Prevalence of Acute coronary syndrome (ACS) in COVID-19 affected patients in public hospital facility of Pakistan, a retrospective study COVID-19 association with ACS

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Data availability statement:

Data openly available in a public repository that issues datasets with DOIs.

Abstract

Introduction

COVID 19 infection is a devastating viral disease-causing multiorgan damage and severity of the complications. Several studies have reported the major effect of COVID 19 on the respiratory, cardiac system as well as on other organs. There has been an increased prevalence of the COVID-19 infection observed in patients with the acute coronary syndrome (ACS) because of many unknown reasons.

Methods

This is a retrospective multicentered study conducted on the 80 patients, in the Allied hospital facility of Pakistan, in March-April. The research subjects were categorized into COVID (50) and non-COVID groups (30) with 50 males and 30 females having acute coronary syndrome, STEMI, NSTEMI, myocardial infarction, unstable angina, global ischemia, IHD, inferior wall ischemia, Anterolateral wall, MI and AHF.

Results

A total number of 80 patients, 50 COVID, and 30 Non-COVID with 50% male and 50% female in the COVID group having a mean age of 56.92 ± 7.92presented during the March/April 2020. Patients were admitted to the hospital with oxygen saturation of 76.9 ±14.323 % and lung involvement of 38 ± 16.35 %. 96% of the COVID 19 patients had comorbidity of hypertension and the highest prevalence of NSTEMI was observed in 22% patients, 12% Inferior wall ischemia, unstable angina, anterolateral wall myocardial infarction and STEMI. However, 10% Global ischemia, 8% MI and IHD and 4% AHF were observed.

Conclusion

COVID 19 is prevalent in patients having acute coronary syndrome (ACS). ACS patients with hypertension are at high risk of COVID19 infection and aggravation of the cardiac implications.

Keywords: acute coronary syndrome (ACS), Prevalence, COVID-19, retrospective

Table1 Acronyms and abbreviations

ACRONYMS

Acronyms	Abbreviations
ACS	Acute Coronary Syndrome
CVD	Cardio Vascular Diseases
SARS COVID-19	Sever acute respiratory distress COVID-19
DM	Diabetes mellitus
HTN	Hypertension
IHD	Ischemic heart disease
AHF	Acute Heart Failure
MI	Myocardial Infarction
STEMI	ST-elevated myocardial infarction
NSTEMI	Non-ST-Elevation Myocardial Infarction
WHO	World Health Organization
RT-PCR	Reverse Transcription–Polymerase Chain Reaction
SOB	Shortness of Breath
HRCT	High-resolution Computed Tomography

Introduction

The outbreak of severe acute respiratory syndrome coronavirus known as COVID-19 has been associated with the poor outcomes of the infections in CVD patients (Aghagoli et al., 2020). The high transmission rate of the infection leads to stay-at-home policy worldwide with a high rate of morbidity and motility. There are several documented case reports and researches related to the prevalence of COVID-19 in patients with or without cardiovascular disease. The critical analysis of several COVID-19 cases reported major manifestations of respiratory distress, multiorgan failure (Zaim, 2020; Wang, 2020) (Mokhtari, 2020) and cardiovascular complications. Patients with certain underlying diseases and critical health implications presented worsening of pneumonitis, multiorgan failure and cardiovascular complications during the incubation period of the virus (Kunutsor and Laukkanen, 2020). As of August 2, 2021, 215 million cases of COVID 19 have been reported globally with a mortality rate of 4.48 million with the highest number of cases in the United States, 38.7 million infected and 636 thousand deaths (WHO, 2021) novel). Studies have suggested that systemic inflammation that also triggers respiratory distress in the COVID -patients are the reason for cardiomyocytes damage (Sandoval, 2017). The viral infectious entity alters the intracellular coupling cause interstitial oedema in the cardiomyocytes (Buja, 2020) and parenchymal myocytes (Archer, 2020 #145), fibrosis, both pulmonary and cardiac (Wigén, 2020). The increased surge of hospitalisation was observed in this time of crisis

Myocardial injuries are characterized as substantial sensitivity of the body to the cardiac troponin levels which are also further associated with the increased cardiac morbidity and mortality (Sandoval and Thygesen, 2017). The infection in cardiac muscles, myocarditis, has been involved with the infections in the Sinoatrial node and atrioventricular node. As per Liu et al., the cardiac infection spreads in 3 steps, the proliferation of the virus into the myocardium, activation of immune response (T-cells and cytokine production) and finally progressive cardiac dilation (Babapoor-Farrokhran, 2020). However, in the case of COVID -19 infection, one of the most frequent complications observed is bradycardia. Until now, only case reports have linked the association of arrhythmia with the COVID-19 infection with high degree AV block with Sinus node dysfunction (Peigh, 2020) and normal electrocardiogram imaging (Kir, 2020). Complete myocardial fibrosis of the interstitial septum has been considered as the unique complication attribute of COVID-19. Lampropoulos et al. found severe symptomatic sinus arrest

along with myocardial fibrosis OF the left ventricle, interatrial septum and intraventricular septum. (Lampropoulos, 2020)

According to the Center for Disease Control (CDC) presence of comorbidities in old age people predicts high vulnerability to infection and worse prognosis, specifically in patients with cardiovascular diseases(Park et al., 2020). Preexisting cardiovascular complications predict a higher rate of mortality in such patients (Aghagoli et al., 2020). In the UK during the second wave of COVID, a 5.1% mortality rate was recorded in COVID 19 patients among 28969 cases of CVD (Wu et al., 2021). Rashid et al. reported in March 2021 4% of the COVID-19 patients with CVD and (Rashid et al., 2021). A systemic analysis of 15 studies (Kunutsor and Laukkanen, 2020). A study found that among total severe COVID-19 cases admitted in the hospital, 25% of those cases had heart diseases, 58% of the cases were hypertensive while 44% had arrhythmia (Wang et al., 2020). Myocardial injuries and arrhythmias are common in covid -19 patients. The increased incidence of the myocardial implications in COVID-19 patients has been associated with the induction of cardiotoxicity, sepsis during hospitalization, inflammation, thrombosis by rupture of plaque, mismatch of the demand and supply along with electrolyte imbalance of the myocardial supply (Kunutsor and Laukkanen, 2020) as in figure1. COVID-19 infection was present in 4% of patients hospitalized with an ACS in England and is associated with lower rates of guideline-recommended treatment and significant mortality hazard.

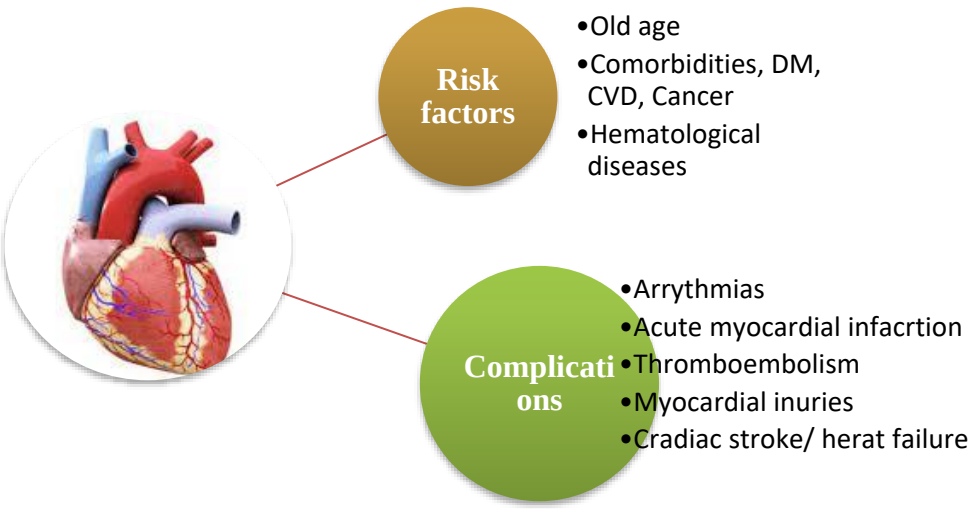

Figure 1Cardiovascualr complications and associated risk factors for COOVID-19 patients

DM* (Diabetes mellitus), CVD**(cardiovascular complications)

Methodology

This study is a retrospective cross-sectional study of the patients admitted to the public sector Allied Hospital Faisalabad, Pakistan during the 1-month tenure of the study. A total of 80 patients were admitted to the hospital in the selected time range. A total of 80 consecutive patients admitted to the hospital were selected for the study. Patients were divided into COVID-19 and non-COVID-19 groups based on the confirmatory test. The COVID positive patients were isolated in the COVID-19 isolation ward of the Allied hospital facility and the other patients were admitted to the respective wards.

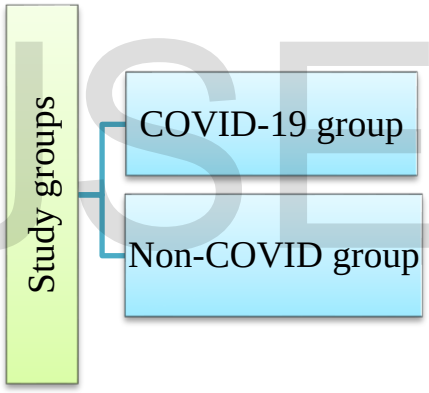

Figure 2 Study groups

In the initial assessment, the patients were confirmed for the COVID 19 by Real-Time Polymerase Chain Reaction (RT-PCR) and High-resolution computed tomography (HRCT) test. The severity of the oxygen saturation and involvement of the lungs in percentage was evaluated at the time of admission and evaluated after frequent intervals. The COVID patients at the time of admission showed physical symptoms of dyspnea, high body temperature, malaise, shortness of breath (SOB) and cough. The initial history record described the consistent deteriorating condition since the past few days. All the COVID patients were admitted to the isolation ward of the hospital facility with proper Standard Operating Operations (SOPs). The non-COVID patients with suspected symptoms of COVID infection, fever, shortness of breath (SOB) was

also evaluated for the infection by PCR and HRCT in the initial assessment. Allied Hospital of Faisalabad is a public sector hospital with an average open door patient count of approximately1000 and multiple specialized wards. It was designated by the government as an isolation center for the COVID 19 patients. After the initial assessment of the patients, the medical and family history was evaluated. The record of comorbidities, patients' history of disease and medication was obtained from the patients and the attendee of the patient having the severity of the symptoms figure 3.

Inclusion criteria

- Patients must have a Cardiovascular system complication
- The patient must be positive for COVID
- Any patients with comorbidities like Hypertension (HTN), Diabetes mellitus (DM) were also selected
- Patients having severe cardiac conditions with a prolonged hospital stay were also included

Exclusion criteria

- Patients diagnosed with COVID during the hospital stay were excluded

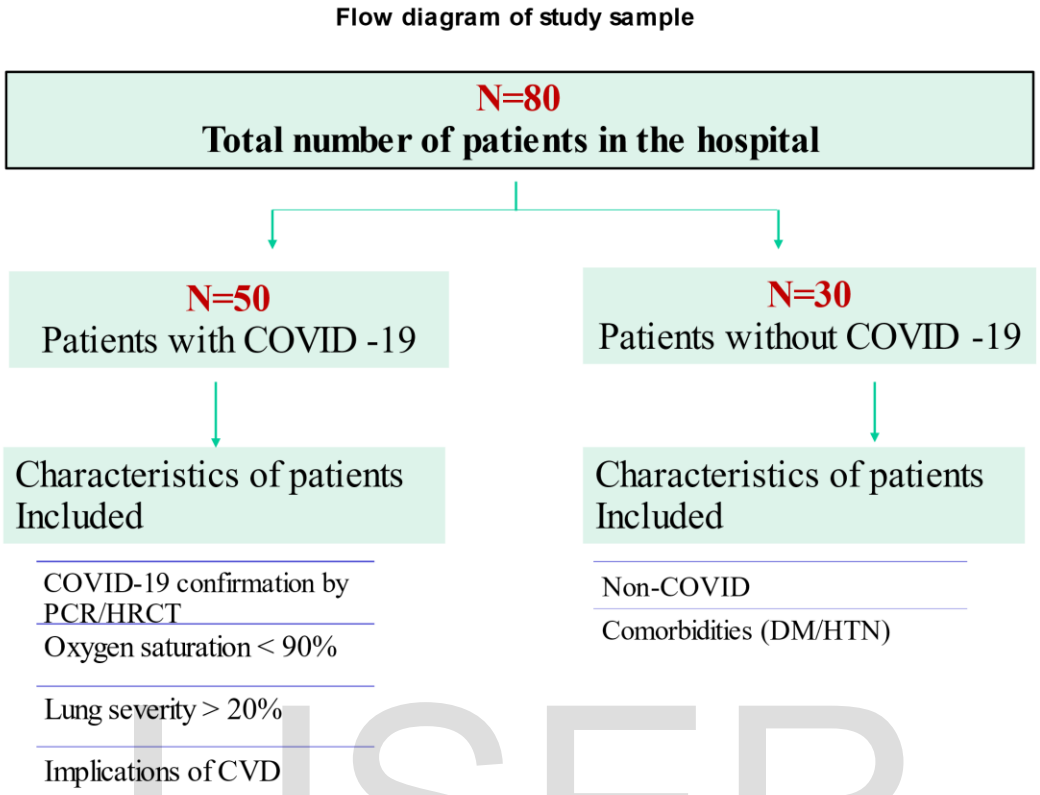

Figure 3 flow diagram of study sample

Data collection

Data was collected from the Allied Hospital Faisalabad, Punjab, Pakistan. Data was collected manually by clinical record files of the patients provided by the Hospital administration of the COVID isolation wards. The data collected for the descriptive, clinical, laboratory, medications and outcomes of the COVID positive patients along with certain cardiac conditions was collected. The raw data was in the form of the patient's description of age, gender, hospital admission, O2 saturation at the time of admission, the severity of the lung involvement at the time of admission and recovery/death outcomes. The medical history including family history, type of ACS condition, comorbidities, presence of any immunosuppressant disease, vaccination status is recorded. The symptoms description of the patients containing 'COVID 19 symptoms' and other 'comorbidity symptoms' are recorded. The oral temperature along with COVID confirmation tests, Polymerase chain reaction (PCR) and High-resolution computed tomography

(HRCT) The history of drug abuse and medications used as treatment strategy of COVID and previous medications used for the ACS condition is also recorded.

Definitions of the study and ethical considerations

The oral temperature was defined at ≥ 38℃ (Han et al., 2020) recorded at the time of admission and follow up visits. Confirmation of the COVID was defined by HCRT and RT-PCR testing at the time of initial admissions. Nasopharyngeal samples were obtained from the suspected patients according to the protocol described by the world health organization (WHO) (Ye et al., 2020). Tests for confirmation of covid were conducted at the laboratory of the allied hospital Faisalabad. During data collection, all ethical grounds and privacy of data were maintained. This study was approved by the Ethical Review Committee, Faisalabad Medical University.

Data analysis

The Statistical Package for Social Science Program version 24 (SPSS-24) was used for the descriptive and statistical analysis. Demographic, clinical, medication and laboratory data were subjected to descriptive statistics and presented in the form of numerals (N) and percentage (%). The collected data included categorical and countable variables. The categorical variables were statistically analyzed by SPSS while continuous data were subjected to descriptive statistics by using SPSS.

Results

The 80 patients analyzed in this study were analyzed for the high risk of COVID 19 in the patients with cardiovascular diseases. The patients with confirmed COVID-19 n=50 (62.5%) was characterized into the symptomatic history and possible complications of the cardiac injury depicted in Table 1. All the COVID-19 patients were admitted with the similar physical symptoms fever, shortness of breath, dyspnea, malaise (100%). 50% of the COVID patients were male and 50% were female. The confirmatory test for COVID-19 was performed on both COVID and non-COVID patients having shortness of breath and high temperature. In non-COVID patients 46.6% patients had a high fever, 16.6% had shortness of breath, 26.6% had malaise and 43.3% showed cough but the HRCT/PCR were negative for the presence of COVID -19 infection. 10% of the COVID-19 patients had a history of smoking, family history was also evaluated in patients reported to be 46% had diabetes and 52% had hypertension while non-

COVID group 3% had a history of smoking, 5.4% were diabetic, and 73.33% were hypertensive. The vaccination status of the patients was recorded, 0% of the COVID patients were vaccinated while in the non-COVID group 14.33% (n=6) were vaccinated with Pfizer.

All the patients had low oxygen saturation (%) mean (SD) 76.9 (±14.323) and increased lung involvement in the spread of infection (%) mean (SD) 38 (±16.351). The clinical characteristics of the overall COVID patients have been described in Table 2. Among the 50 COVID patients. Among the 50 COVID patients' different percentage of implications of the myocardial injuries and complications were observed, 10% (n=5) global ischemia, 12% (n=6) STEMI, 22%(n=11) NSTEMI, 12%(n=6) Unstable angina, 8% (=4) ischemic heart disease, 12% (n=6) inferior wall ischemia, 12% (n=6) Anterolateral wall myocardial infarction, 8% (n-4) myocardial infarction, 4% (2) AHF. However, the non-COVID group (N=30) relatively had a smaller number of cardiovascular complications, 3.33% (n=1) global ischemia, 13.33% (n=4) unstable angina, 10%(n=3) IHD and 6.66% (n=2) Myocardial infarction.

The comorbidities were also recorded, in the COVID-19 group 11.5% had diabetes, 96% were hypertensive, 4% had asthma and 2% were pregnant females. However, 4% of the patients had no comorbidities. In the non-COVID group, 86.6% had diabetes, 70% were hypertensive, 33.3% had asthma, 16.66% had thyroid disease. At the end of the hospital stays 56% of the COVID-19 recovered and 28% died due to the severity of the symptoms and underlying conditions. 16%of patients were still admitted to the hospital.

The COVD-19 patients were provided with Moxifloxacin (100%), Aspirin (100%), Dexamethasone (100%), Metoclopramide (100%), Heparin (100%), Streptokinase (100%), and Paracetamol (100%). However, the other medications were also provided for comorbidities, Atorvastatin (44%, n=22) for lowering cholesterol, Insulin (46%, n=23) for glucose control in diabetics, Furosemide (38%, n=19) for edema and high blood pressure, Salbutamol inhaler (8%, n=4) for patients having asthmatic events, Leflunomide (2%, n=1) for arthritis, Clopidogrel (28%, n=14) for preventing blood clots, Amlodipine (36%, n=18) for high blood pressure and angina pains Figure 7. Few numbers of patients were also given with nitrates (2%, n=1), methylprednisolone (4%, n=2), Tocilizumab (2%, n=1), piperacillin tazobactam (4%, n=2) for their other complications as described in the Table 3.

Table 2 Characteristics of the COVID-19 and non-COVID-19 groups in accordance with the percentage

Characteristics	**Specific aspects**	**Results of indicated groups**	
		COVID (N=)	**Non-COVID (N)**
Sample size		50	30
Gender (%)	Male	25 (50%)	14 (46.6%)
	Female	25 (50%)	16 (53.3%)
Age (Mean)		56.92 ±7.9	42 ±8.9
History n (%)	Smoking	5/50 (10%)	10/30 (3%)
	Diabetes	23/50(46%)	18/30 (5.4%)
	Hypertension	26/50(52%)	22/30 (73.33%)
COVID-19 symptoms	Fever (>37.9)	50/50 (100%)	14/30 (46.6%)
	SOB	50/50 (100%)	5/30 (16.6%)
	Malaise	50/50 (100%)	8/30 (26.6%)
	Diarrhea	50/50 (100%)	0
	Cough	50/50 (100%)	13/30 (43.3%)
COVID-19 confirmation test	PCR	50/50 (100%)	-
	HRCT	50/50 (100%)	-
COVID-19 severity	O_2Saturation at the time of admittance (%)	76.9 ±14.323	-
	Lung's involvement (%)	38 ±16.351	-
Type of ACS	Global Ischemia	5/50 (10%)	1/30 (3.33%)

	STEMI	6/50 (12%)	-
	NSTEMI	11/50 (22%)	-
	Unstable angina	6/50 (12%)	4/30 (13.33%)
	IHD	4/50 (8%)	3/30 (10%)
	Inferior wall ischemia	6/50 (12%)	-
	Antero lateral wall MI	6/50 (12%)	-
	MI	4/50 (8%)	2/30 (6.66%)
	AHF	2/50 (4%)	-
Co-morbidities	DM	23/50 (11.5%)	26/30 (86.6%)
	HTN	48/50 (96%)	21/30 (70%)
	Asthma	2/50 (4%)	10/30 (33.3%)
	PG-	1/50 (2%)	0
	Uterine cancer	1/50 (2%)	0
	Thyroid disease	0	5/30 (16.66%)
	None	2/50 (4%)	0
Presence of immunosuppressant disease	-	0	3 (10%) (rheumatoid arthritis)
Vaccination status	Vaccinated	0	4/30 (14.33%)
	Not vaccinated	50/50 (100%)	0
Mortality rate	Recovered	28/50 (56%)	24/30 (80%)
	Death	14/50 (28%)	0
	Admitted	8/50 (16%)	6/30 20%)

Table 3 The medication used for the sample groups

Medicine	Number of recurrences in COVID 19 N (%)	Number of recurrences in non-covid N (%)
Moxifloxacin	50/50 (100%)	5/30 (16.66%)
Aspirin	50/50 (100%)	5/30 (16.66%)
Dexamethasone	50/50 (100%)	0
Metoclopramide	50/50 (100%)	0
Heparin	50/50 (100%)	15/30 (50%)
Streptokinase	50/50 (100%)	7/30 (23.33%)
Paracetamol	50/50 (100%)	7/30 (23.33%)
Atorvastatin	22/50 (44%)	0/30
Insulin	23/50 (46%)	26/30 (86.66%)
Furosemide	19/50 (38%)	4/30 (13.33%)
Salbutamol Inhaler	4/50 (8%)	15/30 (50%)
Leflunomide	1/50 (2%)	3/30 (10%)
Clopidogrel	14/50 (28%)	2/30 (6.66%)
Amlodipine	18/50 (36%)	0
Nitrates	1/50 (2%)	0
Methylprednisolone	2/50 (4%)	0
Meropenem	1/50 (2%)	0
Tocilizumab	1/50 (2%)	0

piperacillin tazobactam	2/50 (4%)	0

Figure 3 reports the types of ACS recorded in the study groups, COVID and non-COVID groups. The highest percentage was observed for the NSTEMI, 22% in the COVID patients and 13.33% unstable angina in the COVID-19 patients. Figure 4 illustrates the comorbidities in the research groups, 96% of the COVIVD patients had hypertension while 70% of the non-COVID patients had hypertension while 86.6% of patients had diabetes mellitus (DM). Other than these major comorbidities, thyroid diseases, uterine cancer and asthma were also observed in the groups as comorbidity. Figure 5 illustrates the outcome of the patients admitted to the hospital in the selected study tenure. The COVID group observed a 56% rate of recovery and 28% mortality rate while 16% were still admitted to the hospital. On the other hand, the non-COVID group observed an 80% recovery rate with 20% still admitted to the hospital. Figure 6 illustrates the overview of the medications used for the study groups Figure 6.

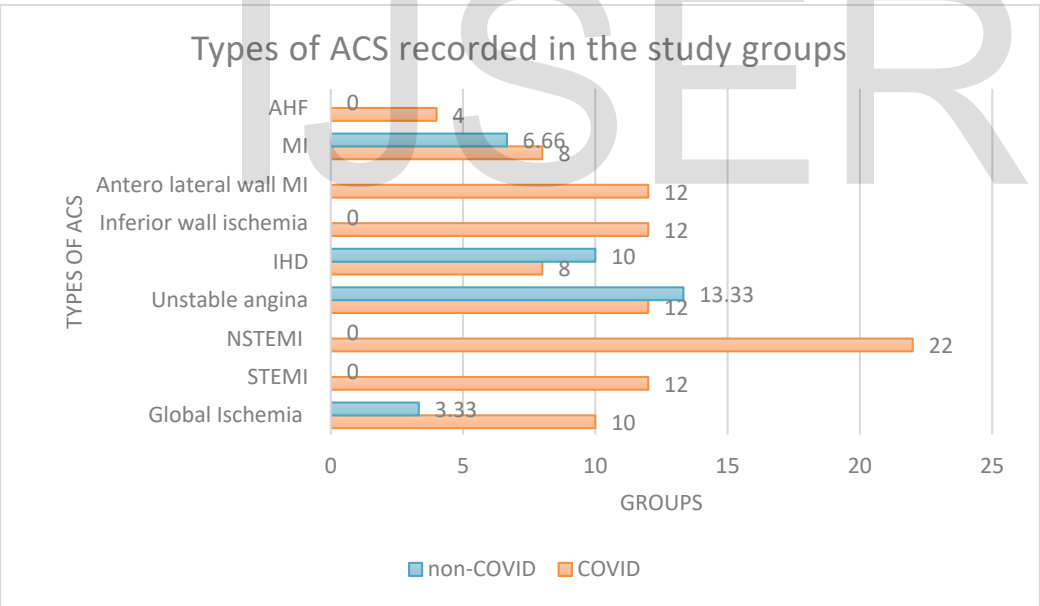

Figure 4Type of ACS recorded in the patients with COVID-19 and non-COVID groups admitted to the hospital

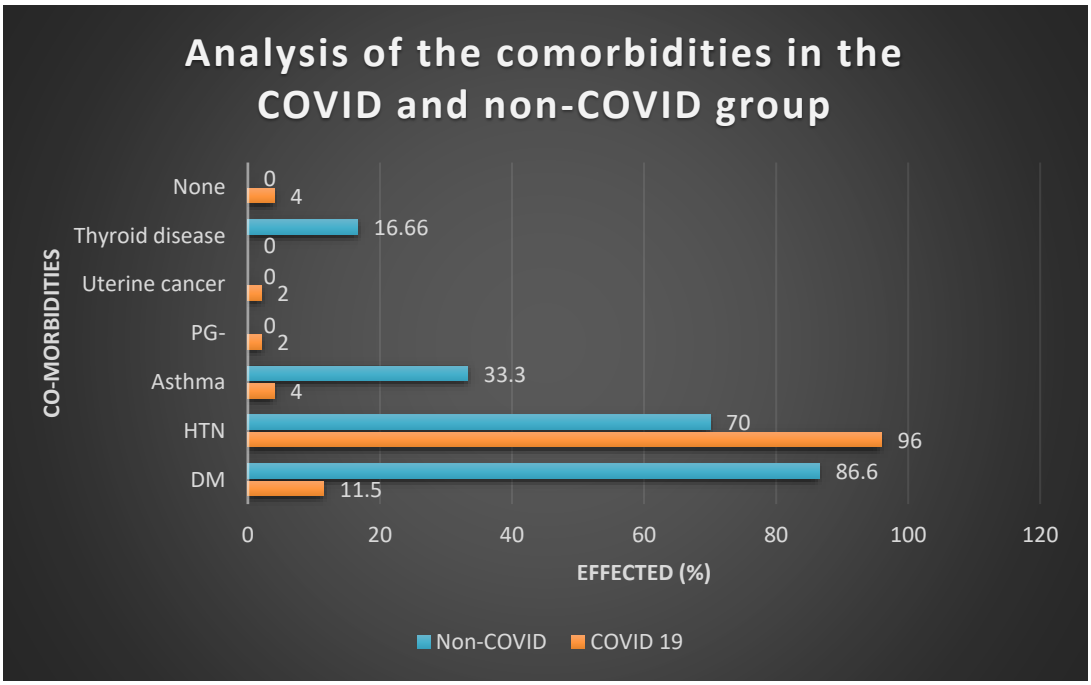

Figure 5 Illustration of the Co-morbidities in the covid and non-covid groups

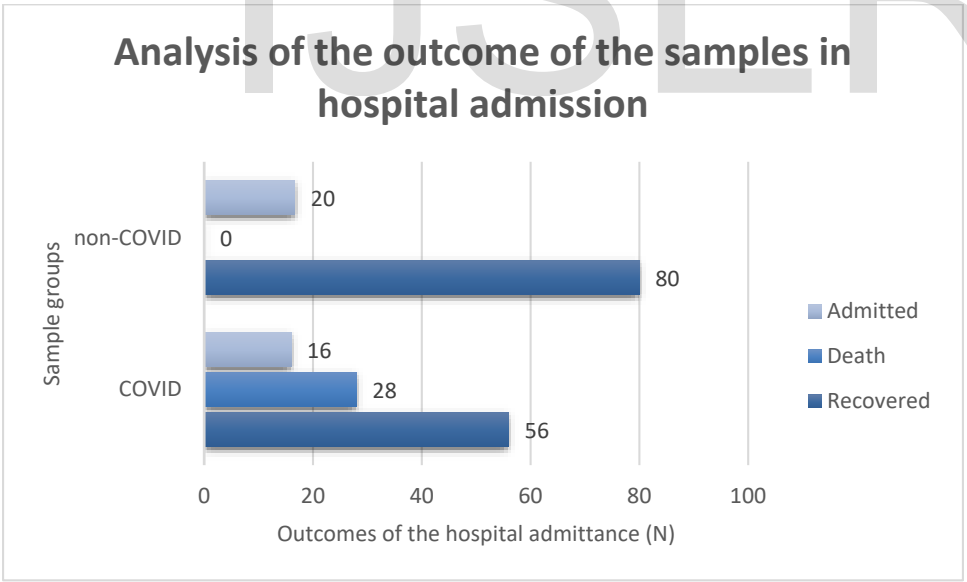

Figure 6 Illustration of the outcomes of hospital admittance in the COVID and non-COVID groups

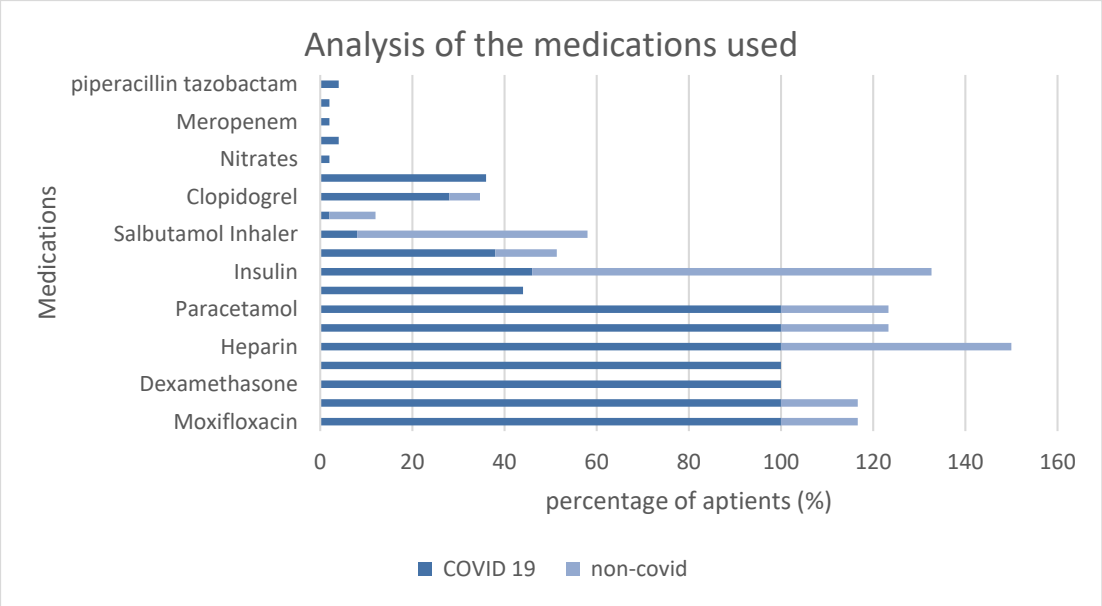

Figure 7 Medication overview used for the study groups

Discussion

Acute coronary syndrome has been reported to decrease the rate of hospitalization worldwide. However, the decreased hospitalization can be due to the stay-at-home policy measures. The findings of the study have reported the prevalence of COVID-19 in patients with the acute coronary syndrome. The highest prevalence was observed for the NSTEMI in the covid patients. The COVID patients also had a high rate of hypertension, 96% as comorbidity and as a family history 52%. The patients affected with COVID-19 were treated with Azithromycin, Moxifloxacin, Ivermectin, Monteleukast, Omeprazole, Heparin, Clopidogrel, Aspirin Dexamethasone, Hydrocortisone and more severe patients were given Tocilizumab. The patients were taking heparin, Atorvastatin, Aspirin, Clopidogrel, Furosemide, Spironolactone etc. -- Other than NSTEMI, COVID patients were also observed to have a high percentage of STEMI, myocardial infarction, ischemic wall ischemia, Anterolateral wall MI, global ischemia, unstable angina, IHD, IHF, inferior and Anterolateral wall ischemia.

The patients having ACS tested positive for the COVID-19 infection are reported to have increased protein fragmentation of clotting, D-dimers in the blood reflecting an enhanced thrombogenicity in the COVID-19. The patients admitted to the hospital had less severity of chest pain in myocardial infarction (MI) (Matsushita, 2021). A study has reported in Austria a

low rate of ACS admittance rate in the hospitals having a significant increase in the infarction and mortality rate (Metzler et al., 2020). The cardiac interventions in addition to COVID 19 should be clinically individualized. The possible mechanism of myocardial injury, myocardial infarction is designated to hyper inflammation, cytokines release, hypoxemia and respiratory failure, physiological downregulation of the ACE 2 receptors, hypercoagulation ability leading to thrombosis, increased risk of endothelial injury (Bavishi, et al., 2020). The increased inflammatory response in the COVID 19 can increase the risk of CVD complications like arrhythmias, heart failure, electrolyte disbalance. It was reported by Bavishi, et al., (2020) that 7.4% of the patients admitted to a hospital facility in Manhattan had cardiac arrhythmia which increases the risk of bradycardia and tachycardia in COVID 19 patients. Other than arrhythmias acute myocardial injuries can also occur in conjunction with other diseases in the clinical course. The Chinese Clinical Guidance for COVID 19 recommends an increased concentration of the myocardial enzymes and biomarkers in COVID 19 patients.

Conclusion

The effect of the COVID 29 virus on cardiac physiology is not well established, however, it has been proposed to affect the patients with the acute coronary syndrome to some extent associated to have comorbidities. Based on the research, there is a need to discover the relation between the extent of severity and prevalence of the COVID 19 in ACS patients and other cardiovascular complications. The histological, pathological, autopsies and more rigorous research can identify the risk factors leading to the COVID 19 in cardiac patients which can further elucidate the mechanism as well.

In addition, we recommend researchers consider how imaging methods may be used to detect abnormalities in heart function in infected patients, as well as further scrutiny of cardiac blood chemistry. These findings will ultimately assist providers in detecting clinicopathological signs as early as possible that may help predict disease severity and better inform treatment management.

Study Limitations

The confirmation for the intervention strategies for COVID 19 patients require further researches.

Conflict of interest:

There is no conflict of interest.

Acknowledgement:

None

Summary:

- **What is known:**
  Patients affected with viral disease COVID-19 there is prevalence of ACS in post-COVID-19 patients.
- **What study adds:**
  This study shows the prevalence of ACS in post-COVID19 patients and increase incidence of deaths associated with this combination of diseases.
- **Clinical significance:**
  This study has a very impactful clinical significance as it shows association of COVID-19 and ACS.

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