

Research Article

Cardiology: Open Access

Impact of Covid-19 in the Field of Cardiology in Karachi Pakistan

Khalida Soomro^{1*}, Zaman Baloch M²

¹Interventional Cardiologist at Zia Uddin University Hospital Karachi, Pakistan

²Assistant Professor Cardiology in Indus Medical College Tando Muhammad Khan, Pakistan

*Corresponding author

Khalida Soomro, Interventional Cardiologist at Zia Uddin University Hospital Karachi, Pakistan.

Submitted: 20 Jul 2022; Accepted: 28 Jul 2022; Published: 06 Aug 2022

Citation: Khalida Soomro (2022). Impact of Covid-19 in the Field of Cardiology in Karachi Pakistan. Cardio Open, 7(3): 275-281.

Abstract

The COVID-19 pandemic caused by the Corona-virus has brought new changes to the worldwide healthcare system. Healthcare delivery is experiencing drastic changes due to the pandemic. This unprecedented surge in COVID-19 infections led many governments around the world to implement population lifestyle changes to limit the spread of infection. To identify the differences in demographics, clinical characteristics, admission, diagnostic and therapeutic procedures, affect cardiovascular services and changes adopted in hospital's emergency room triage. We analyzed key performance services offered in cardiology department in tertiary care hospitals. There has been a more than 50% drop in the number of Cardiac patients presenting to the cardiac dept. of these hospital. All areas of cardiology service provision sustained significant reductions, which included outpatient clinics, investigations, procedures and cardiology community services such as heart failure and cardiac rehabilitation. In line with government guidelines, cardiology services had to alter the delivery of care by adopting virtual clinic models, redeployment of staff to the acute medical services and rescheduling of non-urgent procedures. Dealing with the increased COVID-associated CV risk burden and becoming acquainted with potential new e-cardiology approaches aimed at integrating the cardiology practice are relevant new challenges brought by severe acute respiratory syndrome coronavirus 2 infection and its sequelae in Middle-income countries like Pakistan.

Keywords: Cardiovascular (CV), Low and Middle-Income Countries (LMICs), Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), Coronavirus Disease of 2019 (covid-19), Percutaneous Coronary Intervention (PCI).

Background

Since its emergence in early 2020, the novel severe acute respiratory syndrome, coronavirus 2 causing coronavirus disease 2019 has reached pandemic levels, and there have been repeated outbreaks across the globe [1,2]. Patients with pre-existing cardiovascular diseases are prone to more severe complications from COVID-19 infections in millions of people who survived infection worldwide. The etiological agent of Covid-19 infection has potential consequences on the cardiovascular system its self, can infect the heart, vascular tissues, and circulating cells through ACE2 (angiotensin-converting enzyme 2), the host cell receptor for the viral spike protein. Acute cardiac injury is a common extra pulmonary manifestation of COVID-19 with potential chronic consequences. This unprecedented surge in COVID-19 pandemic has changed the delivery of medical care across the world and led many governments around the world to implement population-based lifestyle changes through social

distancing, shielding and lockdown measures to limit the spread of infection.

There is a growing body of data noting the impact of Covid-19 on cardiac services, patient access to care and cardiovascular outcomes from developed countries. Whereas per reports of the few studies conducted on procedural volumes and case fatalities in Low- and middle-income countries including Pakistan have mixed findings regarding the effects of COVID-19. There are many challenges to the delivery of effective cardiovascular care in LMICs. These include lack of specialized care in rural areas, misdiagnoses, gaps in treatment, gender and ethnic disparities and cost restraints. It is worth maintain about one study conducted in tertiary care hospital in Karachi* reported that COVID disproportionately affects males, resulting in a more severe illness and higher mortality rates in Table-1.

TABLE NO 1. AGE AND GENDER DISTRIBUTION OF COVID-19 CASES IN KARACHI, PAKISTAN 70000 60000 50000 40000 ■ Female 30000 ■ Male 20000 10000 21--30 31--40 41--50 51--60 11--20 61--70 71--80 91 ---10 ABOVE

Table 1: Age and Gender distribution of Covid-19 Cases in Karachi, Pakistan

This may be partly due to the fact Women in our region of the world face many challenges in accessing timely healthcare facility due to cultural barriers, reliance on males in the family for transport, lack of education, and prioritizing the health of male family members over their own. Understandably, all these

Urban Area

factors are amplified during the pandemic and lockdowns. The Study shows 935 patients suffered from Covid-19 (March to July 2020) 497 (62.1%) male suffered vs female 303 (37.8%). Patient from Rural Areas were combatively less than Urban Patients 116 (14.5%) vs 684 (85.4%) in Table 2.

Demographics Pre-COVID (Mar-July 2019) COVID (Mar-July 2020) P Value n = 2552n = 1749 (68.5%)n = 801 (31.4%)Age (Mean ±SD) 60.7 ± 15 61.7 ± 15 0.24 Gender Male 1028 (58.8%) 497 (62.1%) 0.09 Female 719 (41.1%) 303 (37.8%) Area Rural Area 318 (18.2%) 116 (14.5%) 0.01

Table 2

SARS-CoV-2 had more prominent impact on people with cardiovascular disease and its risk factors (e.g., hypertension, diabetes, and obesity) as suggested by the same study in Table 3.

684 (85.4%)

1429 (81.7%)

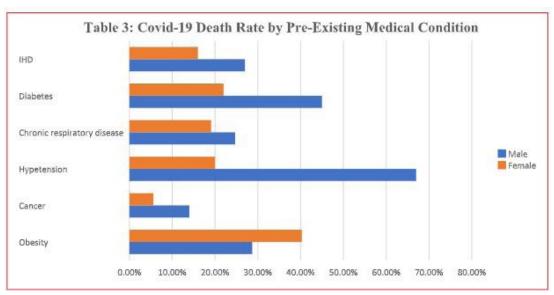


Table 3: Covid-19 Death Rate by Pre-Existing Medical Condition

Impact of SARS2 Seen on Cardiology Admissions and Myocardial Infarction

During the peak periods there was a marked reduction in patient (ACS) chest pain/breathlessness presentations almost a 53% significant (p = 0.047) reduction in admissions in cardiology ward and coronary care unit (CCU), there was a 40% drop in the number of patients diagnosed with myocardial infarction and non-significant reduction in ST elevation Myocardial Infarction, but significant reduction in Type I NSTEMI, Unstable angina and Heart failure [3-6]. There was rise in type II myocardial injury during the COVID period. A reduction in the proportion of STEMI patients achieving a DTB time of \leq 90 minutes was

observed which was related to the thrombolysis-first approach in many small-town centers in Pakistan [7,8]. No significant difference was observed in both groups for tachy-arrhythmia, brady-arrhythmia, stable coronary artery disease, non-cardiac chest pain and symptoms. There was no significant effect of the COVID-19 pandemic on in-hospital mortality. PCI volumes decreased, primarily driven by the deferral of non-urgent procedures. Mainly resulted in a fall in NSTEMI and PCI cases, potentially because of patients deferring contact with healthcare institutions in Table 4.

Table 4: Reduction of ACS, Heart Failure, and Arrythmias

Diagnosis (n = 2552)	Pre-COVID n = 1691 (66.2%)	COVID n = 861 (33.7%)	Reduction
ACS Presentation (n = 805)	526 (31.1%)	279 (32.4%)	53%↓
STEMI (n = 137)	110 (6.5%)	27 (3.1%)	24.5%↓
NSTEMI (n = 405)	276 (16.3%)	129(14.9%)	46.7% ↓
Unstable angina (n = 184)	140 (8.2%)	44 (5.1%)	31.4%↓
Type II MI (n = 352)	152 (8.9%)	200 (23.2%)	24%↑
Heart Failure (n = 310)	250 (14.7%)	60 (6.9%)	24%↓
Tachyarrhythmia (n = 259)	177 (10.4%)	82(9.5%)	46.3%↓
Brady arrhythmia (n = 100)	60 (3.5%)	40 (4.6%)	66.6%↓

Cardiology Outpatient Service

In line with NHS guidance on implementing COVID-19 work patterns, Overall number of patients referred from primary care to cardiology face-to-face outpatient clinics dropped by 78% [9]. We adopted telephone and video consultation services to minimize exposure risks to patients and staff in major urban areas we were not able to set up secure remote working access and establish virtual clinics using technology-enabled care in rural area people due to lack of awareness and literacy rate in these areas mostly. Moreover, the overriding importance of minimizing potential patient exposure, led new and return clinic appointments to more thorough triaging into online or face to face clinics depending on need and focusing on urgency of referrals performed, appropriate investigation and, if necessary, within 24 hours of receipt of the referral instead of clinic assessment, and telephone consultation. Outpatient Clinics Activity during Covid 19 Pandemic of General Practitioners and in Cardiology Department of Major Tertiary Hospital.

Despite changes to service delivery, the practice of referring of patient's and discussing patients in local and regional multidisciplinary team (MDT) meetings in major cardiac centers in Pakistan was maintained. However, the MDT meetings were performed via video especially for Primary PCI in major cardiac center in Punjab and AKUH and satellite centers of NICVD in 12 centers in Sindh only.

Impact on Cardiac Lab Investigations

Acute cardiac injury, inferred from elevations in cTnT (cardiac troponin) levels, is reported in 8% to 62% of patients hospitalized with COVID-19 and is associated with greater disease

severity, including need for mechanical ventilation, and death. As for as CVD is concerned significant fall was observed in the number of performed acute cardiac tests and markers was observed with a 46% reduction in cardiac troponin T (cTnT) blood tests. Moreover, 75% fewer N-terminal-pro B-type natriuretic peptide (NT-proBNP) blood tests performed both in primary and secondary care indicating a reduction in patients presenting with symptoms and signs of heart failure.

Impact on the Other Cardiac Test

In the beginning of pandemic, there was an increase in the number of patient cancellations to the other diagnostic procedures of cardiology department, with the exception of computed tomography coronary angiography (CTCA). Requests for cardiac investigations during the lockdown intervals were triaged into urgent and routine, routine investigations were rescheduled. Therefore, the number of ETTs and outpatient echocardiograms dropped by 47% and the uptake of ambulatory cardiac monitors dropped by 82%.

There was a parallel reduction in investigations like transoesophageal echocardiography (TOE) and functional assessments of myocardial ischemia with dobutamine stress echocardiograms (DSEs); all routine DSEs were postponed until the settle down. Cardiovascular imaging volumes, including elective echo, nuclear stress testing, ETT, cardiac MRI and Holter monitoring suffered a large decline in cardiology departments of tertiary care centers in Table 5.

Table no 5. Reduction of Investigations

CTnT

NT-ProBNP

ECGS

ECHO

ETT

47%

Ambulatory Cardiac Monitors

Cardiac Imaging

0% 10% 20% 30% 40% 50% 60% 70% 80% 90%

Table 5: Reduction of Investigations

This Delay may-be due to patients from rural areas using various means of transport (e.g., public, buses, and private cars) sometimes take up to 24 to reach in major cardiac Centers apart from fear of the pandemic. Thus, statistically significant drop in patients coming to Cardiac Centers from rural areas was noted. As the COVID cases numbers will decrease, patients who delayed their cardiac tests will return, and a gradual catch-up to pre-COVID volumes can be achieved. Meanwhile many diagnostic cardiology staff were redeployed to the CCU, the cardiology ward and acute medical wards to support existing nursing staff.

Coronary Angiography and PCI

Data on PCI volumes provide some insights into how COVID-19 has affected elective procedures. There was a significant decrease in PCI cases from before to during the COVID-19 pandemic, primarily driven by the deferral of non-urgent procedures in Pakistan. The decline in PCI started with the onset of the COVID-19 pandemic and reached a nadir during the government-imposed 'circuit breaker'. The fall can be explained by guidance from the Ministry of Health in Pakistan to individual institutions to postpone non-urgent cases to free up bed space in anticipation of a surge in COVID-19-related admissions. However, Patients with acute MI had greater proportion of NSTEMI in comparison to STEMI patients in most of the major multi-specialty Institution [10-13]. An overall decline in both STEMI and

NSTEMI numbers identical to other studies was found, but only reduction in the latter was statistically significant. A reduction in the proportion of STEMI patients achieving a DTB time of ≤ 90 minutes was related to the thrombolysis-first approach pursued by small towns of Pakistan; primary PCI was performed only if the patient was known to be COVID-19-negative or as rescue therapy in the event of failed thrombolysis with medical staff in full personal protective equipment. The reason for difference in DBT time from other countries was due to various local reasons also. Other studies with similar findings have attributed differences in DTB time to the time taken to perform preadmission screening chest X-rays and to ascertain travel and contact histories and symptomatology in patients whose COVID-19 status is unknown. Nevertheless, despite the increase in DTB time, there was no significant effect of the COVID-19 pandemic on in-hospital mortality. For NSTEMI and STEMI, Overall, there was a significant decrease in PCI cases from before to during the COVID-19 period (13,589 versus 11,949; p=0.020). Primary PCI remained largely constant. (Gender differences in both elective and urgent cardiovascular procedures has been reported that COVID disproportionately affects males. (Female patients were significantly less likely to undergo elective diagnostic coronary angiography and angioplasty 8.2% male vs. 3.3 % female during the pandemic) with appropriate protocols and systems.

Table 6: Impact on Cardiac surgery and Interventional Procedures

Management (n = 1381)	Pre-COVID n = 964 (69.8%)	COVID n = 417 (30.1%)	Reduction
PCI (n = 234)	174 (18.0%)	60 (14.3%)	34.4%↓
Coronary angiography (n = 184)	129 (13.3%)	55 (13.1%)	42.6%↓
Primary PCI (STEMI n = 105)	82 (8.5%)	23 (5.5%)	28.0%↓
CABG (n = 110)	74 (7.6%)	36 (8.6%)	48.6%↓
Cardiac Imaging (n = 717)	481 (49.8%)	236 (56.5%)	49.0%↓
Device Implantation (n = 31)	24 (2.4%)	7 (1.6%)	29.1%↓

There was, however, a significant drop up-to 1/2 of reductions in number of referrals of elective coronary angiography and cardiac surgery was seen. This decrease was partly due to the reduction in patients presenting with chest pain and myocardial infarction but also due to the prioritization of patients needing urgent coronary angiography. That was the reason that 32% reduction in the number of urgent coronary angiography. A possible explanation is that patients were presenting late to hospital with more severe ischemia requiring urgent angiography, having resisted earlier appropriate admission because of fears of contracting the virus. Similarly, there was prioritization of coronary artery bypass grafting, leading to a significant reduction in the number of cardiac surgeries performed to only one from ten during this period.

Impact on Other Cardiac Procedures

Direct Current Cardioversion and Cardiac Device Implantation Data from cardiac centers shows an insignificant Increase in both tachy- and Brady arrhythmias e.g., increase in admission with atrial arrhythmia, ventricular arrhythmia and Brady arrhythmia during COVID. Some elective and necessary Cases procedures during COVID-19 started to fall following complex device consultation with patients and management. These Cardiac procedures were performed as priority groups; the ratio of local device procedures was 1/3. During pandemic pacemaker implantations was only performed in complete heart block or symptomatic second-degree heart block. In symptomatic bradycardia patients such as those with sinoatrial node, disease or pacemaker generator replacements were only done during the COVID-19 period if capacity allowed. Remaining cases were postponed and booked for end of COVID-19. The pacemaker follow-up service was also reconfigured. Pacemaker patients were established on home monitoring systems and reviews were performed via telephone consultation.

Similarly, the number of patients transferred from tertiary care following complex device (cardiac re-synchronization therapy (CRT)/implantable cardioverter defibrillator (ICD)) implantation and electrophysiology studies dropped significantly. The coronary angiography services were restructured with a focus on regional centralization especially in case of NICVD satellites and major cardiac institutes due to reduction of inter-hospital patient transfer in various regions of Pakistan.

Heart Failure

Along with ACS, the number of heart failure patients was also dropped by 30% depending on the trends in heart failure symptom presentation and NT-ProBNP measurements across primary and secondary care during the COVID period also due to reluc-

tance to visit the hospital out of fear of contracting COVID 19, which has a major role to play in reduced HF presentation. The heart failure emergency services were offered in emergency department of every tertiary care hospital. In order to optimize patients' care during the lockdown intervals, strategies to educate and empower patients were adopted to facilitate the up titration and optimization of treatment.

Cardiac Rehabilitation

There was a 60% reduction in the delivery of cardiac rehabilitation, which changed from the usually face-to-face service to virtual service via telephone call; supervised online exercise sessions and supervised exercise sessions took place randomly. PB and heartrate monitoring took place randomly the COVID-19 pandemic and will likely continue to be a permanent part of cardiac rehabilitation after the service is restored to full capacity.

One of the Study conducted Agha Khan University Hospital revealed the data from single center as follows which can be simple example for decreasing cardiac services in Karachi, Pakistan [14]. Out 2976 patients presenting with cardiac complaints to the emergency department (ED), 2041 (69%) patients presented during the pre-COVID period, and 935 (31%) patients presented during the COVID period. There was significant reduction in acute coronary syndrome (ACS) (8% [95% CI 4–11], p < 0.001) and heart failure ($\downarrow 6\%$ [95% CI 3–8], p < 0.001). A striking surge was noted in Type II Myocardial injury (†18% [95% CI 20–15], p < 0.001) during the pandemic. There was reduction in cardiovascular admissions (coronary care unit p < 0.01, coronary step-down unit p = 0.03), cardiovascular imaging (p < 0.001), and procedures (percutaneous coronary intervention p = 0.04 and coronary angiography p = 0.02). No significant difference was noted in mortality (4.7% vs. 3.7%). The percentage of patients presenting from rural areas declined significantly during the COVID period (18% vs. 14%, p = 0.01).

Overall, the reasons for these reductions are multifactorial and include the restructuring and prioritization of services, reduced access to primary care, and patients' reluctance to seek medical help due to fear of contracting the virus. Thus, the healthcare system had tried to restructure to minimize patient contact with healthcare professionals, limit or reschedule hospital visits and outpatient clinics, postpone non-urgent procedures, and adopt telephone and video-assisted consultations [15,16]. More extreme lifestyle changes through shielding were implemented for those deemed to be most vulnerable, such as those with cardiac transplants, complex congenital heart disease and advanced heart failure in order to reduce their exposure risk in line with

government guidelines, cardiology services had altered the delivery of care by adopting virtual clinic models, redeployment of staff to the acute medical services and rescheduling of non-urgent procedures, while at the same time dealing with the cardiac complications of COVID-19 such as myocarditis, myocardial infarction, ischemic heart disease and heart failure as the leading cause of death [17-20]. Several service users in primary and secondary care settings are established through cardiac rehabilitation, heart failure outpatient and inpatient cardiology services. Adverse consequences for some patients presenting with worsening of their underlying cardiac conditions have been inevitable. Consequently, cardiology services should be ready to offer them urgent input and early intervention.

Conclusions

The COVID-19 pandemic has led to a significant reduction in all sections of cardiology services including referrals to outpatient clinics, investigations, cardiology admissions, number of patients diagnosed with myocardial infarction, cardiac procedures, interventions and community services such as heart failure and cardiac rehabilitation. Indicating a significant drop in the diagnostic blood tests performed during the COVID-19 pandemic. Results of studies conducted in Pakistan are consistent to western literature indicating similar epidemiological impact. However, there are indications that the impact has been disproportionate for women and patients from rural regions. LMICs such as Pakistan, with their resource-limited healthcare systems and healthcare inequities, are poorly equipped to deal with the challenges of a global pandemic. The experience gained from the current outbreak will be vital in dealing with any future challenges. Health care authorities need to be cognizant of the fallout from delayed cardiac care and prepare for future burden of increased cardiovascular morbidity and mortality. The restructuring of health services for assessment and preparation for the recovery phase should be based on these findings there is need for COVID-19 work pattern established technology at the heart of the delivery of care where virtual clinics using telephone and video consultation will be a long-lasting legacy and MDTs and meetings using video conferencing will be the norm. Question rise here that use of these communication technologies will be positively received by healthcare workers and patients in middle income countries where there is lack of awareness from communication technologies and decrease literacy rate. The pandemic has ignited the need to develop new pathways of care models and protocols and has prompted a new era of medical-nursing collaboration and resilience according to our regional situation. These changes are needed to prepare for the potential rebound surge of clinical activity.

References

- Yoganathan, A., Sajjad, M., & Harky, A. (2020). Cardiovascular disease and the impact of COVID-19. Journal of Cardiac Surgery, 35, 2113.
- UK, G. (2020). Number of coronavirus (COVID-19) cases and risk in the UK.
- 3. Meenakshisundaram, R., Senthilkumaran, S., Thirumalai-kolundusubramanian, P., Joy, M., Jena, N. N., Vadivelu, R., ... & Chandrasekaran, V. P. (2020). Status of acute myocar-

- dial infarction in Southern India During COVID-19 lock-down: a multicentric study. Mayo Clinic Proceedings: Innovations, Quality & Outcomes, 4(5), 506-510.
- Wu, J., Mamas, M., Rashid, M., Weston, C., Hains, J., Luescher, T., ... & Gale, C. P. (2021). Patient response, treatments, and mortality for acute myocardial infarction during the COVID-19 pandemic. European Heart Journal-Quality of Care and Clinical Outcomes, 7(3), 238-246.
- Moroni, F., Gramegna, M., Ajello, S., Beneduce, A., Baldetti, L., Vilca, L. M., ... & Azzalini, L. (2020). Collateral damage: medical care avoidance behavior among patients with myocardial infarction during the COVID-19 pandemic. Case Reports, 2(10), 1620-1624.
- Sokolski, M., Gajewski, P., Zymliński, R., Biegus, J., Ten Berg, J. M., Bor, W., ... & Ponikowski, P. (2021). Impact of coronavirus disease 2019 (COVID-19) outbreak on acute admissions at the emergency and cardiology departments across Europe. The American journal of medicine, 134(4), 482-489.
- Moreno, R., Alonso, J. J., Caballero, R., del Corral, E., Elízaga, J., Asenjo, R. M., ... & López-Sendón, J. L. (2020). Influence of age and gender on arrival of patients with ST-segment elevation acute myocardial infarction to tertiary centers during COVID-19 pandemic. Experience of Madrid, Spain, STEMI network (Codigo Infarto Madrid). The American journal of emergency medicine.
- Tam, C. C. F., Cheung, K. S., Lam, S., Wong, A., Yung, A., Sze, M., ... & Siu, C. W. (2020). Impact of coronavirus disease 2019 (COVID-19) outbreak on ST-segment–elevation myocardial infarction care in Hong Kong, China. Circulation: Cardiovascular Quality and Outcomes, 13(4), e006631.
- 9. NHS England. Operating framework for urgent and planned services in hospital settings during COVID-19, 2020.
- Li, Y. H., Huang, W. C., & Hwang, J. J. (2020). No reduction of ST-segment elevation myocardial infarction admission in Taiwan during coronavirus pandemic. American Journal of Cardiology, 131, 133-134.
- 11. Rattka, M., Dreyhaupt, J., Winsauer, C., Stuhler, L., Baumhardt, M., Thiessen, K., ... & Imhof, A. (2021). Effect of the COVID-19 pandemic on mortality of patients with STEMI: a systematic review and meta-analysis. Heart, 107(6), 482-487.
- 12. Chew, N. W., Sia, C. H., Wee, H. L., Jia-Da Benedict, L., Rastogi, S., Kojodjojo, P., ... & Loh, P. H. (2021). Impact of the COVID-19 pandemic on door-to-balloon time for primary percutaneous coronary intervention results from the Singapore western STEMI Network. Circulation Journal, 85(2), 139-149.
- 13. Bhatt, A. S., Moscone, A., McElrath, E. E., Varshney, A. S., Claggett, B. L., Bhatt, D. L., ... & Vaduganathan, M. (2020). Fewer hospitalizations for acute cardiovascular conditions during the COVID-19 pandemic. Journal of the American College of Cardiology, 76(3), 280-288.
- Adnan, G., Shams, P., Khan, M. A., Ali, J., Rahman, N., Tipoo, F. A., ... & Faheem, O. (2021). Impact of COVID-19 on Cardiovascular Disease Presentation, Emergency Department Triage and Inpatient Cardiology Services in a

- Low-to Middle-Income Country—Perspective from a Tertiary Care Hospital of Pakistan. Global Heart, 16(1), 86.
- 15. Remuzzi, A., & Remuzzi, G. (2020). COVID-19 and Italy: what next?. The lancet, 395(10231), 1225-1228.
- 16. Scottish Government. Coronavirus (COVID-19): nursing and community health staff guidance, 2020.
- 17. Government of Pakistan. Government of Pakistan Health Advisory Platform; 2020.
- 18. Public Health England (PHE). Guidance on shielding and
- protecting people who are clinically extremely vulnerable from COVID-19, 2020.
- 19. Clerkin, K. J., Fried, J. A., Raikhelkar, J., Sayer, G., Griffin, J. M., Masoumi, A., ... & Uriel, N. (2020). COVID-19 and cardiovascular disease. Circulation, 141(20), 1648-1655.
- Zaim, S., Chong, J. H., Sankaranarayanan, V., & Harky, A. (2020). COVID-19 and multiorgan response. Current problems in cardiology, 45(8), 100618.

Copyright: ©2022 Khalida Soomro. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Cardio Open, 2022 https://opastpublishers.com Volume 7 | Issue 3 | 281