

MONITORING OF CARDIOVASCULAR PHYSIOLOGICAL VARIATIONS BASED ON PSYCHOLOGICAL STATE AT COVID-19 COMPULSION OVER MYOCARDITIS PATIENTS

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Abstract: Whole world is fighting COVID-19 pandemic & there's no vaccine available, to check the spread of this virus people have to be quarantined and isolated. People are facing lot of psychological distress, there's rise in panic, hatred, anxiety, & depression among the people. Societal discrimination is also faced by the suspected as well as people who got cured.

Cardiovascular diseases, hypertension, diabetes etc. are comorbidities associated with the SARS-CoV-2 virus infection. In myocarditis heart gets weakened, there are many reports of myocarditis in the people affected by COVID-19 as well as people who have pre-existing myocarditis and got infected. Hypertension, hypoxemia, virus induced myocarditis, immune mediated systemic inflammation, all contribute to myocarditis and are on rise in the COVID-19 patients further worsening condition of patient with myocarditis. Also, the suffering due to the viral infection is increased in such patients.

This review mainly focused on psychological effect of SARS-CoV-2 virus & the cardiovascular physiological variation it causes in myocarditis patients and the way it can further worsen it.

Keywords: COVID-19; myocarditis; psychological distress; hypertension; inflammation.

I. INTRODUCTION

Coronaviruses is a big group of viruses & most of them has made their target the respiratory pathway; the first Human coronavirus was found in the year of 1965. After 2003 five human coronaviruses has been discovered (1) of which the most widely known are- as follow (a) SARS virus (Severe-acute-respiratory-syndrome virus) first appeared in the humans in the wake of 2003 in China, (b) MERS virus (Middle-east-respiratory syndrome virus) transmitted from the camels to human therefore the illness caused by it is called as camel flu. It was discovered in the year 2012, in the country Saudi Arabia & (c) finally the one which has become a global pandemic SARS-CoV-2 virus, speculated to have originated in the wet markets Wuhan, China as the captured live wild animals are also sold there and remains in close contact with humans. It causes the disease called as COVID-19 also sometimes known as novel coronavirus disease. It shares genomic similarity up to 79.6% with SARS virus.(2) COVID-19 disease mostly affects the respiratory tract but it has been found that it also has a profound effect on the cardiovascular system. As the cure is currently being discovered the only method to check it's spread is isolation, quarantine & use of protective equipment which has put a lot of mental distress on the people. In this review we discuss the cardiovascular variations that occur in the pe

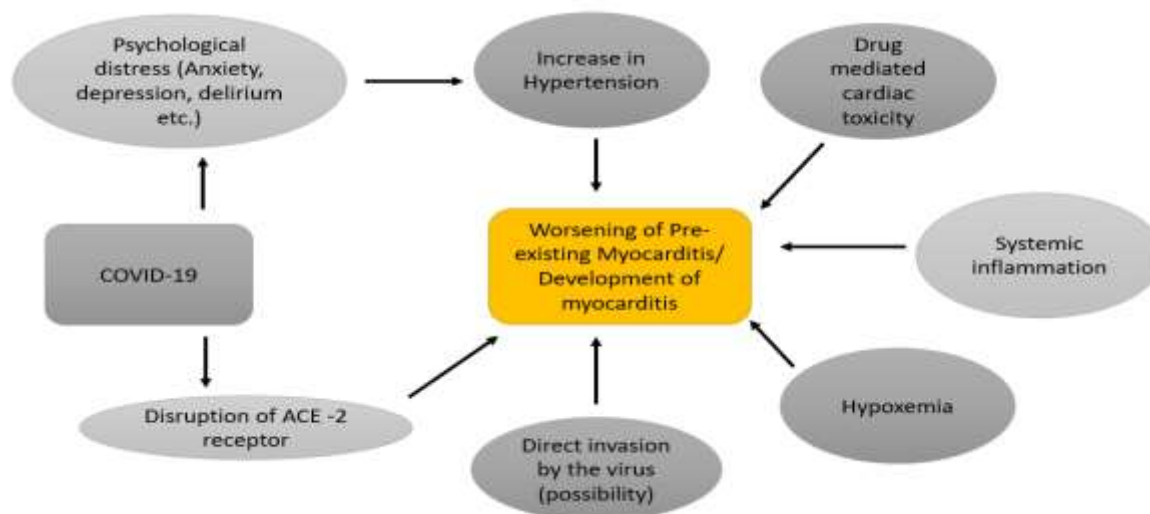


Fig: Above illustration gives a brief about different conditions related to COVID-19 that is associated with myocarditis .

A lot of mental stress is in the people, many cases of myocarditis has also been reported during this infection but not much has been studied about, 'what will be the impact of psychological distress in the patient with pre-existing myocarditis?'

The cardiac diseases are major comorbid conditions linked with the COVID-19 & chances of mortality are also increased therefore this study is really required at this time.

2. Literature survey:

This literature review is specifically based on monitoring of cardiovascular physiological variations based in psychological state at COVID-19 compulsion over myocarditis patients.

Nishiga, Wang (2) evaluated that COVID-19 infection is linked with cardiovascular disease, the SARS-Cov-2 itself can cause cardiac arrhythmia, damage to myocardium, thrombosis in veins, as well as several conditions associated with acute coronary syndrome. It was revealed from their systemic study that there is 37.5% rate of mortality in individuals with increased cardiac troponin T level, & in individuals with some CVD as well as aggravated level of cardiac troponin T the rate of mortality was found to be 69.4% They also revealed that the drug-disease interactions are also becoming a major problem & patients with underlying cardiovascular disease are worst hit with an increased chance of death.

Vellas, Delobel (3) in their finding it is illustrated that older people are prone of getting infected by the virus & especially those with comorbidities are at a very high risk in comparison to those younger people and healthy adults. They suggest that the development of complication in the older people may be due to decline in immunity due to aging i.e. immune-senescence and inflammation that occur with aging i.e. inflamm-aging.

Oliveira, Oliveira (4) revealed that the best method to detect and diagnose the coronavirus is by amplifying its nucleic acid. This amplification can be done by using technique of "RT-PCR" which has set the benchmark for diagnosis but it is tough to use because it requires skill and time. They also tell us about other methods for the COVID-19 detection such as "ELISA".

Zhou, Xie (5) have determined that in comparison to SARS-CoV, the newer virus SARS-CoV-2 also called COVID-19 is more hazardous, have wider spread, whole family is at a greater risk, also it has greater chance of infecting and mortality is also increased. In infected children initially there are gastrointestinal system is affected which further leads to grave conditions. Similarly, in case of newborns if the mother is infected critical complication occurs in them. They also detected that lactate dehydrogenase and neutrophils amount is increased in children but the level T-cells (CD8+ & CD4+) are decreased.

Pascarella, Strumia (6) investigated that the COVID-19 spreads from 1 person to another and also when a person comes in contact with a contaminated surface. Its main symptoms include headache, gastrointestinal problem, dry cough, fever, difficulty in breathing, feeling exhausted and pharyngitis. Best prevention is maintaining hygiene, wearing protective kits in public. As there is no permanent cure for it, still some drugs being used such as antivirals like remdesvir, antimalarial drugs like hydroxychloroquine and also some respiratory therapies which shows some improvement. Till now remaining quarantined is the best method to keep in check it's spread.

Tu, Chien (7) found that the health institutes are trying to discover the novel coronavirus vaccine as quickly as it can be done but it is a time taking process because it has to be tested for its clinical safety and efficacy. They also tell us that drug repositioning is being done of the existing antivirals like favipiravir (viral replication is hindered) and of other drugs used in diseases such as malaria such as chloroquine (pathway of endosomal entry is hindered), as it is a rapid approach to keep in check the pandemic. These drugs can either target the replication cycle of the virus or can affect the immune system (enhances immune response against the virus or increases the inflammatory response against the virus).

Wei, Liu (8) investigated that in case of immunocompromised patient such as those undergone organ transplantations, and are taking immunosuppressants for a long period of time there are chances of recurrences. From their work come to find recurrence of SARS-Cov-2 infection in an elderly patient after 11 days of complete relieve from clinical symptoms, the individual had hypertension since 10 years and with transplanted liver was taking immunosuppressant since 11 years. Therefore, extended quarantine might be required in case of immunocompromised patients.

Lafaie, Célarier (9) illustrated that reinfection due to novel coronavirus in elderly was firstly observed in April,2020. It was observed in case of female geriatric patient there was reoccurrence of COVID-19 which took place after gap of several weeks in-between. All the cases of re-infection were proven to be more deadly. Immuno-senescence can be the reason that led to re-infection & there might be presence of some sanctuary site for the virus in the patient body.

Gonçalves, Gonçalves (10) in their research on 176 obese old individuals found that hypertension was the most predominant comorbidity associated with COVID-19 where 72.2% had it. On second number diabetes stood with 40.9%. Deficiency of vitamin-D was also observed in 94.2% of the individuals. Deficiency of vitamin-D and obesity is predominant in patients admitted in ICU due to COVID-19 and are also critically sick.

Quagliariello, Bonelli (11) discovered that people with cancer are at a greater risk of being infected by COVID-19, & progress of the infection is more severe in them. Also, the extent of severity of infection depends on the type of therapy person is receiving, the type of malignancy and other comorbidities that are coexisting such as hypertension, diabetes etc. Their finding revealed that heart of patients is greatly damaged in COVID-19 if the cancer patient is also taking cardiotoxic substance during the treatment.

Islam, Riaz (12) in their research found that out of 1016 individuals main comorbid conditions associated with COVID-19 was diabetes mellitus with 35% prevalence after that hypertension which was present in 16.6% of the individuals. Then COPD was present in 16.6% of the people and lastly there were 7.8% individuals with severe heart diseases. The danger was higher in case of the patients with chronic kidney disease, COPD and progressive damage to the liver i.e. chronic liver disease.

Bailey, Dmytrenko (13) have determined using a bioengineered cardiac tissue that the COVID-19 virus infects particularly cardiomyocytes. After the infection there was inflammation of cardiomyocytes i.e. myocarditis, mortality of the cells was also observed, contraction of the cardiac tissue was also impaired & immune cells started becoming active. The result obtained are similar to the tissue obtained from a COVID-19 patient after post-mortem. Entry of virus takes place only after it integrates with ACE2 enzyme and expression of endosomal cysteine proteases.

Ozieranski, Tyminska (14) have proposed the hypothetical mechanism by which myocarditis occurs during the course novel corona virus infection. The cardiac troponin release may due to direct invasion by the virus leading to myocarditis, low concentration of oxygen in the blood i.e. hypoxemia, systemic inflammation, inflammation of the endothelium, and myocardial infarction. It is suggested that more endomyocardial biopsy data is needed for better understanding. Also autopsy data can also be used to understand the inflammatory state that patients undergo due negative effect of immune system during COVID-19 infection.

Cuomo, Menozzi (15) suggested that major clinical indicator in SARS-CoV-2 infection can be myocardial injury or acute myocarditis. Brain natriuretic peptide, level of troponin, MRI of heart, echocardiogram (ECG) helps in detection. It was assumed that the pathogenesis of myocarditis may be due COVID-19 mediated through immunological response.

Madjid, Safavi-Naeini (16) observed that in novel coronavirus infected patients there is increases in the inflammation which can lead to the inflammation of vessels, myocardium and also cardiac arrhythmia. They suggest that risk factors associated with cardiovascular diseases should be carefully observed and controlled as the chances of mortality is increased in such patients.

South, Diz (17) illustrated that the SARS-CoV-2 enters the host by integrating with the ACE-2 enzyme, this knowledge can be used to target the virus entry by blocking ACE-2 enzyme or reducing its formation. Cardiac, renal, gastrointestinal, lungs and brain tissues express this enzyme therefore they are at prime risk. Their work also tells us that it is to be considered that ACE-2 enzyme is an important enzyme of renin-angiotensin-aldosterone system, and hypertension or cardiovascular patients who are being treated using RAAS blocker & statins may be at higher risk of infection because the amount of ACE-2 enzyme gets alleviated.

Pechère-Bertschi, Ponte (18) conducted a single centre study that weather to discontinue angiotensin-converting-enzyme 2 inhibitors and angiotensin receptor blockers or not. As ACE2 aids the virus in infecting the host by integrating with it but ACE inhibitors and ARBs are also providing protection against inflammation in acute-respiratory-distress syndrome. Their work reveals that the use of ACE inhibitors and ARBs should be continued.

Babapoor-Farrokhran, Gill (19) found that damage to the ACE2 receptors lead to several cardiac conditions like coronary failure, improper functioning of heart, & disease of the heart muscles i.e. cardiomyopathy. I-troponins & T-troponin are the main biomarkers in case of myocardial injury, during injury their level increases. The mechanism by which the novel coronavirus damages the myocardium is not properly understood but several possible mechanisms have been proposed like-bodywide inflammation, direct invasion on myocardial cells leading to myocarditis, lack of oxygen supply, amplified cytokine action by T helper cells, collagen accumulation myocardium interstitium of heart i.e. its fibrosis, activation of immune system mediated by interferons & rupturing of deposited plaque in coronary vessels.

Matsumori, Yamada (20) demonstrated that damage to cardiac muscle in myocarditis may be due to cytokines. Cytokines also reduces the intensity of the heart muscle contraction. A major role is of TNF- α in the development of myocardial injury. In 13 individuals' number of interleukins (1- α , 2, 6 & I-fl), interferons (α & γ), TNF (α & fl), & stimulating factors (granulocyte-macrophage, granulocyte & macrophage) were measured who were also affected by myocarditis. The number of cytokines increased in myocarditis patients indicating that they might have an important role in the development of myocarditis.

FAHR (21) determined that 75% of the chronic myocardial illness are associated with hypertension. It is one of the main aspects that leads to chronic myocarditis. Infection is just a small factor in causing myocardial illness, instead it is the weakened state of heart when infection plays a major role in pathogenesis of a myocardial disease.

Frustaci, Francone (22) have detected that hypertension makes a person more vulnerable towards infections targeting cardiac system. Their work revealed that in comparison to people who don't have hypertension myocarditis was more common in individuals with hypertensive heart disease (a cardiac condition that occurs due to hypertension and high blood pressure) and left ventricular dysfunction. In 64.28% cases (total 28) having both myocarditis & hypertensive heart disease no pathogen found. It implies possibility of some other mechanism such as "immune-mediated mechanism or a stress-mediated release of segregated antigens (i.e. myosin) from myocardiocytes" (22).

Fofana, Latif (23) have detected that the lockdown, isolation and fear of the pandemic has affected the mental health of the people. There is a rise in the negative emotions, psychological disorders linked with depression and anxiety. Due to the limited resources the fear and unpredictable future of SARS-CoV-2 infection is putting a lot of pressure. To decrease the negative emotions & improve the mental condition of people such as migrants, healthcare workers, & also the general population.

Rahman, Hoque (24) determined that greater psychological discomfort during the novel coronavirus crisis were found in the smokers, people who consume alcohol, females, people who are more scared, & person with underlying mental health issues. Their investigation showed that alleviated level of fear was linked with alcohol consumption, people who are in age group of 30-59, change in the employment conditions and status, people who are taking care of the suspected patients & infected patients.

Dubey, Biswas (25) detected several unusual behaviours in people like paranoia, over stocking, confusion due to spread non-reliable and misinformation that is rapidly spreading about COVID-19. Also, there is an increase in depression & anxiety among the people, and there are several cases of occurrence of post-traumatic-stress-disorder in people due to the disease along with the isolation. Their work also revealed that there is an increase in racism, increased hatred towards people belonging to different culture and ethnicity among the people. Healthcare workers are also experiencing psychological disturbances such as mental exhaustion, stress, depression etc. Children lifestyle became upside down which may lead to psychological suffering. Homeless people are forced to be quarantined which increased fear among them.

Velayudhan, Aarsland (26) have discovered that people with dementia & are infected by the novel coronavirus have a higher chance of being delirium. Among the infected demented people there is a development of psychoneurotic conditions in 98% of them. These neuropsychological symptoms can also worsen during the infection or after getting cured due to social burdens. Mismanagement of these psychoneurotic symptoms can enhance the disease and may also cause death.

Peng, Mo (27) found that among the infected, isolated & quarantined people due to COVID-19 depression was more common in younger individuals. People with less education, are single, not married are the ones' that are getting more depressed, suffers from anxiety, insomnia, which may lead to post-traumatic-stress disorder in the long run. Hyperarousal was more observed in the depressed groups.

Qiu, Shen (28) evaluated that the main reason for fear of the COVID-19 is due to these reasons: knowledge that to check the viral spread quarantine is essential, virus can also spread from one person to another & declaration by WHO that it is a public health emergency of international concern. Their work reveals that fear decreased among the people as time passed. To tackle this situation there should be a well-coordinated and planned system to care of public mental conditions such as tele medicine, public reach towards health facility and resources should be improved and strengthened, people such as old, kids, immigrants & females should be given special attention, & the detection, monitoring of the epidemic, management system should be implemented to reduce the mental distress and fear among the people.

Rogers, Chesney (29) have conducted a systemic search and found that in COVID-19 patients admitted who are admitted in ICU 65% (26/48 patients) of them had confusion and anxiety was present in 69% (40/58 patients) of the patients. but altered conciseness was also observed in 21% (17/82 patients) of patients in another investigation although they died later. 2 cases of patient with affected brain functioning due to hypoxia and 1 case of inflammation of brain i.e. encephalitis was observed. There was improper executive functioning in 33% (15/45 patients) after discharge in a different study was seen. Additionally, help of data from acute ill patients of coronavirus infections (SARS, SARS-2 MERS viruses) were also taken and it was observed that out of 129 case depression was in 42 patients, sleep disorder in 54, anxiety in 46 & memory impairment was seen in 44.

Sensoy, Gunes (30) in their finding 91 individuals were taken who had proof of SARS-CoV-2 infection, & using a questionnaire the depression level and anxiety level were determined. It was found that increased level of anxiety around 44% and people with depressed mood were 24%. Hospitalized individuals had more anxiety in comparison to those who were not hospitalized. The symptoms of anxiety is suggested to be linked with hypertension, a comorbid condition in COVID-19 infection.

Every-Palmer, Jenkins (31) evaluated that New Zealand's quick action has halted the community transmission of SARS-CoV-2 but the strict lockdown had negative psychological impacts. In the online survey it was found that 30% had some psychological problems. Anxiety was present in 16 % with mild & high severity. 39% had a feeling of not being healthy. Younger individuals with no work, who are alone, not with family, with poor health, their condition was poorer. 2% individuals attempted suicide, 2% made plans for suicide whereas 6% individuals had idea of suicide. But 62% of the people were enjoying work from, spending time with family. Therefore, there is a presence of significant psychological distress among the people.

5.Literature Evaluation:

COVID-19:

COVID-19 or novel coronavirus disease is a viral disease caused by Severe-acute-respiratory-syndrome virus 2, belonging to the same group of coronaviruses from which Severe acute respiratory syndrome virus (SARS/SARS-CoV) and Middle east respiratory syndrome virus (MERS) originated. It first appeared in China's metropolitan city of Wuhan in the month of December, 2019.

But it is different from them in many aspects such as strength of infection, fatality and spread. Currently no vaccines are available but the efforts are being done at rapid pace to discover one. But to tackle this problem currently repurposing is being done of already existing antiviral (favipiravir) and other drugs such as antimalarials (chloroquine/hydroxychloroquine) to reach a solution quickly. The drugs were divided in different categories depending upon their target such as (a) target the replication cycle of the virus or (b) can affect the immune system (enhances immune response against the virus or increases the inflammatory response against the virus). (7)

SARS-CoV-2 is able to transmit from one human to another human by air droplets from coughing, sneezing, or by coming in contact with a contaminated surface. The main symptoms associated with it are headache, dry cough, pharyngitis, difficulty in breathing, affected gastrointestinal system & feeling of tiredness. (6)

Older people are more prone to acquiring this disease, the reason is suggested to be immunosenescence i.e. decline in immunity due to aging & inflammation that starts to appear as the person age i.e. inflammaging. (3) Children initially show symptoms related to affected gastrointestinal, also in newborns critical complication can occur if mother is infected, the amount of lactate dehydrogenase

and neutrophils is increased but the level of T-cells (CD8+/CD4+) are decreased.(5) The best method to investigate and detect the disease is by amplifying the genetic material (DNA/RNA) which can be done by techniques like RT-PCR which has currently set the benchmark for diagnosis & ELISA

COMORBIDITIES ASSOCIATED WITH COVID-19:

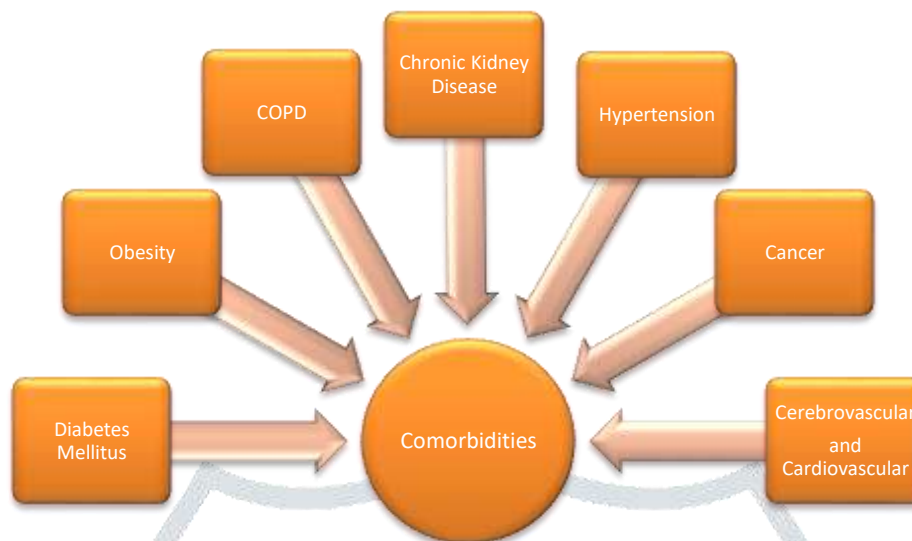


Fig: - Depicts comorbidities linked with SARS-CoV-2.

People with cancer is at a greater risk of being infected by COVID-19, & progress of the infection is more severe in them. Also, the extent of severity of infection depends on the type of therapy person is receiving such as radiotherapy, chemotherapy or combinations of therapy etc., the type of malignancy and other comorbidities that are coexisting such as hypertension, diabetes etc. Findings revealed that cancer patients are at a great danger in COVID-19 because the health of the heart gets compromised & during therapy if the cancer patient is also taking cardiotoxic substance then the condition may worsen. (11) In case of 176 geriatric obese individuals they were found to be at grave danger from SARS-CoV-2 infection because they are mostly at risk of and commonly have hypertension (72.2%) & diabetes mellitus (40.9%) which are the common comorbid condition usually found in COVID-19 disease. But in the critically sick patients' deficiency of vitamin-D was observed and the prevalence of deficiency was found in 94.2%. (10) An if we consider all age group then among 1016 individuals diabetes mellitus was with 35% people after that hypertension which was present in 16.6% of the individuals. Then COPD was present in 16.6% of the people and lastly there were 7.8% individuals with severe heart diseases. The danger was also higher in case of the patients with chronic kidney disease, COPD and those with progressive damage to the liver i.e. chronic liver disease. (12) Critical case of novel coronavirus disease can develop in the individuals with progressive damage to liver i.e. chronic liver disease. It is suggested that many factors play a role in causing damage hepatic cells. Patients who underwent liver transplantation are at intermediate risk as compared to individuals with liver cirrhosis who are at higher risk of getting infected by SARS-CoV-2 and the prognosis is also severe. (32) Individuals suffering from chronic kidney disease is at more risk of contracting many infections as well as CVD because of disrupted state of immune system in them. The immunocompromised state makes CKD individuals vulnerable towards other infections. The chances of infection by SARS-CoV-2 virus is 3 times more in individuals having CKD. Death of 15-25% of the CKD individuals happens who are fighting this viral infection and also undergoes hemodialysis (33)

Many incidences of re-infection of novel coronavirus,2019 disease was also noted after several weeks & days & the patient had symptomatic relief. Till now the observed reasons were found to be (a) in case of immunocompromised individuals such as those who underwent organ transplantation & are taking steroids for suppression of immunity. Here, a paradox occurs that immunosuppressant may reduce the intensity of systemic inflammation but may also downregulate the immune system leading to increased chances of infection & reinfection, (8) (b) another cause can be weakening of immunity due to aging i.e. immunosenescence & inflammation that occurs with increasing age i.e. inflamm-aging, (c) or there might be some safe site also called as sanctuary site for the virus in the patient body. (9)

Table 2: Table showing prevalence of different comorbidities linked with COVID-19.

Total number of patients involved	Data sources	Patients of Hypertension. (%)	Patients of diabetes mellitus (%)	Patients of Cardiovascular disease. (%)	Other diseases. (%)
18	YOUNG, ONG (34)	22.22	5.55		5.5(Hyperlipidemia)
138	Wang, Hu (35)	31.2	10.1	14.5	7.2(Malignancy)
1591	GRASSELLI, ZANGRILLO (36)	49	17	23	8(Malignancy), hypercholesterolemia (18)
1096	GUAN, LIANG (37)	15.8	9.24	11.7	Malignancy (1.5)
41	CHEN, ZHOU (38)	15	20	15	NR

Implications in CVD patients:

In case people diagnosed with COVID-19 it was observed that the viral infection increases the intensity of cardiovascular disease may be due to the systemic inflammation that it causes. It was found that the virus can itself cause cardiovascular disease or aggravate the underlying cardiovascular illness. (16) Infection by SARS-CoV-2 virus causes cardiac arrhythmia, damage to myocardium leading to myocarditis, thrombosis in veins, as well as several conditions associated with acute coronary syndrome. The drug-disease interactions are also becoming a major problem & patients with underlying cardiovascular disease are worst hit with an increased chance of death. (2)

Using a bioengineered cardiac tissue, it was revealed that the COVID-19 virus movement is directed towards the cardiomyocytes, after the infection there was inflammation of cardiomyocytes i.e. myocarditis, necrosis of the cells was also observed, contraction of the cardiac tissue was impaired & immune cells became active. The result obtained are similar to the tissue obtained from a COVID-19 patient after post-mortem.(13) Also increased level of cardiac troponin T was observed in patients & it is linked to increased chances of mortality, increased occurrences of arrhythmias. In the patients who succumbed to this viral disease increased level of troponin T & N-terminal pro b-type natriuretic peptide (NTproBNP) was observed. Higher level of troponin T can be taken as an indicator that individual is more prone to be infected by the coronavirus-2019. The mechanism by which the novel coronavirus damages the myocardium is not properly understood but several possible mechanisms have been proposed like- body wide inflammation, direct invasion on myocardial cells leading to myocarditis, lack of oxygen supply, amplified cytokine action by T helper cells, collagen accumulation myocardium interstitium of heart i.e. its fibrosis, activation of immune system mediated by interferons & rupturing of deposited plaque. (19)

For entry into the host body, SARS-CoV-2 virus there must be expression of ACE2 enzyme with which it integrates using a protein present on its body called SPIKE and also expression of “endosomal cysteine proteases” are required. ACE-2 receptors are present on heart tissue, renal tissue, gastrointestinal tissues, pulmonary tissues and also in brain therefore they are at prime risk of being affected and giving rise to underlying illness or inducing diseases. It is to be considered that ACE-2 enzyme is an important enzyme of renin-angiotensin-aldosterone system, and hypertension or cardiovascular patients who are being treated using RAAS blocker & statins may be at higher risk of infection because the amount of ACE-2 enzyme gets alleviated and chances of infection will increase. But it has been observed that use of ACE inhibitors is found to be beneficial in combination with the angiotensin receptor blocker in individual suffering from ARDS. (17)

COVID-19 & it's psychological effect:

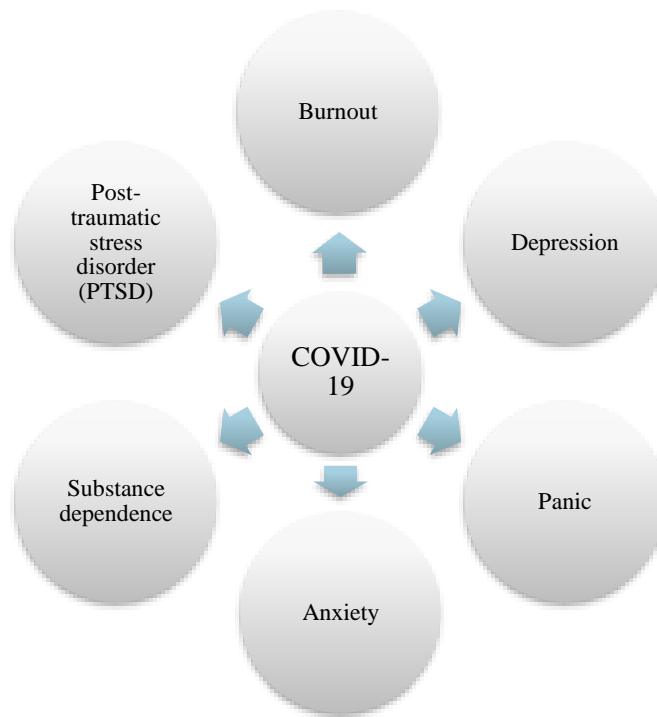


Fig: Psychological effect on people, as well as on affected people during COVID-19.

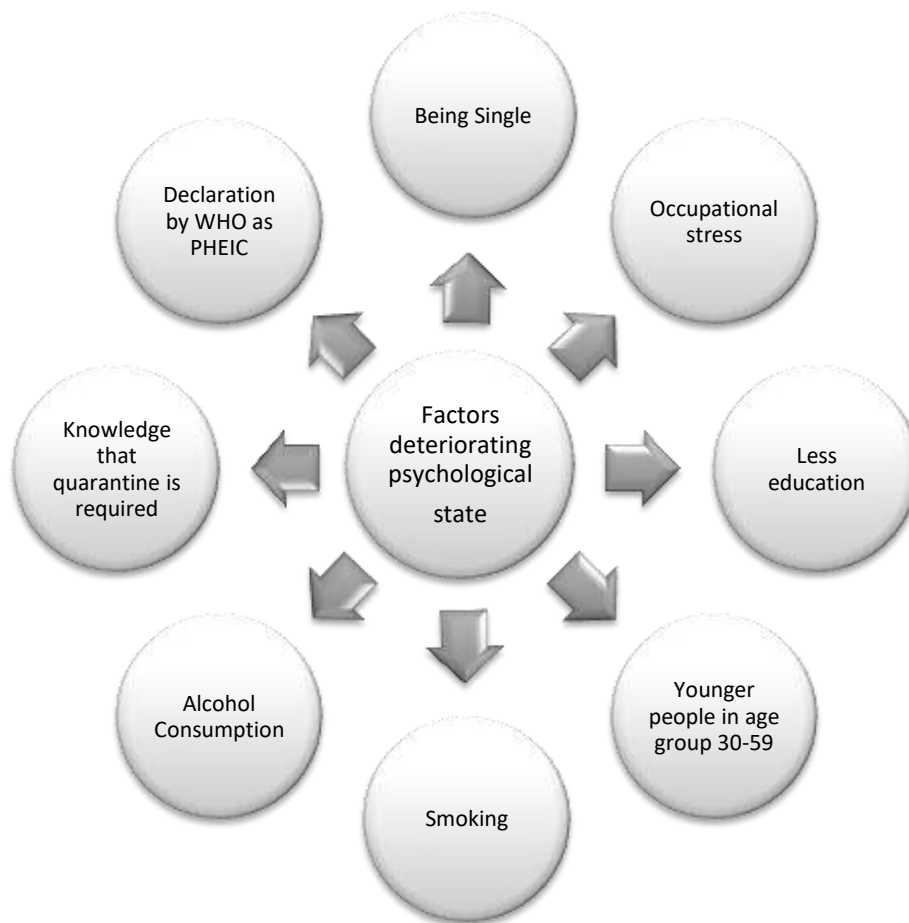


Fig: Depicted factors that worsen the psychological disorder during the COVID-19.

Table 3: Table showing different psychological distress found in people during COVID-19.

<u>Source</u>	<u>Sample Size</u>	<u>Psychological Effect</u>	<u>Country</u>
Qiu, Shen (28)	52730	35% Psychological distress (More distress in male than female, in people of age group 18-30 highest in case of migrants.)	China, Hong Kong, Macau and Taiwan
Sensoy, Gunes (30)	91	24% with depression, 44% with anxiety & hypertension in 27%	Turkey
Rahman, Hoque (24)	587	245 people with comorbidities including psychological distress	Australia
Peng, Mo (27)	2237	6.21% depression 6.46% depression 7.44% depression 3.7% depression	Shenzhen, China Nanjing, China Vietnamese outpatient Chongqing, China
Wang, Pan (42)	1210	Psychological impact on 54% Sever anxiety in 28.8% Severe depressive symptoms 16.5% Severe stress level 8.1%	China
Li, Yang (43)	1563	50.7% with depressive symptoms 44.7% anxiety 36.1% sleep disturbance	China
Every-Palmer, Jenkins (31)	N. R	30% had some psychological problems. Anxiety was present in 16 %. 39% had a feeling of not being healthy. 2% individuals attempted suicide. 2% made plans for suicide 6% individuals had idea of suicide.	New Zealand
Rogers, Chesney (29)	58 40 82 45	Agitation in =69% Delirium =65% Altered consciousness =21% Dysexecutive syndrome =33%	France

Due to COVID-19 there is rise in negative emotion that is affecting the mental health of the general population. There's a rise in depression, anxiety, fear, mental exhaustion and hypertension. There is a need to decrease the negative emotions & improve the mental condition of people such as migrants, healthcare workers, & also the general population. (23) Psychological disturbance was found more in case of smoker, alcohol consumers, females, & people who are already affected by a psychological disease. Panic was observed more in case of consumers of alcohol consumers, in people whose job status changed because they have to meet their financial needs, 30-59 age group because they are more aware and consume more information & people who look after suspected and confirmed patients of novel COVID-19 disease. (24)

Knowledge that to check the viral spread quarantine is essential, virus can also spread from one person to another & declaration by WHO that it is a public health emergency of international concern also contributed to panic. (28)

People with less education, without any partner are also found to have more psychological distress. (24)

Due to panic, fear & misinformation of unpredictable future many unusual behaviors were observed such as over stocking of emergency supplies. Paranoia & delusions were also seen. Due to increasing stress, anxiety as well as the misinformation's there is increase in hatred toward people of different ethnicity and different culture. (25)

In people who are demented have higher rate of delirium & 98% of the people with dementia develop neuropsychiatric problem. Mismanagement of these conditions can worsen the progress of the COVID-19. (26) Available data are less only 3 cases has been reported where psychological problem occurred because of lack of oxygen supply to brain or inflammation of brain i.e. encephalitis. It confirms the report of coronavirus invasion on the CNS leading to inflammation of brain and spinal cord (encephalomyelitis). (31)

COVID-19 & Myocarditis:

Table 4: It shows the no. of hospitalized individual infected with COVID-19 & then diagnosed to be with myocardial injury.

Source	No. of Individuals	Data indicating myocarditis	With Myocarditis/Suspected Myocarditis
Ruan, Yang (39)	68 fatal case	Myocardial damage 7% Myocardial damage & respiratory failure present in 33%	Possibility of myocarditis
Wang, Hu (35)	36 ICU patients	Elevated level of Hs-cTI (5.6-26.4) & CK-MB (12-35)	Suspected
Guzik, Mohiddin (40)	120 individuals	Elevated level of NT-proBNP (27.5% case) & cTnI (in 10% deceased)	Suspected
Ma, Liu (41)	84 patients	Abnormal echocardiogram & cardiac enzyme levels. (15.48%)	4.8% with myocarditis
Nishiga, Wang (2)	41 patients	Elevated level of Hs-cTI (12.19%)	Myocardial Injury present
Nishiga, Wang (2)	191	Acute cardiac injury (17%)	Suspected
Nishiga, Wang (2)	416	Cardiac injury (20%)	Suspected

Inflammation of the heart muscles i.e. myocarditis/cardiomyopathy is cause of many comorbid conditions associated with SARS-CoV-2 virus, & it is also a complication that occurs with coronavirus 2019 disease. Generally the symptoms that occurs with myocarditis is increase in heart rate, faster rate of breathing, difficulty in breathing and oedema, there is also presence of indicators related to heart failure.(15) From an experiment conducted using bioengineered cardiac tissue it was shown that after the COVID-19 infection, indicators showing inflammation of cardiac muscle i.e. myocarditis was observed such as necrosis of the cells was also observed, contraction of the cardiac tissue was also impaired & accumulation of immune cell (macrophages) occurred. And it was confirmed after similar result was obtained from the tissue of a COVID-19 patient after post-mortem. Within the cardiac cells the COVID-19 virus replicates, & it can be concluded that the virus has a role in causing myocarditis. Another cause of myocarditis can be inflammation due to macrophages and fibroblast that occurs during the infection, (13) aggravated action of cytokine caused by T-Cells, increased actions of immune system due to interferons & rupturing of deposited plaque in coronary vessels. There are several indicators that signifies cardiomyopathy and inflammations and which were present in the individuals who had myocarditis and were also positive for SARS-CoV-2 virus some of them are aggravated level of BNPT (N-terminal prohormone of brain natriuretic peptide), cardiac troponin I, & high-sensitivity C-reactive protein. In some case no signs of pulmonary distress instead people reported symptoms related to CVD and later were found positive for the viral infection. (19) The cardiac troponin release may due to direct invasion by the virus leading to myocarditis, low concentration of oxygen in the blood i.e. hypoxemia, systemic inflammation, inflammation of the endothelium, and myocardial infarction. (14) In patients with aggravated levels of cardiac troponins the prognosis of the disease usually severe, therefore it can be used as a marker to indicate the severity of COVID-19 at initial stage. (41)

Up to 75% of the illness related to myocardial injury have been found to be associated with hypertension. Only during the weakened state of heart, the infection which is a minor contributor becomes a major cause of myocardial injury. Hypertension is a significant contributor associated with chronic myocarditis. (21) Myocarditis is more commonly observed in patient with hypertension as compared to non-hypertensive one. Mechanisms that might be involved are (a) immune system activity brought by virus, (b) due antigen segregations some component which remain separated gets released due to stress (22) & (c) cytokines may have an important role in development of myocardial injury.

Therefore, it can be said hypertension might be a factor for causing myocarditis as well in the people with pre-existing myocarditis hypertension can further worsen it & deteriorate heart condition leading to other cardiac diseases.

Conclusion:

Myocarditis can be considered as a serious complication during COVID-19 & can lead to critical case and may also cause death. The psychological distress & panic during this pandemic has caused increase in anxiety, depression and hypertension which contributes in myocarditis & can further worsen it leading to weakening of heart. Weakening of heart makes it more prone to infections. Therefore attention should be given to reduction of fear and psychological distress among the public. & misinformations should be controlled. Amount of cardiac troponin, high-sensitivity C-reactive protein & NT-proBNPs can be measured for the detection of abnormalities and injury to the heart. Also ECG records can also be used. Hypertension & other psychological problems should be closely monitored.

References:

1. Kahn JS, McIntosh K. History and recent advances in coronavirus discovery. *The Pediatric infectious disease journal*. 2005;24(11 Suppl):S223-7, discussion S6.
2. Nishiga M, Wang DW, Han Y, Lewis DB, Wu JC. COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives. *Nature reviews Cardiology*. 2020;17(9):543-58.
3. Vellas C, Delobel P, de Souto Barreto P, Izopet J. COVID-19, Virology and Geroscience: A Perspective. *The journal of nutrition, health & aging*. 2020;24(7):685-91.
4. Oliveira BA, Oliveira LC, Sabino EC, Okay TS. SARS-CoV-2 and the COVID-19 disease: a mini review on diagnostic methods. *Revista do Instituto de Medicina Tropical de Sao Paulo*. 2020;62:e44.
5. Zhou MY, Xie XL, Peng YG, Wu MJ, Deng XZ, Wu Y, et al. From SARS to COVID-19: What we have learned about children infected with COVID-19. *International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases*. 2020;96:710-4.
6. Pascarella G, Strumia A, Piliago C, Bruno F, Del Buono R, Costa F, et al. COVID-19 diagnosis and management: a comprehensive review. *Journal of internal medicine*. 2020;288(2):192-206.
7. Tu YF, Chien CS, Yarmishyn AA, Lin YY, Luo YH, Lin YT, et al. A Review of SARS-CoV-2 and the Ongoing Clinical Trials. *International journal of molecular sciences*. 2020;21(7).
8. Wei L, Liu B, Zhao Y, Chen Z. Prolonged shedding of SARS-CoV-2 in an elderly liver transplant patient infected by COVID-19: a case report. *Annals of palliative medicine*. 2020.
9. Lafaie L, Célarier T, Goethals L, Pozzetto B, Grange S, Ojardias E, et al. Recurrence or Relapse of COVID-19 in Older Patients: A Description of Three Cases. *Journal of the American Geriatrics Society*. 2020.
10. Gonçalves TJM, Gonçalves S, Guarnieri A, Risegato RC, Guimarães MP, de Freitas DC, et al. Prevalence of obesity and hypovitaminosis D in elderly with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Clinical nutrition ESPEN*. 2020;40:110-4.
11. Quagliariello V, Bonelli A, Caronna A, Conforti G, Iovine M, Carbone A, et al. SARS-CoV-2 Infection and Cardioncology: From Cardiometabolic Risk Factors to Outcomes in Cancer Patients. *Cancers*. 2020;12(11).
12. Islam MZ, Riaz BK, Islam A, Khanam F, Akhter J, Choudhury R, et al. Risk factors associated with morbidity and mortality outcomes of COVID-19 patients on the 28th day of the disease course: a retrospective cohort study in Bangladesh. *Epidemiology and infection*. 2020;148:e263.
13. Bailey AL, Dmytrenko O, Greenberg L, Bredemeyer AL, Ma P, Liu J, et al. SARS-CoV-2 Infects Human Engineered Heart Tissues and Models COVID-19 Myocarditis. *bioRxiv : the preprint server for biology*. 2020.
14. Ozieranski K, Tyminska A, Jonik S, Marcolongo R, Baritussio A, Grabowski M, et al. Clinically suspected myocarditis in the course of SARS-CoV-2 infection: fact or fiction? *Journal of cardiac failure*. 2020.
15. Cuomo G, Menozzi M, Carli F, Digaetano M, Raimondi A, Reggianini L, et al. Acute myocarditis as the main clinical manifestation of SARS-CoV 2 infection. *Infectious disease reports*. 2020;12(2):8609.
16. Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential Effects of Coronaviruses on the Cardiovascular System: A Review. *JAMA cardiology*. 2020;5(7):831-40.
17. South AM, Diz DI, Chappell MC. COVID-19, ACE2, and the cardiovascular consequences. *American journal of physiology Heart and circulatory physiology*. 2020;318(5):H1084-h90.
18. Pechère-Bertschi A, Ponte B, Wuerzner G. [Renin-angiotensin-aldosterone blockers and Covic-19 infection : friends or enemies ?]. *Revue medicale suisse*. 2020;16(693):1003-7.
19. Babapoor-Farrokhran S, Gill D, Walker J, Rasekhi RT, Bozorgnia B, Amanullah A. Myocardial injury and COVID-19: Possible mechanisms. *Life sciences*. 2020;253:117723.
20. Matsumori A, Yamada T, Suzuki H, Matoba Y, Sasayama S. Increased circulating cytokines in patients with myocarditis and cardiomyopathy. *1994;72(6):561-6*.
21. FAHR GE. HYPERTENSION HEART: THE MOST COMMON FORM OF SO-CALLED CHRONIC MYOCARDITIS. *Journal of the American Medical Association*. 1923;80(14):981-4.
22. Frustaci A, Francone M, Petrosillo N, Chimenti C. High prevalence of myocarditis in patients with hypertensive heart disease and cardiac deterioration. *2013;15(3):284-91*.
23. Fofana NK, Latif F, Sarfraz S, Bilal, Bashir MF, Komal B. Fear and agony of the pandemic leading to stress and mental illness: An emerging crisis in the novel coronavirus (COVID-19) outbreak. *Psychiatry research*. 2020;291:113230.
24. Rahman MA, Hoque N, Alif SM, Salehin M, Islam SMS, Banik B, et al. Factors associated with psychological distress, fear and coping strategies during the COVID-19 pandemic in Australia. *Globalization and health*. 2020;16(1):95.
25. Dubey S, Biswas P, Ghosh R, Chatterjee S, Dubey MJ, Chatterjee S, et al. Psychosocial impact of COVID-19. *Diabetes & metabolic syndrome*. 2020;14(5):779-88.
26. Velayudhan L, Aarland D, Ballard C. Psychiatric and neuropsychiatric syndromes and COVID-19. *The lancet Psychiatry*. 2020;7(8):663-4.
27. Peng M, Mo B, Liu Y, Xu M, Song X, Liu L, et al. Prevalence, risk factors and clinical correlates of depression in quarantined

population during the COVID-19 outbreak. *Journal of affective disorders*. 2020;275:119-24.

28. Qiu J, Shen B, Zhao M, Wang Z, Xie B, Xu Y. A nationwide survey of psychological distress among Chinese people in the COVID-19 epidemic: implications and policy recommendations. *General psychiatry*. 2020;33(2):e100213.
29. Rogers JP, Chesney E, Oliver D, Pollak TA, McGuire P, Fusar-Poli P, et al. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic. *The lancet Psychiatry*. 2020;7(7):611-27.
30. Sensoy B, Gunes A, Ari S. Anxiety and depression levels in Covid-19 disease and their relation to hypertension. *Clinical and experimental hypertension (New York, NY : 1993)*. 2020:1-5.
31. Every-Palmer S, Jenkins M, Gendall P, Hoek J, Beaglehole B, Bell C, et al. Psychological distress, anxiety, family violence, suicidality, and wellbeing in New Zealand during the COVID-19 lockdown: A cross-sectional study. *PloS one*. 2020;15(11):e0241658.
32. Cabibbo G, Rizzo GEM, Stornello C, Craxì A. SARS-CoV-2 infection in patients with a normal or abnormal liver. *Journal of viral hepatitis*. 2020.
33. D'Marco L, Puchades MJ, Romero-Parra M, Gimenez-Civera E, Soler MJ, Ortiz A, et al. Coronavirus disease 2019 in chronic kidney disease. *Clinical kidney journal*. 2020;13(3):297-306.
34. Young BE, Ong SWX, Kalimuddin S, Low JG, Tan SY, Loh J, et al. Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore. *Jama*. 2020;323(15):1488-94.
35. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *Jama*. 2020;323(11):1061-9.
36. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *Jama*. 2020;323(16):1574-81.
37. Guan WJ, Liang WH, He JX, Zhong NS. Cardiovascular comorbidity and its impact on patients with COVID-19. *The European respiratory journal*. 2020;55(6).
38. Chen C, Zhou Y, Wang DW. SARS-CoV-2: a potential novel etiology of fulminant myocarditis. *Herz*. 2020;45(3):230-2.
39. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive care medicine*. 2020;46(5):846-8.
40. Guzik TJ, Mohiddin SA, Dimarco A, Patel V, Savvatis K, Marelli-Berg FM, et al. COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. *Cardiovascular research*. 2020;116(10):1666-87.
41. Ma K-L, Liu Z-H, Cao C-F, Liu M-K, Liao J, Zou J-B, et al. COVID-19 Myocarditis and Severity Factors: An Adult Cohort Study. 2020:2020.03.19.20034124.
42. Wang C, Pan R, Wan X, Tan Y, Xu L, Ho CS, et al. Immediate Psychological Responses and Associated Factors during the Initial Stage of the 2019 Coronavirus Disease (COVID-19) Epidemic among the General Population in China. *International journal of environmental research and public health*. 2020;17(5).
43. Li W, Yang Y, Liu ZH, Zhao YJ, Zhang Q, Zhang L, et al. Progression of Mental Health Services during the COVID-19 Outbreak in China. *International journal of biological sciences*. 2020;16(10):1732-8.

