

Coronavirus Disease: Anxiety, Stress, Fear and Heart Health

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SARS-CoV-2, a member of the family of respiratory viruses known as coronaviruses, has turned out to be the most powerful killer of the century [1]. The 1918 influenza (H1N1) pandemic was the most severe pandemic in recent history. Cardiovascular diseases caused an estimated 18 million deaths, globally, in 2017. Even vascular diseases, which have reigned as the number one killer worldwide for over a century, have not caused such a panic [2,3]. Why this panic then, one may ask? It is because, it is new, novel, limited tests are available, and there is currently no cure or robust treatment protocol. As such there are more controversies, confusion, politicization and conspiracy theories. This virus has spread to all the countries, except Antarctica. Infection rate, test positivity and case fatality may vary from country to country, but its fear has shut down half of the world and created unprecedented health and economic crisis [4]. Coronavirus disease (Covid-19) pandemic has brought down the world to its knees and is considered the public health workers' 'nightmare'. According to the Johns Hopkins Covid-19 tracker (coronavirus.jhu.edu), as of this writing, globally, there are over 16 million infected individuals and 645,192 confirmed deaths in the short duration of 6 months. The US, Brazil, India, Russia and South Africa are the top five ranking countries, in terms of number of positive cases recorded. The most advanced nation, the United States of America has the highest number of infected individuals (4 million) and deaths (150,000). This pandemic has brought down the prestige of public health flagship agencies such as the US Center for Disease Control (CDC) and Prevention, US Food and Drug Administration (FDA) and the World Health Organization (WHO). The US administration has withdrawn its membership from the WHO. The absence of a Global Leadership has caused, confusion, created unwanted anxiety, increased the stress levels, and seriously affected the heart health.

Prestigious Mayo Clinic website says, "For many people, anxiety is high as a result of pandemic. This is not bad at all, anxiety and fear are natural protectors of people's lives. These responses trigger flight-or fight response, that motivates people to act in primitive sense—usually to run or fight. However, an unknown or not easily understood danger, can increase people's anxiety". Covid-19 pandemic seems to induce stress, anxiety, fear, sadness, loneliness and depression. According to Harvard Heart Letter dated October 2017, anxiety and heart disease has a complex connection. Chronic anxiety can change the body's stress response, the combination of hormonal and physiological reactions. People with anxiety and stress may have emotional ups and downs that can cause high blood pressure and heart rhythm disturbances. Platelets may become "stickier", activate the coagulation cascade, making the blood more likely to clot, increasing the odds for a heart attack. For many people, the uncertainty surrounding coronavirus is the hardest thing to handle. We just do not know how exactly we will be impacted, or how bad things might get? That makes it all too easy to catastrophize into, overwhelming dread and panic. The Centers for Disease Control and Prevention has a web page, with information on dealing with fear, anxiety and stress brought on by the coronavirus pandemic.

Chronic stress as well as acute stress, can be harmful for the heart health. In a first of a kind study, researchers from Radiology Department of Weil Cornell Medical College, New York, report a link between regional brain activity and subsequent cardiovascular disease, amygdalar activity independently and robustly, predicted cardiovascular disease events [5]. These findings provide novel insights into the mechanism through which emotional stressors, can lead to cardiovascular diseases. We at the University of Minnesota, discovered a

unique phenomenon called, “membrane modulation”, which restores the function of drug-induced refractory (dysfunctional) platelets. This phenomenon is modulated by endogenous catecholamines, and the restoration of platelet function is alpha adrenergic receptor mediated [6-8]. We hypothesized from these observations, that adrenaline indeed could work as a ‘double edged sword’ when it comes to modulation of platelet function, meaning it could restore the function of refractory platelets and arrest bleeding, or in situations of extreme emotional trauma lead to acute vascular events, such as heart attack or stroke.

Having said that, we need to provide a couple of scenarios, to make this latter point clear. Case in point is the excess cardiovascular deaths reported during an unprecedented earthquake in Los Angeles (1994). Researchers from the Heart Institute, Los Angeles, concluded their findings in NEJM (1995), “The Northridge earthquake was a significant trigger of sudden death due to cardiac causes, independently of physical exertion. This finding along with the unusually low incidence of such deaths in the week after the earthquake, suggests, that emotional stress may precipitate cardiac events in people, who are predisposed to such events [9]”. On January 18, 1991 during the Gulf war, the day of the first strike (Scud Missiles from Iraq) on Israeli cities, a 58% increment in total mortality, a 77% excess in women and 41% excess in men occurred. This excess mortality occurred largely in the targeted Tel Aviv-central coastal and Haifa regions from cardiovascular causes and mainly out of hospital, significantly more in women than men (*JAMA* 1995;273 (15):1208-1210. In the next example we describe, it is the men who had excess events, suggesting the effect of stressor is gender neutral. This stress related “trigger” of acute events are not just limited to such calamities, it could occur at other situations, where emotional outbursts occur, whether the stressor is acute or chronic.

According to an article in the European Heart Journal, “The 18th FIFA World Cup 2006 in Germany enthused millions of people worldwide, but only little is known about the association of such an event with cardiovascular events [10,11]”. German researchers in an article in NEJM (2018), concluded, that viewing a stressful soccer match more than doubles the risk of an acute cardiovascular event. In view of this excess risk, particularly in men with known coronary heart disease, preventive measures are urgently needed [12]”. Several studies have demonstrated that there is low frequency of heart attacks during the night and a peak frequency onset of nonfatal myocardial infarction (MI) during 7 to 11 A.M. A hypothesis has been proposed that this condition results from ischemia secondary to the formation of platelet aggregates on an atherosclerotic coronary lesion. Corroborating evidence comes from observations, that during this period of the day (early morning), blood catecholamines (epinephrine and norepinephrine) increase and induce activation of circulating platelets. Studies have demonstrated the protective role of aspirin and adrenergic blockers from early morning heart attacks [13-15]. The seriousness of the sudden death is heightened by observations, that approximately a third of patients present with sudden death as their first manifestation [16]. In view of such observations, there are concerted efforts to prevent infarctions before they occur and this new and emerging area of research, investigates inciting events which “trigger” MI, arrhythmias and sudden death.

Researchers from Cardiovascular Center, Division of Cardiology, Tufts Medical Center, Boston summarize their concerns in the July (2020) issue of *JAMA* under the title, “Fear of Coronavirus Disease 2019-An Emerging Cardiac Risk”. “While early fears of widespread death and overwhelmed hospitals, have played an important role in sounding alarm about this pandemic and motivated important social distancing measures, these fears are also causing substantial harm. In this Viewpoint, using cardiac disease as an example, we explore the hazards associated with the pandemic and initial response”. The authors continue, “We argue that clinician’s ability to modulate fear-a sensitive but nonspecific response to threats-will be a major determinant of the magnitude of the pandemic’s effects [17]”. In an earlier editorial, we wrote that coronavirus disease is a public health worker’s ‘nightmare’. Discussing the risks associated with natural disasters, the researchers from Tufts Medical College, report that after Hurricane Katrina, in New Orleans, the rate of acute coronary syndrome occurrence increased by three-fold, the following year and the evidence for increased rates of MI persisted for several years. In view of these observations, they speculate, “If the COVID-19 presents a similar hazard to the entire nation or worldwide, it is likely that we will see 1 million to 2 million additional coronary events, that are directly attributable to the current Covid-19 crisis [17]. The authors conclude, “To minimize the negative outcomes of this pandemic, we must keep patients from dying of fear-both of the pandemic and their fate in the

hands of medical institutions". The purpose of writing this editorial, was not to increase the anxiety, stress and fear in the minds of general public or the readers, but to create general awareness of this condition.

It is an unprecedented frightening time. We are amid a worldwide pandemic from the most pathogenic microbe of unknown origin. Everything about this novel virus is novel and new. For majority of the people, the uncertainty surrounding the coronavirus is the hardest thing to handle. Despite the fact, that acquiring this virus and getting hospitalized is less than 1% and risk of death from this disease is also less than 1%, the very thought of getting infected with this virus, getting isolated from the loved ones, sends chills through the body, because no cure exists at this time for this disease. Having said that, we want to assure the readers, that there are number of write ups on this topic, including web pages by the CDC (www.cdc.gov), NIH (www.nih.gov), WHO (www.who.int) and various other professional organizations (adaa.org). After the FIFA World Championship match 2006 in Germany, for the first time in history of sports, all players had to undergo a medical examination. As far as the viewing spectators at the stadium, as well as on the internet (3.2 million spectators), the organizers realized it was difficult to manage. Whether it is the unexpected earthquake, viewing a highly competitive sports, facing unprecedented Covid-19 pandemic, or just day to day anxiety, stress or fear, the endogenous hormones (stress hormones) are elevated and activate circulating platelets. If the person has preexisting risk for CVDs, he or she would be at an increased risk for ischemia and myocardial infraction. Supporting this observation, studies have shown that aspirin or adrenergic receptor blockers or a combination of both the drugs, offer significant protection under such conditions.

David Ropeik an instructor in risk management at the Harvard School of Public Health, writes in the New York Times (April13, 2020), "There has never been a time in modern history, when every person is seriously worried about the same thing at the same time". He further continues, as with other calamities, it is the bad news that gets the most attention, not the apparent fact that most people, who become infected develop no symptoms or only mild ones and recover fully within few days. With such a worldwide pandemic, fear is gripping not just people who are ill with the coronavirus, but those who need urgent medical care. In the NEJM (2020), Kaiser Permanente reported a drop of nearly 50 percent in heart attack admission in its Northern California hospitals [18]. This is not just a stray observation. Similar findings have been reported in Northern Italy [19]. These observations are hard to explain, when compared to the known facts about the effect of anxiety, stress and fear of heart health. Is it possible that this reduction in rate of admission is due to the fear of patients that they would get this deadly virus infection at the hospitals? Only time will tell us, as to what the real reasons for such decline in rates of admission for MI, during the Covid-19 pandemic and how or what contribution these emotional upheavals played in the severity and fatality of Covid-19. In a short essay on this very important topic, it is not possible to cover all aspects of this unprecedented crisis. We did not make any attempt to discuss anxiety, stress and fear related to job loss, financial constraints, loss of lives of loved ones and the uncertainties of future [20]. Readers are urged to refer to original articles, comprehensive reviews, professional society guidelines on this topic.

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