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Review Article

COVID-19 and Emerging Trends in Diabetes Mellitus

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Abstract

Background: COVID-19 has been plaguing the entire world for more than two years and there has been no sign of eradication of it as new mutant forms constantly and regularly arise from the previous versions in order to evade the immunity gained through natural infection and vaccination.

Summary: Diabetes mellitus was in itself an epidemic before the arrival of COVID-19. Diabetes is considered as the worst comorbidity to have in times of COVID-19 as the complications created by diabetes is huge. In addition, several other diseases grip the body post diabetes such as CVD, renal impairment and so on. Obesity can also be seen among diabetic patients as the blood sugar levels are not maintained properly. All these fall out effects coupled with the deadly impact of COVID-19 makes it difficult to manage such patients clinically.

Conclusion: The connection between COVID-19 and new developments in diabetes necessitates a thorough and interdisciplinary approach due to its complexity. The domains of endocrinology and infectious diseases must continue to work together to better understand the underlying processes and create long-term care plans, treatment plans, and preventative measures for those who suffer from both illnesses.

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INTRODUCTION

Coronavirus disease 2019 or COVID-19 is the still evolving deadly disease, which has taken the whole world at its whims and fancies. The novel coronavirus has since its inception from the Wuhan city of China, the virus spread to almost every part of the world due to its extremely high transmissibility of itself. Novel coronavirus, which is named as such due to its novelty, belongs to the corona viridae family. However, its predecessors like SARS-COV and MERS-COV, which have caused previous similar outbreaks, were largely contained in certain geographical areas of the planet ^[1]. On the contrary, the novel coronavirus knows no geographical boundaries and spreads to every nook and corner of the planet. Even the remotest portion of the inhabited land were affected by the pandemic, which was status after elevating it from public health emergency of international concern. It is one of the most destructive events in the past hundred years of human civilizational history that has caused such widespread destruction as caused by COVID-19^[2-4]. More than 6 million people lost their lives owing to the clinical complications created by COVID-19. Moreover, many people were having preexisting chronic diseases, which was found to be counterproductive, and in fact fatal for such patients as comorbidities in times of COVID-19 is the worst thing to have. Viral mutations can give rise to new variations, such as the virus that causes COVID-19, SARS-CoV-2. Certain mutations may have an impact on the virus's traits, such as how quickly it spreads, how sick people get from it, and how well it reacts to medications or vaccinations. The virus can spread more quickly from person to person if certain changes occur in the spike protein or other parts of the virus. Increased instances and maybe greater rates of community transmission may result from this. The capacity of the virus to be identified by antibodies generated after vaccination may be impacted by mutations in the spike protein, particularly those found in locations targeted by vaccines. In the case that the mutation modifies the spike protein substantially, vaccination efficacy against infection may be compromised. The world was completely taken aback as the pandemic of COVID-19 spread like wildfire [5-6]. The constant

travel through hosts around the world prompted mutations which are hard to negotiate as there is no drug available to deal with the particular strains. Vaccinations have been covering almost all the inhabitants of the world but still the need of the booster dosages can be felt as the waning immunity provided by these drugs are a point of concern. The recent resurgence in cases of infection from various countries is attributed to this phenomenon of mutation. Comorbidity is the chief decision maker in producing either severe or mild clinical outcomes ^[7-8]. Persons with diabetes mellitus are at the forefront and thus are more vulnerable to the infection. In addition, the bidirectional relationship between COVID-19 and diabetes mellitus, which needs to be, studied more. Since the start of the pandemic, there has been a great deal of research and worry about the connection between COVID-19 and diabetes mellitus. People with diabetes, especially those with poorly managed blood sugar, appear to be more susceptible to serious disease from SARS-CoV-2 infection. Individuals with diabetes, particularly those with other comorbidities, are more likely to develop COVID-19 and experience severe consequences and worse outcomes. This entails a greater chance of dying young, being admitted to critical care units (ICUs), and needing mechanical ventilation. Diabetes may increase a person's susceptibility to viral infections such as COVID-19 and hinder their capacity to recover from them by compromising their immune system's ability to fight infections. In this article, a comprehensive overview of diabetes and its clinical manifestation among patients is comprehensively overviewed.

METHODOLOGY

A comprehensive and detailed strategy was followed while researching about the said topic, "covid 19 and emerging trends in diabetes mellitus". The results were chosen from research databases all over the world. Research databases like PubMed, google scholar, MEDLINE, Embase etc. were researched thoroughly with keywords like "Diabetes mellitus" or "COVID-19" or "Bidirectional relation". Articles in languages other than English were filtered out and were not taken into consideration. The editor's note was also filtered out.

ost COVID-19 is important along with
n their non-diabetic counterparts.
ne virus ^[10] .
pharmacological interventions must be
ndent risk factors for COVID-19 ^[12] .



COVID-19 and comorbidities

The huge loss of lives and livelihood around the world has prompted the researchers and medical professionals to seek the cure at the earliest to get rid of the deadly impact unleashed by the virus. Initially all were in surprise and even medical professionals along other governmental agencies were in awe about dealing with the situation. The health care professionals mostly relied upon ad hoc measures to deal with the growing infections ^[13]. The highly contagious nature made it extremely difficult to contain in it one geographical area like its predecessors of SARS and MERS. COVID-19 knew no boundaries and spread rampantly all across the world. The disproportionate impact can be seen among certain sections of population, which bore more brunt than others did. This section of population mainly includes elderly, pregnant women and persons already suffering from various chronic diseases also known as comorbidities. In all these clinical conditions, the patients are undergoing immunosuppressive state and thus these chronic diseases consume the majority of the immune system response. Novel coronavirus is well versed in exploiting these anatomical loopholes and starts to multiply and affect the person in an adverse way in a fast manner. In fact, the majority of the fatalities caused by the COVID-19 pandemic has been from this section of the population ^[14]. Thus, it is essential that trends must be established in order to safeguard these persons from the deadly impact of the novel virus. Prior to the arrival of the COVID-19, various chronic diseases like cardiovascular

diseases, liver and kidney ailments, diabetes mellitus, obesity and so on were plaguing the whole world and the healthcare sector was already under stress in dealing with these anomalies. In addition, after the arrival of the COVID-19, things changed for the worse and along with health care infrastructure, the persons suffering from these chronic diseases started to fall one by one. Novel coronavirus enters through bodily openings like the mouth and nose and starts to penetrate the cells of the thoracic as well as pulmonary region. Viruses are the quasi-living pathogens, which gains entry, in case of novel coronavirus, through Angiotensin Converting Enzyme 2 (ACE 2) receptors, which acts as the gateway for the entry of the virus inside the cell of the host ^[15, 16]. Without a host, the viruses are not able to reproduce and are in dormant state but as soon as the environment-like host in this case humans are available then they thrive on the nutrition of the cell. They multiply in the cell rapidly and then burst open the cell thus triggering organ failure. The presence of the ACE 2 receptors can be found on various vital organ systems like cardiovascular, renal, hepatic, neurological and so on. In addition, immunosuppressive states make the clinical condition for the virus more favorable to grow.

Diabetes mellitus and COVID-19

Diabetes mellitus is an increasing menace prior to the arrival of the COVID-19. Diabetes mellitus is the disease which has an impact on the utilization of glucose in the blood which is the primary energy source for the body and brain. It is important to

supply the glucose to all the cells and muscles so that they can carry it through any repair or formation of new cell activities. There are mainly three types of diabetes mellitus seen among patents. Type 1 (T1DM), Type 2 (T2DM) and gestational diabetes among gravid women which is of temporary nature. T1DM is when the pancreatic cells are being destroyed, especially beta cells which have influence on insulin levels which in turn controls the blood sugar levels. The level of insulin hormone is almost nil or dangerously low. In T2DM there is imbalance of the insulin and it fluctuates thus affecting proper control of the blood glucose levels. Its onset can be predicted from the increasing age and obesity. In 2019, prior to the arrival of the COVID-19, diabetes itself took 4.2 million lives all over the world. More than 463 million are suffering from the diabetes menace. Such is the extent. Not just that, diabetes mellitus becomes the inviter of other chronic diseases like CVD, atherosclerosis, stroke, heart attack, renal failure and so on [17, 18]. These diseases coupled with diabetes can have a huge impact on the quality of life of the patient. Diabetes and COVID-19 have an interesting relationship. Diabetes mellitus is said to be the worst comorbidity to have in times of COVID-19. As diabetes is a chronic lifestyle disease which weakens the body from inside and the immunity to fight the external pathogenic invasions like novel coronavirus becomes weak. Various other organs withstand the worst of the fall out impacts of the diabetes and thus causing multi organ failure among the COVID-19 sufferers. Several studies after having the data pool accumulated over the past one year have suggested that the susceptibility to the COVID-19 infection has also been found to be higher among the diabetic patients than their nondiabetic counterparts ^[19-21]. After analyzing several post mortem reports of fatal cases of COVID-19, a sizable chunk among them were having diabetes mellitus as comorbidity. The need for sophisticated medical care like ICU and mechanical ventilation has been seen on rise among such patients than non-diabetic patients. Taking lessons from previous similar outbreaks of SARS and MERS, the susceptibility of the diabetic patients was also high in those outbreaks. The clinical management of patients becomes difficult as the patient is undergoing treatment for comorbidity and COVID-19 only adds up to the woes of the patient. The clash of the medicines of the two or more treatments can have detrimental impact on the course of the patient's clinical outcome. Infections originating from the bacterial or viruses have an impact that is more dreadful on the diabetic patients. In a Chinese study done in the most affected province due to pandemic, more than 20 percent of COVID-19 had diabetes mellitus. The age group, which are highly susceptible and are diabetic, are 55 to 75 years of age. Acquired diabetes is a lifestyle disease and takes decades to form. However, if it is acquired then it will not leave the person until the end of his life term. In a study in China, patients with diabetes have a higher chance of developing cardiovascular diseases and this is not feasible for the betterment of the patient [22, 23]

There are certain enzymes and chemicals present in the body which are essential for the proper daily functioning of life. These enzymes can fluctuate if any distortion is present in the form of disease. These are called bio indicators as these can indicate the worsening clinical condition of the patient. These bio indicators are monitored regularly, they can be very helpful in preventing undesirable situations. Novel coronavirus triggers inflammatory response throughout the body which is harmful if not controlled in time. Various studies have already indicated that the need o the invasive ventilation has been found on rise among the patients of COVID-19. There was already the crumbling situation in the health care sector not all across the world and the health care infrastructure was capable enough to cater the demand in pre COVID-19 era itself but after the arrival of the COVID-19 the situation worsened and the health care infrastructure collapsed completely. The sophisticated care was facing scarcity and was in limited numbers hence the fatality rate rose in millions all over the world. The percentage of the ICU patients for COVID-19 having diabetes mellitus stood at 22 percent while for non-diabetic patients it stood at 10.1 percent. A holistic study in China among 1099 COVID-19 patients found out that 7.4 percent of the overall population had diabetes and 16.2 percent of them obtained a severe clinical outcome ^[24-26].

Although on the contrary, people with diabetes have a chance of contracting the disease as others and the susceptibility issue is not present there in this case. It is not coming as a surprise as the primary entry point for the virus and its action is the upper thoracic region which is almost the same in the overall population. Internal bodily dynamics came into play in later parts and changed the clinical outcome of the patients. Also, as the condition evolved around the world and people got to know about vulnerability according to the comorbidity they have, people started to follow non-pharmacological interventions (NPI's) such as wearing masks, sanitizing hands at regular intervals, not going in public places etc which would have been effected in susceptibility parity between diabetic and nondiabetic patients. Type 2 diabetes in particular brings on the high risk factor along with it such as cardiovascular diseases, obesity. advanced age and so on. A proper and maintained level of glucose in the blood stream throughout the pandemic period as it is important that the patient does not slip into a hyperglycemic situation. One study done in the United Kingdom's clinical facility treating COVID-19 found that the risk of obtaining fatal clinical outcomes among the diabetic patients having COVID-19 for T1DM IS 2.86-fold and for T2DM is 1.8-fold. All these patients were compared to the patients having no diabetes mellitus either T1DM or T2DM^[27].

As the novelty of the disease was such that the government had no other option at the start of the pandemic to put up lockdowns all over the world and impose movement restrictions for the sake of controlling the pandemic condition as the virus was raging and spreading all over the world at rapid pace ^[28]. Hence, this has resulted in people being confined to their homes and residence and no outing was almost allowed except in case of emergency. This has taken a toll on various stakeholders such as patients with diabetes who need to consult their physician on a regular basis. Moreover, the physical activities were almost completely stopped which are essential in case of diabetes patients as they need to control their blood sugar level by maintaining a healthy lifestyle which includes regular workout ^[29-31].

COVID-19 and diabetes a bidirectional relation

People who get COVID-19 may have changes in their blood sugar levels or, in rare circumstances, develop diabetes. During a COVID-19 infection, some people-especially those without a prior history of diabetes-may have hyperglycemia, or elevated blood sugar. A diagnosis of new-onset diabetes may result from this, and it may last only during the infection time or permanently. Stress-induced hyperglycemia can be brought on by severe disease, infections, or stress brought on by illnesses like COVID-19. This can result in transient rises in blood sugar levels. This could be similar to diabetes, although it might go away as the sickness passes. Delays in glucose metabolism due to COVID-19 can result in reduced glucose tolerance. Blood sugar levels are greater in those with impaired glucose tolerance than in healthy people, but not high enough to be considered diabetic. During a COVID-19 infection, certain people may be more susceptible to new-onset diabetes ^[32]. A family history of diabetes, obesity, advanced age, and pre-existing medical disorders including hypertension or cardiovascular disease are risk factors. Uncertainty surrounds the precise processes via which COVID-19 can cause diabetes to develop. It is thought that the virus may, nonetheless, directly impair pancreatic function, incite an inflammatory response that affects the synthesis and use of insulin, or worsen pre-existing insulin resistance. During a COVID-19 infection, it's critical to keep an eye on blood sugar levels, particularly in people with risk factors or those who are unwell for an extended period of time. Increased blood sugar levels may necessitate further assessment and diagnostic procedures to confirm the beginning of diabetes or other glycemic disorders [33].

It has been found through various post COVID-19 follow up studies that there has been abnormal levels of glucose found in the survivors blood for a long duration of time. This was not the case prior to the COVID-19 infection incidence. Along with major vital organs, pancreas also one and along with others it is also attacked by the novel coronavirus hurting the production of glucose controlling hormone called insulin. Impairment of glucose induced secretory cells and beta cells has been observed in those severely affected COVID-19 survivors which is a grave cause of concern as it can have negative impact on the quality of life of the survivors. In addition, chronic inflammation among the adipose tissues can trigger the T2DM along with resistance to insulin which renders it useless. A statistical analysis of over 35865 individuals with COVID-19 screened for the study. The mean age was recorded as 42.6 years and 45.6 percentage participants were women. The study noted a causal relationship between COVID-19 and diabetes after it [34, 35].

It is high time to think about how to safeguard the health and wellbeing of the diabetic patient. Non-pharmacological interventions might help a lot and reap many benefits as the lifestyle diseases can be feasibly dealt with proper and suitable changes in lifestyle. The diet of the diabetic patients must be properly curated so that healthy conditions can be maintained. Diabetic patients are highly prone to erratic changes in their blood sugar levels and thus affecting several vital organ systems like the renal system over a course of time. Various studies also suggested that patients who are not infected with COVID-19 could exercise at home in whatever capacity they can do. Minor exercises at home, which are convenient to do, can be regularly performed. Any kind of physical activity can improve blood sugar levels especially in T2DM. The more the muscles move the uptake of the glucose by the muscles increases and thus maintaining the healthy blood glucose levels. 150 minutes each week has been suggested but the boundaries should be constantly pushed ^[36, 37].

Prevention rather than cure

Not only the patients of COVID-19 suffer throughout their infection duration and hospital stay, there has been a trend that is confirming the fact that novel coronavirus causing COVID-19 is not going to leave easily after testing negative for it. The long term impacts of the COVID-19 has been seen which is termed as a condition of long COVID-19 among the severely ill survivors of the COVID-19. In fact in some cases the long COVID-19 conditions are found among the population which had not been severely ill due to COVID-19. A wide spectrum of long term implications which includes intermittent loss of taste and smell, fatigue, intermittent fever, cough and cold, cardiovascular and pulmonary function impairment and so on. These impacts are not limited to physiological levels and exceed psychological levels as anxiety and depression has also been recorded by the sufferers. All these effects are affecting the quality of life of ones and hinders their pathway to achieve their full potential. Therefore, it is necessary to avoid such implications at any cost and preventive measures are the most feasible option available at the time. WHO and other health agencies have suggested various nonpharmacological interventions ^[38]. These preventive measures include physical distancing, not going out in crowds, especially people having chronic underlying diseases, wearing masks, getting vaccinated along with booster dose and following COVID-19 appropriate behavior. These measures if followed diligently can not only avoid the pain of isolation and quarantine but also long term physiological and psychological issues can also be avoided.

CONCLUSION

Coronavirus in its novel form is going to stay here in its many mutant forms. Hence, one should be following all the COVID-19 appropriate behaviors. It is seen that the curative measures have no established course of treatment and the patients are still treated on ad hoc basis. In addition, the long term impacts are haunting the survivors which gives another reason to pursue the preventive measures as all these miseries can be avoided. Diabetic patients are one of the most vulnerable sections of the population and therefore their wellbeing must be safeguarded.

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