Review Article

DIABETES MELLITUS: WORST COMORBIDITY TO HAVE IN COVID-19 PANDEMIC

ABSTRACT

BACKGROUND: Diabetic patients have shown the worst clinical manifestation of the COVID-19. They are at higher risk of being infected and producing severe clinical outcomes, challenging to manage. Also, the share of the diabetic patient among case fatalities is large.

SUMMARY: COVID-19 is a disease pandemic that has spread worldwide. All sections and age groups of people worldwide have been affected by the pandemic. Diabetes mellitus is the worst disease to have in OVID-19, as studies have shown some adverse clinical outcome that needs sophisticated medical attention. In lack of resources and overwhelmed infrastructure, the availability of these is tricky.

CONCLUSION: More study is needed about the bidirectional relationship between COVID-19 and diabetes mellitus so that a clearer picture can be emerged out of the fogged situation. Diabetes is already grappling the world, which is suggested by increasing the number of diabetic patient's number worldwide. Especially in COVID-19, it has become a challenge to contain the disease along with all these comorbidities. The immunosuppressive state brought about by various underlying medical conditions like diabetes mellitus is suitable ground for novel coronavirus to propagate itself.

KEYWORDS:- Covid and Diabetic, Comorbidity, Covid-19, Long Term Implication

INTRODUCTION

Coronavirus disease 2019 or COVID-19 is the unprecedented disease outbreak turned pandemic that is wreaking havoc worldwide. Every corner of the world inhabited by human beings has been severely affected by the COVID-19 and they are still bearing the brunt enforced upon by the pandemic. More than a hundred million people have been registered to be infected by COVID-19, which is unprecedented and never happened in the past hundred years of human civilization. As of March 6, 2021, 116,061,296 infection cases have been registered worldwide, and 2,580,050 case fatalities have been reported due to the complications attached to COVID-19(1). No other event was so expansive geographically and in numbers as COVID-19 and termed once in a century event. World Health Organization (WHO) has in initial days, termed COVID-19 as pandemic alleviating its status from public health emergency of international concern (PHEIC)(2). It was the first such announcement from WHO since its inception, highlighting the grave situation. United States of America, India, Brazil, Russian Federation, United Kingdom and France are the most affected countries having more than half of the case infections and case fatalities of the total number(3). The new mutated strain of novel coronavirus reported from Brazil, United Kingdom and South Africa is a severe cause of concern as these are supposedly 70 percent more virulent than the present strain(4). The recent resurgence in cases of infection from various countries is attributed to this phenomenon of mutation. Comorbidity is the chief decider in producing either severe or mild clinical outcomes(5). Persons with diabetes mellitus are at the forefront and thus are more vulnerable to the infection. Also the bidirectional relationship between COVID-19 and diabetes mellitus which needs to be studied more(6). In this article, comprehensive overview of diabetes and its clinical manifestation among patients is comprehensively overviewed.

UNDERLYING CHRONIC ILLNESS IN COVID-19 PANDEMIC

Coronavirus disease 2019 or COVID-19 is a deadly disease outbreak turned pandemic(7), haunting the world for more than a year. The COVID-19 is a novel disease pandemic which has no medical history and which makes it difficult to contain in proper way. Ad hoc measures according to condition on the ground has been employed since the outbreak(8). In addition the extremely uncertain behaviors of the coronavirus makes more difficult to contain and defenestrate it from the human society. No prediction can prove true as the COVID-19 is unpredictable and notorious for showing continuously changing pathophysiology. Very few trends emerging out of COVID-19 have been backed by empirical evidences and scientific validations(9). This includes relation between the clinical manifestation of COVID-19 and underlying chronic medical illnesses. Underlying chronic or acute medical illness or comorbidity influences the patient's clinical outcome during COVID-19 to much extent. Comorbidity is the biggest decider whether COVID-19 infected patient will produce severe clinical outcome or not. Various comorbidities which are prevalent among larger masses has been proving major hindrance in containment measures. In fact majority of the case infections reported and case fatalities due to COVID-19 are from comorbid populations. Also comorbid patients after infected with COVID-19 conditions need sophisticated medical attention like intensive care unit

accommodation along with ventilator and oxygen support system. Various comorbidities such as diabetes mellitus, cardiovascular diseases such as hypertension, renal failure, liver ailments, obesity, chronic obstructive pulmonary disorder (COPD) etc. (10). are found in abundance among various sections of population. These comorbidities are proving hazardous during COVID-19 pandemic. These are diseases which are chronic and are acquired due to lifestyle changes. Improper diet which contains high fat and sugar contents along with lack of adequate physical movement and exercise acts as invitation to these comorbidities. These comorbidities are notorious to stay for long with the affected person and in most cases once acquired, it accompanies the person throughout the lifetime. Various medications are involved into suppressing these diseases. These drugs can interfere with the COVID-19 treatment course and patient can slip into severe conditions. Also during comorbidities the patient is already going through immunosuppressive state. As the mechanism of novel coronavirus depends on the immune system. Weakened immune system works as the fertile ground to propagate the infection. The angiotensin-converting enzyme 2 (ACE 2) receptors are present all over the major organ systems of the human body. These ACE 2 receptors acts as gateway to the novel coronavirus. The coronavirus which enters through nose and mouth attaches with host cells and spreads to different parts of the body. The human beings with the weakened immune system are more vulnerable to the faster propagation of this process and they have less time to seek medical attention. Therefore comorbidities acts as vulnerability and makes this section of population as critically vulnerable to infection of COVID-19. Comorbidities affects the population regardless of the age. Old age persons are vulnerable who have comorbidities but young adults are also vulnerable if they have any comorbidities as the health care infrastructure was on the verge of the collapsing and is not able to handle such huge number of influx of COVID-19 infected patients, it necessary to study more on the comorbidities which affects more. Among these comorbidities, several comorbidities have more adverse impact than others due to their pathophysiology. Diabetes mellitus is among worst comorbidities to have in COVID-19 pandemic(11).

DIABETES MELLITUS

Diabetes mellitus, popularly known as diabetes is a metabolic disorder which contains many medical conditions attached to it. It is basically high blood sugar levels for considerably long time in human body. Diabetes needs compulsory medical intervention as it can lead to several other adverse medical consequences which then becomes difficult to handle if left untreated. Diabetes occurs when pancreas which is the insulin producing organ, does not works properly or cells of the body does not respond properly to the produced insulin. There are three types of diabetes viz. Type 1 diabetes mellitus, Type 2 diabetes mellitus and gestational diabetes. Diabetes mellitus initial symptoms includes constant urge to urinate, increased and frequent appetite, increased thirst. More than 450 million people are infected with diabetes mellitus all over the world. The number is ever increasing and need urgent attention to tackle the menace. Diabetes is considered as lifelong disease which can be managed through medications but no complete treatment is available which can cure the diabetes. It is basically a disease which is caused by lifestyle changes such as sedentary lifestyle, unhealthy diet, lack of physical exercise

and so on. It can also transmitted through hereditary mechanism. Along with insulin injections and other medications, other changes such as inculcation of healthy diet, physical exercise are also suggested so that it can be kept under control. Various dietary restrictions are imposed so that blood sugar levels are maintained at healthy levels.

COVID-19 AND DIABETES MELLITUS

Many researchers and medical professionals are terming the diabetes mellitus as worst disease to have during COVID-19 pandemic and gives solid data to back their claims. It is now widely accepted that Diabetic patients infected with COVID-19 produces adverse clinical symptoms more often than any other disease. Diabetic patients needs sophisticated medical care like ventilator and oxygen support system. Clinical manifestation of COVID-19 among such patient is highly complicated to manage as various drugs interferes with each other. Diabetes is a chronic medical condition which prolong in the body for very longtime. It also weakens the immune system which acts as gateway to the novel coronavirus. Various studies and observations have now established that diabetic patients infected with COVID-19 takes longer time to respond to treatment and to recover from COVID-19(12). Also medical attention is required at very early stage of the infection so that necessary steps can be taken in order to treat the patient. There is observed increase of 5 times in need of ventilator support system in case of diabetic retinopathy. Retinopathy, which is the damaging of the blood vessels near the eyes is the phenomenon overserved in Type 1 as well as Type 2 diabetes. The damaging of blood vessels to other parts of the body can create huge medical complications during COVID-19 infection. The underlying medical condition or illness which makes the immune system frail makes the diabetes more difficult to manage clinically during COVID-19 infection. When the blood sugar levels are at unmanageable levels it can damage the immune system response innately present in the human body. The increased level of sugar in blood makes the blood viscous and reduce the fluidity. It can prove extremely harmful as blood is the connective tissue which provides the oxygen and other essential nutrients to various parts of the body. Also antibodies and natural substances used by the body to defend against any external pathogenic invasion is also not supplied adequately resulting in frail innate immune system response. It also delays the healing process carried out by the body mechanism. Already the unmanaged blood sugar levels can act as invitation to the COVID-19 infection as it weakens the immune system. Persons with proper blood sugar levels have to be extra cautious as small changes in their blood sugar levels can increase the risk of contracting the infection. Various studies already established that diabetes is the immunosuppressive medical condition which can invite variety of other infection(13). Also diabetes does not occur alone as it is found commonly among obese patients. It also invites cardiovascular ailments such as hypertension, respiratory decline and chronic lung diseases which can complicate things further. The most feared condition that is invited by the diabetic patient infected with COVID-19 is COVID-19 pneumonia. COVID-19 pneumonia is a critical stage from which very few patients had successfully returned from. It needs sophisticated medical intervention such as oxygen support system and ventilators. Also the chance of developing severe and fatal clinical outcome increase by manifolds. Major part of case fatalities

caused due to COVID-19 infection is associated with the COVID-19 induced pneumonia. Both the types are equally susceptible to the infection and are quite difficult to manage. Data from study conducted in New York hospital suggested that almost 34 percent among 5700 patients admitted for COVID-19 infection were suffering from diabetes, hypertension as well as obesity. These conditions extremely interconnected as one invites the other making things more complicated. General medical observation has suggested abundance of type 2 diabetes mellitus patients over type 1, but no empirical evidence backing is available for the same hence cannot be considered as generalized fact(14). Cytokine dysregulation can be resulted from immune dysfunction which is generally associated to Hyperglycemic condition observed in diabetes mellitus. Old aged patients are most vulnerable if they are having diabetes mellitus to COVID-19 infection and chances of producing fatal clinical outcome is increased multiple times. Diabetic patients have overrepresentation among case fatalities reported due to COVID-19 complications. In an Italian study conducted on case fatalities, 35 percent of case fatalities were found to have link with diabetes mellitus condition which is a grave cause of concern.

LONG TERM IMPLICATIONS OF COVID-19 IN DIABETIC PATIENTS

So far COVID-19 was feared for its clinical manifestation and everybody was worried and concern about how disease will pan out during infection period. But as the time passes, many facets of the disease were uncovered. It is now widely known that COVID-19 is not only adversely affects during infection and incubation period but it affects the concerned individual post recovery too(15). Many cases were reporting certain symptoms that were persisting even after successful completion of the COVID-19 treatment. Although they were tested negative, the disease was haunting even after recovery. Many patients from all over the world reported persistence of symptoms such as extreme fatigue, intermittent loss of taste and smell, occasional and recurring cough, cold and fever, brain fogging which is the condition where person affected is confused while making and decisions, muscle pain, reduction in physical capacity as compared to pre infection condition(16). Also some medical conditions found to have taking place post COVID-19 infection which are not good for the healthy functioning of the human body. Many tests were done to assess the long term implication of the COVID-19 and some serious conditions were seen which were not present prior to infection. These conditions include weakening of the heart muscles reduced blood flow towards heart, wreaking of alveolar tissue resulting in difficulty in diffusion of oxygen, renal damage. Blood vessels were damage due to unregulated flow of blood and so on. This created another cause of worry for the patients affected as they have to seek more medical attention of rehabilitative nature. Diabetic patients are at the forefront of all these long term implications. They not only takes longer time to recover but survivors are destined to experience these persistence of symptoms. Many diabetic patients who recovered from the COVID-19 infection successfully are finding it difficult to control the fluctuating insulin levels. The blood sugar levels are fluctuating between considerably low to unmanageably high levels which is the last thing anyone would wanted. This can pose a serious problem in the long term as diabetic patients are already difficult to manage medically. Steroids are the popular choice of drugs among medical fraternity to counter the severe and critical

COVID-19 cases. Dexamethasone is one of the drugs considered as promising in terms of treating the COVID-19 patients of severe symptoms. But administration of steroids like dexamethasone among dietetic patients can induce inflammatory response which is bad for the patient. Insulin requirements shoots up among such patients. Glucose levels takes considerable amount of time to stabilize and stay at manageable levels post COVID-19 infection. Constant monitoring of the diabetic patient is the key to successfully rehabilitate the patient after COVID-19. More serious cause of concern unearthed after certain observation which reported in reputed endocrinology journal. It suggested that there is a bidirectional relationship among COVID-19 and diabetes mellitus(17). A bidirectional relationship is the relationship in which one quantity influences or induce another and vice versa. In bidirectional relationship, the chance of getting other condition by first and vice versa increases. As many as 14.4 percent of the severe COVID-19 patients admitted to hospitals were found to have newly diagnosed diabetes mellitus. Novel coronavirus is supposedly facilitating the damage of the insulin producing cells which can trigger this bidirectional phenomenon.

PREVENTIVE MEASURES FOR DIABETIC PATIENTS IN COVID-19 PANDEMIC

The unfolding of coronavirus disease 2019 was never expected by anyone and is of unprecedented nature. It's one of the deadliest event in the past hundred years of human civilization which has global coverage along with millions of case fatalities and infection cases. As no past medical records or history has been registered for the SARS-COV-2, there is no established treatment protocol and ad hoc measures are being implemented in order to contain the viral spread of the pandemic. There are two parts in any disease mitigation program. First id curative part which is employed after the disease engulfs the persons or entities. Second is preventive part which mainly focus upon various measures to prevent the disease from happening at first place. The severe symptoms shown in certain age groups and the panning of disease over long term through persistence of symptoms have necessitated the preventive measure need over curative measure. Especially patient with diabetes mellitus must be extra cautions as the clinical manifestation of COVID-19 is of critical nature in most of the diabetic patients and diabetic patients needs more sophisticated medical attention which are scarce In nature. In order to utilize the currently overwhelmed health care infrastructure judiciously, one has to focus on the preventive measure more as it well somewhat lessen the burden on the health acre infrastructure which was almost on the verge of collapse. Further the bidirectional relationship between COVID-19 and diabetes is serious cause of concern. As one induce another, both are serious illnesses. Therefore to avoid all these consequences preventive measures must be popularized and focus upon so that these can be adopted and acquired by the concerned section of society. These includes non-pharmacological interventions like wearing of face masks, sanitizing hands regularly, avoiding going out when unnecessary, wearing of personal and protective equipment's (PPE) kits, maintain physical distancing while around other people(18). These preventive measures are already tried and tested and can be easily directly implemented for the better purpose. In various previous outbreaks of severe acute respiratory syndrome (SARS), Middle Eastern respiratory syndrome (MERS), Ebola and various other contagious

diseases, efficacy of these measures have been tested and these measures have found to be extremely beneficial in the containment and mitigation of the disease. Diabetic patients needs to extra cautious and extra vigilant about their exposure to others as any person can be a potential carrier. Regular consultations with doctors can be virtually done through telemedicine which can be very effective way with minimal risk to stay in touch with medical professionals. Various monitoring devices are now portable and can be kept at home for handy use. These incudes glucose monitoring strips, oxygen level monitoring oximeters. As these devices does not require any sophisticated approach to use, the trip to doctor can be avoided and results can be conveyed after results to doctor virtually. Elderly having diabetic condition must be kept least contacted physically by the outsiders so that they do not get infected. Virtually they can connect with anyone to stay connected and prevent themselves from being lonely(19). Studies on herbal treatment and ayurvedic remedies for controlling diabetes were reported by Ambad et. al. (20) and Deshpande et. al. (21). Studies on risk factors and associated complications of diabetes are available(22-25). Henry and Singh studied the pattern of cutaneous manifestations in patients with diabetes mellitus(26). Effects of Covid on patients with diabetes and their treatment were reflected in studies of Afaque (27), Agrawal et. al. (28) and Subhadarsanee et. al.(29). Gaps in current healthcare context of diabetes in this region are evident(30-35).

CONCLUSION

Diabetes is already grappling the world which is suggested by increasing the diabetic patient's number all over the world. Especially in COVID-19 it has become a challenge to contain the disease along all these comorbidities. The immunosuppressive state brought about by various underlying medical conditions like diabetes mellitus is proving to be suitable ground for novel coronavirus to propagate itself. Therefore utmost care should be taken in order to prevent the disease from happening at first place, as its long term implications are also equally adverse. The bidirectional relationship between COVID-19 and diabetes mellitus is a subject for study but if established then one needs to be extra cautious. Preventive measures are best suited for pandemic like COVID-19 as these are not contained by only curative measure. Combination of both can lead us to solving the puzzle of COVID-19 spread and defenestrating it from our life.

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