= 0.036

Abbreviations: CT = computerized tomography, **LDL**=low density lipoprotein, **LV-EF** = left ventricular ejection fraction, **PCR** = polymerase chain reaction, mg = milligram, **dl**= deciliter, **µl**= microliter, **ng** = Nanogram. **RD**=respiratory distress, **TLC**=total leukocytic count.
**All values included in the Table represent (Mean ± SD)

Management of STEMI patients:

Out of the 1482 STEMI patients, (55.2 %) had anterior infarction. Median patient delay time (defined as the time from onset of symptoms to first medical contact [9], was 5 hours (0.5- 480), while the mean system delay time (defined as the time from first medical contact in our center to wire crossing in the catheterization laboratory [9] was 40.24 ± 7.2 minutes.

Thrombolytic therapy was given to 228 patients (15.4 %), (38.2%) of them were eligible for PPCI but were given thrombolytic therapy due to confirmed or suspected COVID-19 infection on presentation, (71.5%) of thrombolytic therapy was successful.

Patients who underwent PPCI were (74.9 %), of which (85.5%) were stented. It mentioned that (3.5 %) of STEMI patients who underwent PPCI were diagnosed as MINOCA [10], including atherosclerotic vessels with non-significant obstruction. Further management of that group is beyond the scope of this study. While (9.7%) of STEMI patients were managed conservatively (Figure 1).

Management of NST-ACS patients:

Most of the 770 NST-ACS Patients were managed conservatively (78.7 %). GRACE score was calculated for NST-ACS patients with a mean of 111.38 ± 32. It was found that high vs. moderate vs. low risk represented (20.9% vs 27.8% vs 51.3%) respectively.
(Figure 1)

Details on the management of NST-ACS patients were excluded from this part of the current paper, which will be published later.

The impact of COVID status on the site of STEMI and the management plan:

There was no difference between suspected and non-suspected cases regarding the STEMI site and results of PPCI. (Table 3)

We found that COVID-suspected cases underwent less PPCI and received more thrombolytic therapy; they had worse fibrinolysis results in comparison to non-suspected patients, with statistically significant differences between both groups. **(Table 3)**

Table (3): Data on Management Plan of STEMI Cases

	STEMI + Suspected COVID-19		**P-value**
	Yes (n = 419)	**No (n = 1063)**	
STEMI Site			
• Anterior	236 (56.3%)	582 (54.7%)	
• Inferior	157 (37.5%)	424 (39.9%)	= 0.613
• Lateral	26 (6.2%)	57 (5.4%)	
Patient delay time (hours)	29.93±6.6	25.71±3.9	
Door to wire crossing (minutes)	44.31±6.9	48.30±7.1	
Revascularization Strategy			
• **Thrombolytic**	75 (17.9%)	153 (14.4%)	= 0.034
✓ Successful	46 (61.3%)	117 (76.5%)	= 0.044
• **PPCI**	300 (71.6%)	810 (76.2%)	= 0.024
✓ Stented	261 (87%)	688 (85%)	
✓ PTCA	30 (10%)	63 (7.8%)	= 0.182
✓ Others	4 (1.3%)	35 (4.3%)	
✓ Planned for CABG	5 (1.7%)	24 (3%)	
✓ Conservative management	36 (8.6%)	108 (10.2%)	= 0.191

Abbreviations: CABG = coronary artery bypass graft, **PTCA**= percutaneous trans-coronary angioplasty, **PPCI** = primary percutaneous intervention, **PTCA** = percutaneous trans-coronary angioplasty, **STEMI** = ST-elevation myocardial infarction.
*The Chi-square test was used to compare the frequency between groups
**Independent Sample T-test was used to compare the difference in Mean between groups

Patient outcomes according to COVID status:

Our study showed that COVID-19 infection was associated with about 2-fold in-hospital deaths, cardiogenic shock, heart failure, and a 5-fold need for mechanical ventilation, nearly double the percentage of total complications in comparison to non–

COVID patients. COVID patients also needed longer hospital stays, as shown in Table (4).

Worthy of notice that COVID-19 infection contributed to (12.8%) of in-hospital deaths, (14.3 %) of 1-month deaths, and (6.4 %) of 1-year deaths among the study population. Of the 1482 STEMI patients, (9.2%) died within the hospital admission, and (15.4%) died within 12 months of follow–up (Figure 2).

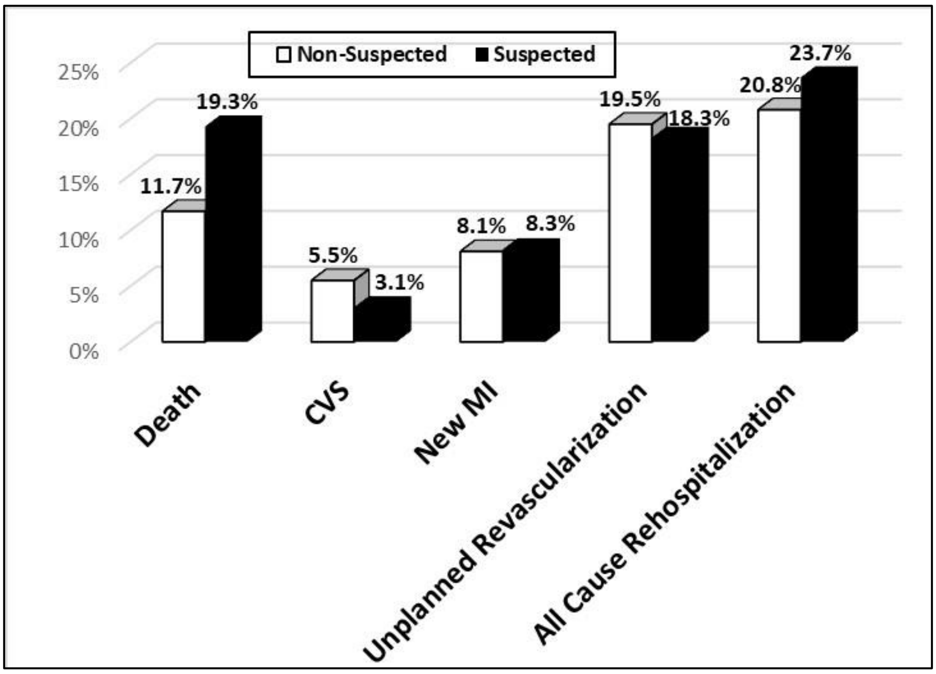


Figure 2: Cumulative 1-year MACE of the total study population
Abbreviations: CVS=cerebrovascular stroke, MI= myocardial infarction.

Table (4): Patients' outcomes and length of hospital stay according to COVID status

	Non-Suspected (n = 1562)	Suspected (n = 690)	P-value*
In-hospital complications:			
• Total	277 (17.7%)	245 (35.5%)	< 0.001
• Death	92 (5.9%)	72 (10.4%)	< 0.001
• MI Mechanical Complications	166 (10.6%)	142 (20.6%)	< 0.001
• Cardiogenic Shock	96 (6.1%)	68 (9.9%)	= 0.002
• VT/VF	58 (3.7%)	34 (4.9%)	= 0.180
• New CHF	58 (3.7%)	125 (18.1%)	< 0.001
• New Heart Block	32 (2%)	26 (3.8%)	= 0.018
• Ischemic CVS	8 (0.5%)	4 (0.6%)	= 0.527
• Intracranial Hemorrhage	1 (0.01%)	3 (0.4%)	= 0.054
• Mechanical ventilation	42 (2.7%)	78 (11.3%)	< 0.001
Length of hospital stay/ days	2.42 ± 0.02	3.08 ± 0.08	< 0.001**
12-month FU Complication	n=1221	n=541	
• Death	90(7.4)	61 (11.3%)	= 0.005
• New CVS	78 (6.4%)	52 (9.6%)	= 0.024
• New MI	99 (8.1%)	45 (8.3%)	= 0.443
• Unplanned Revascularization.	238 (19.5%)	99 (18.3%)	= 0.254
• Hospital readmission	254(20.8%)	128(23.7%)	= 0.807

Abbreviations: CHF = congestive heart failure, **CVS** = cerebrovascular stroke, **MI**= myocardial infarction, **VF** = ventricular fibrillations, **VT** = ventricular tachycardia.

Comparison between during, before, and after COVID-19 regarding ACS admissions and PPCI done:

Using the electronic data archiving system in our hospital to compare the number of patients admitted during similar periods before and after the COVID–19 pandemic (15 months), we found that the number of admissions for ACS patients, in addition to a percentage of PPCI done, decreased about (5%) in comparison to the year preceded COVID-19 pandemic as shown in Figure 3.

The year after the COVID-19 pandemic witnessed an increase in ACS patient admissions by about (15 %) and an increase in the percentage of PPCI done by (5%) with a statistically significant difference (p-value = 0.044) (Figure 3).

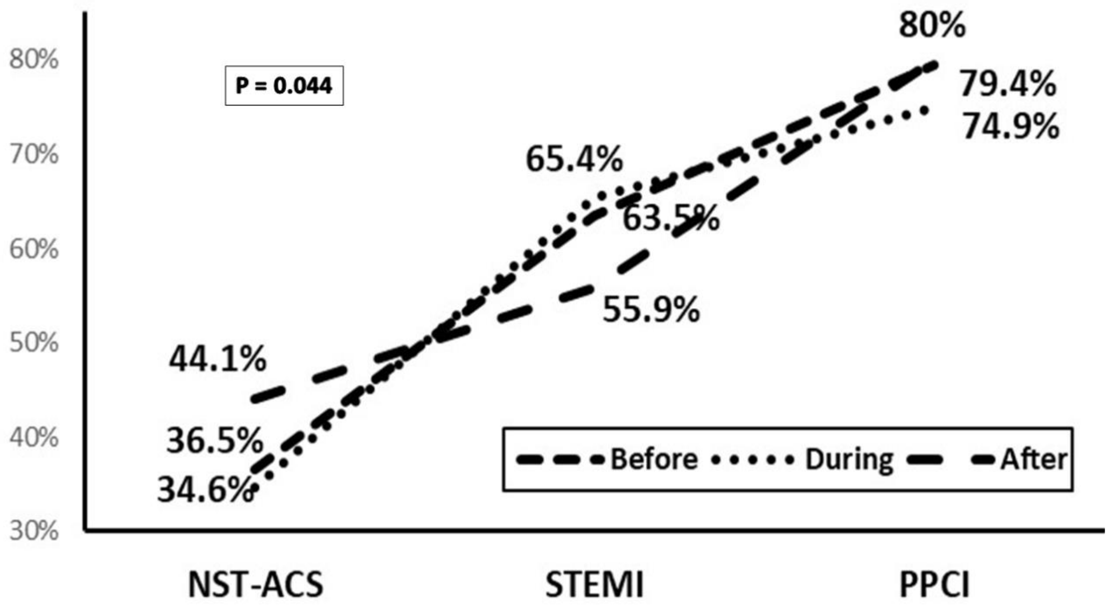


Figure 3: ACS admissions and PPCI before, during, and after the COVID-19 pandemic McNemar test was used to compare frequency on repeated analysis.
*** Data from Assiut University Heart Hospital Database (HIS).

Predictors of MACE:

A multivariate logistic regression model, which included factors suspected to affect the outcomes, showed that COVID-19 infection among STEMI patients was associated with an increase in the in-hospital (OR=5.021, 95%CI= 1.995 – 8.661, P < 0.001) and one year (OR=3.801, 95% CI= 1.451 – 6.019, P= 0.012) MACE among the study population. Also, having one or more high-risk features (ex: cardiogenic shock, pulmonary edema, and VT or VF), uncontrolled diabetes, COPD, CKD, and smoking were found to be associated with more MACE while higher hemoglobin levels and LVEF were associated with a reduction in MACE as shown in tables (5).

Table (5): Predictors of MACE among STEMI patients using multivariate logistic regression analysis

STEMI		
In-hospital predictors	**OR (95% CI) ***	**P value**
Positive COVID-19 Infection	5.021 (1.995 – 8.661)	< 0.001
High-Risk Feature/s	3.801 (1.451 – 6.019)	= 0.012
CKD	3.384 (1.994 – 5.743)	< 0.001
COPD	3.056 (1.577 – 5.933)	= 0.001
Male sex	1.826 (1.417 – 2.354)	< 0.001
Revascularization Time	1.053 (1.030 – 1.075)	0.001
Haemoglobin A1C	1.417 (1.214 – 1.651)	< 0.001
1-year predictors	OR (95% CI) *	P value
High-Risk Feature/s	3.801 (1.451 – 6.019)	= 0.012
Confirmed COVID-19 Infection	3.021 (1.024 – 6.152)	= 0.039
COPD	2.511 (1.428 – 3.991)	= 0.019
Hypertension	1.605 (1.066 – 1.446)	= 0.005
LVEF%	0.944 (0.824 – 0.998)	= 0.045
Age (years)	1.015 (1.002 – 1.029)	= 0.029
Smoking	1.428 (1.019 – 1.923)	= 0.011

Abbreviations: CKD = chronic kidney disease, **COPD**= chronic obstructive pulmonary disease, **GRACE**= Global Registry for Acute Coronary Events, **LVEF**= left ventricular ejection fraction, **STEMI** = ST elevation myocardial infarction., **TLC**= total leukocytic count, **OR**=Odds Ratio; CI, Confidence Interval

** High-risk features = cardiogenic shock, pulmonary edema, and VT or VF[9]

Discussion

The objective of our study was to conduct a registry of ACS patients during the COVID-19 Pandemic. This observational, prospective, longitudinal cohort study was conducted on 2252 adult patients who were presented with ACS in the Cardiovascular Medicine Department of Assiut University Heart Hospital between March 1st, 2020, and May 31st, 2021.

The main findings of our study include:

- Around 4% of the study populations were young ≤ 35 years old, while most of them were >55 years old.
- Two-thirds of our patients had STEMI, and 3.5 % of them were finally diagnosed with MINOCA.
- COVID-19 strongly affected management strategies as STEMI patients with suspected COVID-19 infection received more thrombolytic therapy and underwent less PPCI by 5% compared to archived data for years before and after the pandemic.
- COVID-19-suspected ACS patients needed longer hospital stays and were associated with higher In-hospital and 12-month MACE in comparison to non-COVID-ACS patients.

In the current study, male gender was predominant (71.7%), while females represented (28.3%). Most of the study population were > 55 years old, with a mean age of 60.65 ± 11.7 years. Hypertension and a previous history of dyslipidemia were the most frequent risk factors (44.9% and 37.5 %, respectively). Smoking and CKD were more prevalent among COVID-19-suspected patients. Concerning the STEMI site, (55.2%) had an anterior location.

Similar Egyptian and international studies of ACS patients during the pandemic. ***Reda et al. (2019)***[11] also reported male predominance, with most men presenting with STEMI, while a larger percentage of women had unstable angina and NSTEMI. In our study, STEMI was predominant for both males and females because our hospital, as a tertiary center, is considered the only primary PCI center in Assiut and nearby governorates. The nearest center is distant, taking 3 to 4 hours to reach, in addition to our focus on serving the more critical (STEMI) patients.

Regarding the mean age of presentation, generally, Egyptian patients presenting with STEMI are reported to be younger compared to the European population, possibly due to the younger age of the whole Egyptian population and the higher prevalence and poorly controlled risk factors. ***Shaheen et al. (2020)***[12] Still, our findings agreed with other similar registries that the majority of STEMI patients who presented during the pandemic were relatively older, with more risk factors, with hypertension and dyslipidemia being the commonest [13].

According to our study, the median patient delay time was 5 hours (0.5-480), being longer relative to non-covid periods, which is consistent with other centers worldwide [13]. Also, in our center, this can be further explained by the fact that it is the only PPCI-capable center serving a wide area and has a slow emergency medical system. However, the mean time for revascularization for the total population in this study (40.24 ± 7.2 minutes) was consistent with a previous study in our center, ***Hassan et al., (2018)***[14] before the COVID era, with mean door-to-wire time for the total population (40.15 ± 15.32), indicating an adequate response of the medical team in both circumstances.

In our study, (3.5%) of patients presented with ST elevation in their ECG but had non-obstructive CA, including ecstatic or aneurysmal vessels, myocardial bridge, atherosclerosis with non-significant CAD, and those with non–ischemic etiology. The hypercoagulable state known to be caused by the COVID-19 infection was previously suggested as one of the important mechanisms contributing to the occurrence of MINOCA [15].

MINOCA also could be promoted by hypoxia, tachycardia, and hypotension, which occur in acute respiratory failure **[16]**.

Regarding the effect of COVID-19 on management strategies, most of the STEMI patients in the current study underwent PPCI; thrombolytic therapy was given to (15.4%) while only (9.7%) were managed conservatively. Upon comparison, STEMI patients with suspected COVID-19 infection underwent less PPCI with relatively longer ischemia times. They received more thrombolysis in comparison to non-suspected patients despite the fact that PPCI was still the recommended standard of care for patients with STEMI during the COVID-19 pandemic [17].

Besides other factors, this could have affected the outcome of this group, which will be discussed later. Upon comparison to the numbers in the same center, we found that the total number of admissions for ACS patients, along with the percentage of PPCI procedures performed, all decreased by 5% when compared to the year preceding the COVID-19 pandemic. These findings are in alignment with many Egyptian and international registries and surveys showing the rate of intervention during the COVID era was less than before and after, with a higher percentage treated medically; still, as per guidelines, most of the patients with high-risk ACS underwent invasive strategy. ***Mahmoud et al., (2021)***[18], ***Xiang et al., (2020)***[19].

Regarding outcomes, COVID-19 infection was associated with more In-hospital mortality, cardiogenic shock, heart failure, and the need for mechanical ventilation. COVID–ACS patients needed longer hospital stays, and COVID-suspected STEMI patients showed lower rates of successful thrombolysis, which could be attributed to the thrombogenic effect of COVID together with the later presentation of the suspected group.

Also, within the total study population, COVID-19 infection contributed to (12.8%) of in-hospital deaths, (14.3%) of deaths within one month, and (6.4%) of one-year deaths in our study, with the mortality rate being higher among STEMI patients than NST-ACS cases.

In a multivariate logistic regression model for predictors of MACE, COVID-19 infection was associated with significantly higher in-hospital, 1-month, and 1-year MACE among the study population. These findings are supported by other studies addressing outcomes of COVID-19 patients presenting with ACS during the pandemic. Many previous studies demonstrated the short-term outcome effect of COVID-19 on ACS patients, ***Salinas et al., (2021)***[20].

Among those, ***Xiang et al. (2020)***[19] showed that the outbreak resulted in an upsurge in the in-hospital mortality and heart failure rates. ***Lasica et al. (2022)***[21], in their work on 12,958 patients with 519 COVID-19 positive, demonstrated that patients with both COVID-19 and ACS had elevated in-hospital mortality as well as thirty-day mortality, in comparison to patients with ACS but without a COVID-19 diagnosis. ***Kite et al. (2021)***[22] and ***Alharbi et al. (2023)***[23] illustrated that cardiogenic shock occurred significantly more in COVID-19 patients compared to non-COVID patients.

Regarding the long-term outcomes, by finding that the COVID-19 infection significantly predicts one-year mortality, the current study adds to the limited and conflicting data on the effect of COVID-19 infection on 1-year outcome of STEMI patients, as some trials have shown no difference in one-year all-cause mortality **[16]**.

Çınar et al. (2022)[24] also reported that ACS concomitant with COVID-19 was the only independent predictor of one-year mortality in Patients with ACS and COVID-19.

COVID-19 infection has several effects on the cardiovascular system, coagulation, and inflammatory cascade, with several mechanisms suggested to cause ACS. The injury of the endothelium of the blood vessel and rupture of the atherosclerotic plaque with activation of the coagulation cascade **[21]**. Direct cell invasion by SARS-CoV-2 leads to endothelial damage and activation of variable forms of the inflammatory response **[25]**. COVID-19 also increases levels of D-dimer, fibrinogen, coagulation factor VIII, and von Willebrand factor, with a higher incidence of thrombosis in this disease **[26]**. These mechanisms, together with the delayed presentation of patients, the differences in management strategies in suspected and confirmed cases, and the logistic drawbacks in some countries, all contributed to the worse outcomes noted.

Limitations of the study:

- CT chest and COVID-19 PCR tests were not done for all suspected patients of the study as it was an observational, not interventional, study.
- Some follow-up data (16.3%) were missing due to the large sample size and loss of communication data.

Conclusion:

COVID-19 strongly affected management strategies for ACS, as STEMI patients with suspected COVID-19 infection received more thrombolytic therapy and underwent less PPCI. COVID-19 infection was a strong predictor of in-hospital and 12-month MACE in ACS patients. Efforts are needed to increase public health awareness regarding avoiding delays and seeking immediate medical care for suspected acute cardiac conditions.

List of abbreviations

Abb.	Full Term
Acs	Acute coronary syndrome
Ami	Acute myocardial infarction
Cabg	Coronary artery bypass graft
Ckd	Chronic kidney disease
Chf	Congestive heart failure
Copd	Chronic obstructive pulmonary disease
Corads	The COVID-19 reporting and data system
Ct	Computerized tomography
Ctn	Cardiac Troponin
Cvs	Cerebrovascular stroke
Dl	Deciliter
Ecg	Electrocardiogram
Fmc	First medical contact
Grace	Global Registry of Acute Coronary Events
Ihd	Ischemic heart disease
Kg	Kilogram
Ldl	Low-density lipoprotein
Lv- ef	Left ventricular ejection fraction
Mace	Major adverse cardiac events
µg	Microgram
µl	Microliter
Minoca	Myocardial infarction with non-obstructive coronary arteries
Mvd	Multi-vessel disease
Ng	Nanogram
Nst-acs	Non-ST-elevation acute coronary syndrome
Ptca	Percutaneous trans-coronary angioplasty
Dl	Deciliter
Tlc	Total leukocytic count
Lv- ef	Left ventricular ejection fraction
Ldl	Low-density lipoprotein
Ppe	Personal protective equipment
Cvs	Cerebrovascular stroke
Dcl	Disturbed conscious level
Mvd	Multi-vessel disease
Ppci	Primary percutaneous intervention
Ppe	Personal protective equipment
Ptca	Percutaneous trans-coronary angioplasty
Rd	Respiratory distress
Vf	Ventricular fibrillations
Chf	Congestive heart failure
Ct	Computerized topography
Corads	The COVID-19 reporting and data system
Mace	Major adverse cardiac events
Rd	Respiratory distress
Sars-cov-2	Severe acute respiratory syndrome coronavirus 2
Stemi	ST-elevation myocardial infarction
Tlc	Total leukocytic count

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