Review Article

Effect Of COVID-19 infection in the Patients with Diabetes Mellitus

ABSTRACT: -

Background: - Coronavirus is pandemic virus infection which has recently affected the globe, and as a result, In patients with non-communicable diseases, the associated morbidity and death are substantially greater. One of the most common non-communicable diseases linked to worsening clinical conditions in Corona virus patients is diabetes mellitus (DM).

Covid-19 is a zoonotic illness that was firstly found in Wuhan city of China, and is now recognized a zoonotic disease that spreads from moist animals to people in 2019. The disease has a low fatality rate and only affects the most seriously ill patients. Approximately 80% of the cases involve patients who are seriously to moderately ill. Since the outbreak of the disease, the number of people who have died has continuously increased.

Summary: - The aim for this study is to determine the receptors involved in diabetes and the pathogenetic relationship btw. COVID-19 and diabetes. Both diseases are characterized by inflammation and the release of inflammatory markers. The roles of angiotensin-converting enzyme molecule and dipeptidyl peptidase in COVID-19 and diabetes have been investigated. The effects of glucocorticoids and catecholamines, invasion of pancreatic islet cells, medications used to treat COVID-19, and hence the lockdown policy, may have a deleterious impact on diabetes patients' glucose control. The results of COVID-19 research involving diabetic and non-diabetic patients were also examined. Various medication trials, such as the dapagliflozin and linagliptin trials are still being conducted to see if certain medications are suitable for diabetic people with COVID-19.

Conclusion: -

Diabetes is a risk factor for COVID-19 patients, according to the data, leading to their severity and mortality. This article also contains guidelines and recommendations that may be useful in the management and Avoidance of diabetic individuals who are infected with COVID-19.

Key Words

- Diabetes Mellitus

- Insulin
- Pancreas
- COVID-19
- SARS-CoV2

INTRODUCTION:-

In 2019, (DM) is well-established risk factor for poor clinical outcomes in the individuals having Corona virus Disease.The interaction between these two things, on the other hand, appears to be bidirectional. The present COVID-19 outbreak has had a significant influence on diabetic blood glucose control. The outcomes of these impacts can be divided into two categories: Direct consequences (those that are connected to the viral infection directly) and indirect effects (those that are not related to the viral infection directly) (those related to the impact of the pandemic on the management of blood glucose or the use of proposed treatments for the infection that also affect glucose metabolism). As a result of the COVID-19 infection, patients' metabolisms have altered dramatically, with considerable blood glucose rises. It's assumed to be caused by an increase in Increased insulin resistance and hyperglycemia were caused by cytokines and inflammatory mediators. Additionally, by focusing on ACE2 receptors in pancreatic islets, Corona virus has been associated to the development of acute diabetes mellitus in some individuals, resulting in pancreatic damage. (1).

COVID-19 has been treated using a variety of drugs that have been repurposed. Glucocorticoids, affect the glucose level of blood significantly.when glucocorticoids were used it has been seen that it caused a fewer number of deaths in people who were severely infected with corona virus disease. It can be understood that use of glucocorticoid's alters the homeostasis of glucose by increasing gluconeogenesis while simultaneously increasing insulin resistance in diverse organs. (2)

Several studies have described the COVID-19 pandemic's indirect effects on various communities during the lockdown. Some studies claim that glycemic control has improved, while others claim that there has been no meaningful change or control of glycemia in this population has deteriorated. The current literatures on corona virus and DM will be reviewed in this paper. Corona virus is an infection causing illness caused by a virus i.e.SARS CoV2. It's a ss-RNA virus with crown-like

surface projections under electron microscopy, hence the name. MERS and SARS are both members of the Coronaviridae family and the Coronavirinae subfamily, and they share clinical features with COVID-19 (1). They share biochemical and structural similarities. Myalgia cough, respiratory issues, fever, stomach pain, and a variety of additional symptoms are among the symptoms. (3).

Background:-

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Diabetes mellitus (DM) is a disease and a global health problem that has become much more severe in the previous two decades (1). Diabetes affected 30 million individuals in 1985; By 2010, the no. has rised to 283 million people. Acc. to International Diabetes Federation current global forecast, there will be 495 million diabetics in 2023. By 2045, diabetes is estimated to afflict 700 million people worldwide, Diabetes is connected to end stage of kidney disease, blindness at adult onset, and lower extremity's non-traumatic amputations (4). Increased disability and, in the worst-case situation, life-threatening complications ensue from diabetic complications (5).

The 1st pneumonia case with an unknown cause was discovered in China in early December 2019. A new encapsulated RNA beta-coronavirus has been identified as the pathogen (6) . SARS-CoV-2 pneumonia was quickly identified as an unique illness that quickly spread throughout Wuhan and other Chinese regions, and is now spreading around the world (7). The WHO has called the SARS CoV-2 induced sickness coronavirus disease 2019. The number of sufferers had risen substantially by April 27th, 2020 (9 p.m.) - 2,858,939 people had been infected with the virus, with 203,935 people dying. Symptoms of COVID include dry cough, dyspnea, lymphopenia and exhaustion (8).Clinical signs of SARS-CoV and MERS are strikingly similar (9), (10). It is transmitted mostly through droplets or direct contact, faeces, and respiratory tract infection (11), (12). Due to the disease's novelty, the elements that influence the severity of status and mortality remain unclear. Due to the disease's novelty, the elements that influence the severity of status and mortality remain unclear. The intensity of the symptoms is considered to be influenced by patients with underlying health conditions, persons over 60, and delayed hospitalisation. (13)**,** (14)**,** (15)**.** Furthermore, many people have been affected as a result of the reduction in physical activity imposed by most

governments throughout the world, which is particularly essential for diabetics. All of these effects are significant since In diabetic patients, they increase the risk of infections, hospitalisation, amputations, and death (16).

Discussion:-

Diabetes is one of the most common diseases, and it is also one of the leading causes of a host of costly side effects; it may also force young people out of employment. Furthermore, COVID-19 illness is a rare respiratory disease that has spread around the world, affecting almost 3.5 million individuals and killing 201,949 of them. We discovered 28 studies on diabetes and COVID-19 after doing a comprehensive search. The bulk of studies were not specifically focused on diabetes. The majority of the study was carried out in China. Because of differences in diabetes prevalence between populations. It's vital to conduct more study on various groups. COVID-19 patients with diabetes accounted for 14.5 percent of the total. Diabetes was shown to be prevalent in 54.4 percent of MERS patients and 14.6 percent of H1N1 influenza patients in illnesses comparable to COVID-19. It should be highlighted that patients from various trials were included in multiple studies. In all patients, COVID-19 symptoms include sore throat, fever, dry cough, lethargy, and diarrhoea (17).

Type I Diabeties Mellitus(DM) and Corona virus:

Corona virus patients with T1DM range from 0.150 percent to 28.990 percent, Hyperglycaemia(higher glucose level) has been connected to COVID-19-related issues. 47% people with T-1Diabeties Mellitus had increased level of blood glucose, 46% had raised temperature, 39% had dry cough, 33% had vomiting and excess fatigue, 31% suffered from breathlessness , 27% suffered from nausea , 22% had body/headaches, COVID-19's clinical results in T1DM patients were studied in a multicenter monitoring study in the United States. In addition, 15% of people reported chest pain and stomach, cold, and a loss of smell and taste. Obesity(39%) and cardiovascular problems and hypertension(13%) were the most prevalent comorbidities, whereas the most adverse outcome in these Covid 19 and type I diabetic patients was ketoacidosis. The independent influence of diabetes status and type on in-hospital death among English Corona patients was investigated in a large population study, 1.5% of in hospital Corona virus related fatalities occurred in the people suffering from T1DM v/s 31.4% in patients suffering from T2DM. Unadjusted death rates per 100,000 persons for those with T1DM were 138 compared to 27 for those without diabetes during the course of the study's 72 days. In people with T1DM, When sex, age, deprivation, ethnicity, and

geographic location were taken into account, the odds ratio (OR) for Corona virus related death rate in hospitals was 3.51 (95 percent CI = 3.16–3.90).

A population based research looked at links btw risks variables & Corona virus related mortality in T1DM patients. Corona virus related mortality was shown to be closely correlated with older age and male sex. Mortality which was related to Corona virus was found to be considerably greater in people of African and Asian descent.

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Effect of Corona virus on Diabetes:-

The Corona virus exacerbates diabetes mellitus stress by releasing catecholamines and glucocorticoids into the bloodstream. Glycemic regulation has worsened, and glycation end product synthesis in a number of organs has increased, lowering prognosis (18).

Therapies in the form of drug provided to Diabeties Mellitus among COVID-19 patients:-

Non-insulin antidiabetics, both oral and injectable [summarised in Table 1], as well as insulin, are discussed in connection to COVID-19 therapy and results.Table 1. Corona virus and Anti-diabetics adapted from singh etal. (19)

Table 1. Drugs used in Diabeties

Drugs used in Diabeties	**Benefits**	**Results**
Metformin	It is touted as a powerful medicine that can help individuals with type-II	It can be used in peoples with Type-II Diabetes Mellitus until they are

	Diabetes Mellitus with covid-19 infection live longer.	admitted to the hospital or unless it is contraindicated. It's unclear whether the possible mortality advantage applies to inpatient usage or non diabetic corona patients at this instanttime.
Pioglitazone	Inflammatory indicators might be reduced.	In diabetics with covid-19 infection, there is no strong evidence to justify its use. To fully understand its potential usefulness, more research is required.
Sulfonylureas	There's a chance that the severity of the condition may be reduced.	There has been no evidence of a substantial change in the count of ICU beds booking or the severity of illness with its usage in studies.
DPP 4 inhibitors	It's been suggested that DPP4 is connected with SARS-receptor-binding CoV-2's domain. It may also have anti-inflammatory, anti-fibrotic, and immunomodulatory properties. Several studies have recommended that it be used as a COVID-19 repurposed agent.	There was no substantial difference in rates of death, poor prognosis, or ICU hospitalisation in several investigations. Others, on the other hand, found some advantage in the rate of intubation, the severity of the condition, and the rate of release. To fully understand its potential usefulness, more research is required.
SLGT-2 inhibitors	Dapagliflozin has anti-inflammatory characteristics and reduces lactic acidosis, which might help to restore	There has been no evidence of a substantial difference in illness severity or fatality rates in studies.

	acid-base balance in hypoxia.	
GLP-1 receptor agonists	During acute lung damage, there is an improvement in right ventricular function as well as anti-inflammatory benefits.	There is a scarcity of information. According to several research, there is no discernible change a decrease in the number of ICU admissions or fatalities

Metformin

Metformin is used by the T2DM patients who make up the vast Majority who are on oral antibiotics hypoglycemics, either alone or in combination with other medications.The first-line therapy for type 2 diabetes is metformin. Metformin can cause lactic acidosis as a side effect. This is unusual in the absence of other factors that lead to lactic acidosis, however it can happen in people with renal impairment, severe infections, or sepsis. Individuals with COVID19 who are asymptomatic or have minimal symptoms can continue to use metformin. Metformin should be stopped in patients hospitalised with severe COVID19 infection due to the risk of lactic acidosis (20). It's worth noting that COVID-19 patients using Metformin have reported better health results. Metformin is thought to block viral entrance into cells via activating AMP-activated protein kinase (AMPK) and the B–mammalian target of rapamycin (mTOR) signalling pathway.

Inhibitors of the dipeptidyl peptidase 4 (DPP-4) enzyme

In COVID-19 patients, DPP-4 inhibitors are well tolerated and can be used for an extended period of time. They're associated with a lower risk of hypoglycemia. Because DPP-4 may act as a receptor for a variety of corona viruse, DPP-4 inhibitors may prevent COVID 19 acquisition by preventing this binding. This expected benefit, however, has yet to be demonstrated in clinical studies.

Agonists for the binding site for glucagon as peptide 1(GLP-1 agonists)

Agonists for the glucagon-like peptide-1 receptor (GLP-1 agonists) GLP-1 agonists may produce nausea and vomiting in patients, as well as a reduction in water consumption. As a result, GLP-1 agonist medication raises the Water loss and aspiration pneumonia are both risks. In individuals with severe COVID 19, GLP-1 antidepressants should be avoided. If COVID-19 patients are given GLP-1

antidepressants, they should be constantly watched and their hydration intake should be appropriate. GLP-1 antidepressants may have an anti-inflammatory effect and decrease inflammation of the airways in rats with a rhinovirus (RSV) infection and experimental lung injury. To see if GLP-1 antidepressants have an anti-inflammatory effect in COVID-19 patients, more study is needed.

Sulfonylureas

Because sulfonylureas can cause hypoglycemia in individuals with Serious COVID 19 infection and insufficient ingestion through the mouth, it's best to avoid them. Furthermore, using hydroxychloroquine with insulin at the same time may raise the risk of hypoglycemia.

Does the Corona Virus Affect the Pancreas Directly?

Some publications have hypothesised on how quickly control of glycemia in patients with stable diabetes mellitus with Corona virus deteriorates, necessitating the administration of large insulin dosages, and the chances of SARS CoV-2 invasion of pancreas (21).

The observation of enhanced ACE2 levels in beta cells in islets of pancreas, which might lead to increased the number of islet cells damage and lower the value of insulin output, backs up the prior hypothesis.

COVID-19 and glucose metabolism

SARS-CoV-2 replication in human monocytes is aided by increased glucose levels, and glycolysis aids corona virus replication by generating reactive oxygen species in the mitochondria and activating hypoxia-inducible factor-1 (22). Hyperglycemia may thereby enhance viral multiplication. History of Type 1 DM and Type 2 DM or Hyperglycemia in SARS patients were shown to be independent predictors of mortality and morbidity , validating this hypothesis. Furthermore, Comorbid T2DM promoted a dysregulated immunological response in mice infected with MERS-CoV, resulting in severe and widespread lung damage. Diabetic patients are those who have diabetes mellitus have an increased risk of severe SARS-CoV-2 infection than those without the disease. Increased blood glucose levels also suggest a larger need for medications and therapy, as well as a higher chance of mortality. (23), (20).

CONCLUSION:-

Patients with diabetes should be advised that the corona virus might cause blood glucose levels to rise, and they should follow diabetes care recommendations more strictly during the COVID-19 pandemic. They should take their medication (insulin doses) as directed by their doctors, and they should check their blood glucose levels more frequently than in the past. If a patient's blood glucose levels are consistently higher than normal, they should consult a doctor straight once. In light of recent global quarantine efforts, health-care providers should emphasise proper dietary consumption and physical exercise in diabetes patients. Patients with symptoms like fever, dry cough, or having a rapid jump in their blood glucose level should consult their doctor or clinic very once. Patients should also closely follow their doctor's orders and be wary of remarks circulated via other forms of media (including social media) that frequently contradict scientific findings. Standard procedures by following social distance, wearing an N-95 mask, doing hand wash often, and using sanitizer >70 percent alcohol sanitizer) Both health care workers and their family members should follow stringent recommendations to reduce the risk of spreading infection in persons with diabetes.

Because it produces inflammation and changes immune system responses, Corona virus infection has been shown to have a Sevier influence on diabetic mellitus maintenance, making glycemic control exceedingly difficult. Infection with In patients suffering from diabetes mellitus, In patients of diabetes, SARS CoV-2 raises the risk of thrombosis and makes cardiorespiratory failure more likely. All of these mechanisms are now recognised to have a role in diabetics with COVID-19 having a bad prognosis. Tight glycemic management and the preservation from risk factors of cardiovascular system are critical for individuals with DM during the Corona virus pandemic. For patients at high risk of SARS-CoV-2 infection, medications for diabetes and cardiovascular disease should be changed accordingly. Dexamethasone and hydroxychloroquine, two investigational medications, have showed some promise as therapeutic agents (24-30).

Finally, the global pandemic of COVID-19 offers serious health hazards, particularly to those with diabetes. Because current immunizations are not 100 percent effective but can provide protection for a limited period of time, it is suggested that both doses of vaccine be given to lower the risk of infection and mortality from the corona virus. Because the vaccination isn't 100 percent effective, we'll need to take extra measures including social isolation, masking, and self quarantining. The optimum care strategy for diabetic patients, as well as the permanent cure of diabetes mellitus through gene therapy, should be the focus of future research.(31-36)

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