

**Review Article**

**MANAGEMENT OF DIABETES WITH COVID-19: A REVIEW**

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**ABSTRACT**

**Objective:** As of now, the world is struggling with a serious pandemic of disease 2019 Coronavirus (COVID-19), which was emerged from Wuhan in China, originated by the novel coronavirus 2019 (SARS-CoV-2). COVID-19 is a viral illness, which is occurring on a large scale in every nation of the globe. Symptoms of coronavirus mainly include fever, fatigue, cough, headache, pneumonia and in severe condition, there is respiratory distress. The deadly virus alarmed the world to be on high alert as the number of rising cases and the death toll rising as the day passes.

**Methods:** We have searched for articles of preference and interest systematically in sources like Google Scholar, PubMed, and other outlets.

**Results:** Management in the case of diabetes is really necessary to decrease their mortality. Certain management parameters need to be followed to take care of patients suffering from both diseases.

**Conclusion:** In this review, we highlighted the role of different medicines like chloroquine, lopinavir, and hydroxychloroquine for the remedy of this pandemic. We also discussed the chest Computed tomography functions and Real-time polymerase chain reaction for the screening of the outbreak. The center of attention of this review majorly on the care of diabetes throughout the time of the COVID-19 epidemic.

**Keywords:** Coronavirus, Diabetes, Medicines, Chloroquine, RT-PCR

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**INTRODUCTION**

Respiratory disorders are the primary cause of death and morbidity and impact the lives of more than a billion people across the world. Children and young kids are highly vulnerable [1]. Global health is usually enhancing, with lesser persons dying due to infectious diseases and thus surviving long enough in many cases to develop chronic diseases [2]. Chronic respiratory diseases (CRDs) are acknowledged as a crucial source of unintended death in the population globally. CRDs are a disease of the airway and the additional structure of the lungs adds up to a large formation of major illness. Curable long-standing respiratory disease includes asthmatic diseases, respiratory allergic reaction, chronic obstructive pulmonary diseases (COPD), lung disease, and pulmonary fibrosis [3]. Symptoms of this disease are chest illness, cough, and phlegm, shortness of breath [4]. The risk factors for CRDs include smoking, obesity, indoor air pollution, outdoor air pollution, unhealthy diet, lack of exercise, allergens, and biomass fuel combustion in low-middle income countries (LMICs) [5].

In December of 2019, an epidemic origin from COVID-19 takes place in the Hubei Province of Wuhan, China. Up to 22<sup>nd</sup> March 2020, the overall number of 306,506 cases of COVID-19 were turned up in hundreds of nations across the globe. As a beta coronavirus, SARS-CoV-2 expose to danger the global health due to excessive mortality rates [6]. The zoonotic virus is not reviewed to be extremely infectious to living organisms up to the epidemic of a severe acute respiratory syndrome (SARS-CoV) in 2002 and 2003 respectively, in Guangdong province of China, was the coronavirus spread before the times in humans mainly give rise to a mild infection in immune-competent peoples. Ten years later, SARS, a new and another dangerous pathogenic coronavirus, is the Middle East Respiratory Syndrome coronavirus (MERS-CoV) comes out in countries of middle east [7]. COVID-19 is one of the critical viruses that fundamentally select the respiratory system of living [8]. In late 2019, a crowd of persons was divulged to their nearest hospitals with an untimely screening for pneumonia with an unspecified cause. Most of the persons were epidemiologically attached to the seafood and wet animal, vastly marketed in Wuhan [9, 10].

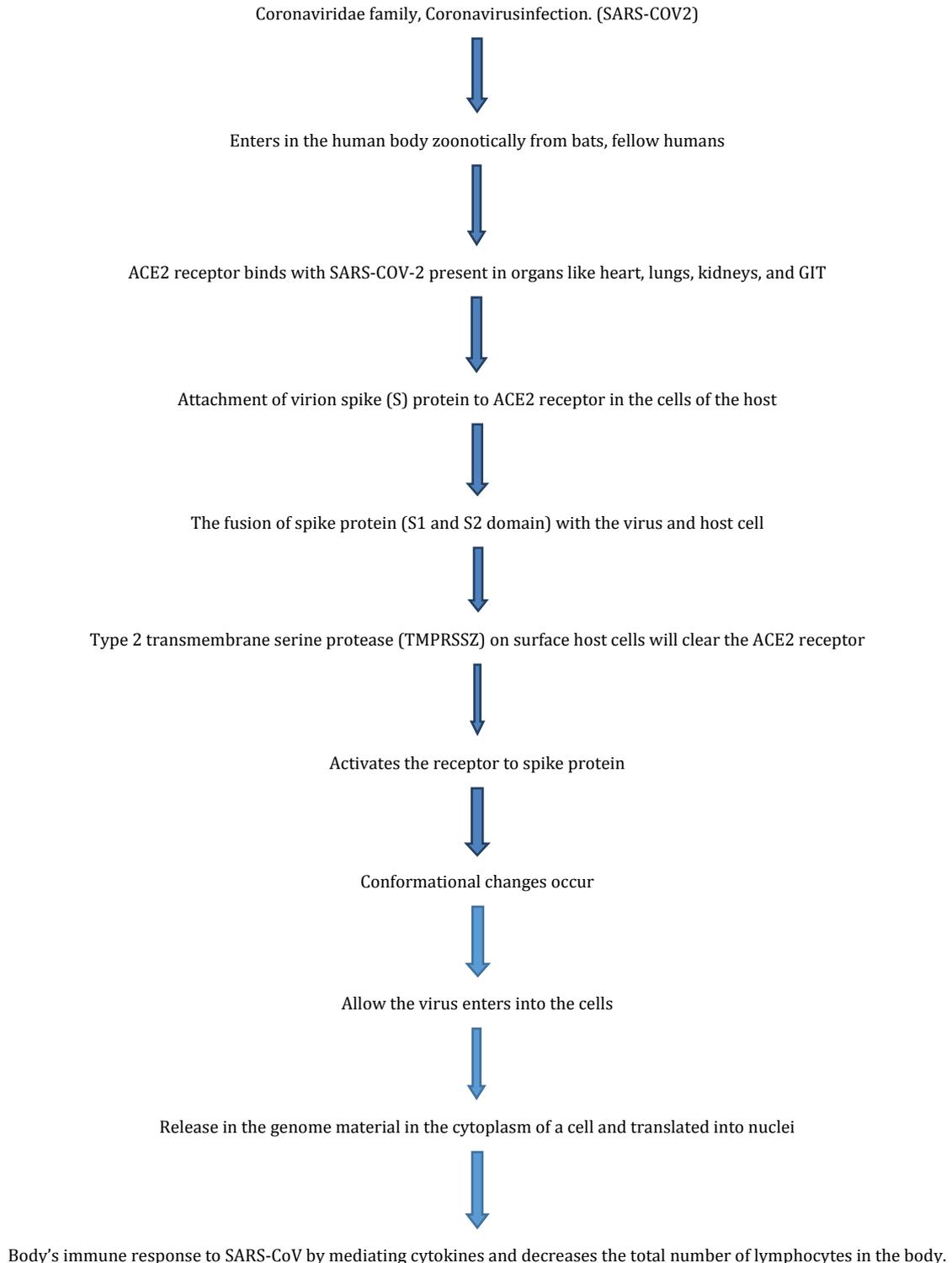
Coronavirus is swathe and single-stranded ribonucleic acid. The four major structural proteins hidden in the corona viral genome is the spike (S) protein that is linked to the angiotensin-converting enzyme-2 (ACE-2) receptor and arbitrates eventually attached between the swathe and host-cell membrane to encourage viral entrance into the host cells [11, 12]. As of 16 February 2020, the virus has given rise to a total of 70,548 infections in mainland China and Japan 413 infections [13]. This was the seventh known coronavirus, which gives rise to infection in humans [14]. Two other extraordinary examples SARS-COV and MERS-COV, previously which get down in Southern China and resulted in 8098 infections and 774 deaths in 29 countries from 2002 to 2003 and then later on raised in Saudi Arabia and their it caused 2458 infections and 848 deaths in 27 countries by 2019 [15, 16]. On 17 February 2020, the State Council of China clenched a news topic briefly which suggested that Chloroquine phosphate, a drug for the diagnosis of malaria, had revealed the mark of effective and acceptable safety in treating COVID-19 [17]. Chinese public health clinics and other scientific communities took immediate action for timely allow of the recognition of new pathogens and split the viral genome sequence across the globe [18]. SARS-CoV-2 is primarily spread from human contact or zoonotically to humans through respiratory droplets in contact with air, which is typically free in the through coughing or sneezing by an infected person. Most of the droplets from coughing or sneezing usually fall within a few meters of a person; this states that the probability of transmission is very low if each person maintains a distance of at least 2 meters [19]. The COVID-19 genetic sequence makes for the fast production of RT-PCR diagnostic point of care tests listed for 2019-nCoV [20].

**Pathogenesis**

Coronavirus binds to the specific cellular receptors via the Virion spike (S) protein, this triggers the cell fusion of the spike into (S1 and S2 domain) of the coronavirus, and it is accountable for the selection of the virus's host tropism [21]. The subunits S1 and S2 formed from the precursor cleavage, so S1 helps us to dictate tropism in cells and host's viral range, and S2 is divided into heptad repeat 1 and heptad repeat 2 (HR1 and HR2), which helps in the

fusion of cell membrane and the pathogen. When HR1 binds with HR2 to form a six-helix bundle structure. This results in newer non-infection indicated human contact transmission of the pathogen via

air droplets by coughing, sneezing, or direct and indirect physical contact [22]. In this flow chart, we explained how the virus reached the host cell and the body reaction towards the virus [22, 23].



### Symptoms

COVID-19 patients may have symptomatic or asymptomatic coronavirus in them. After an incubation time of around 5.2 d, COVID-19 symptoms emerge [24]. There was between 6 and 41 d of onset of COVID-19 mortality symptoms and an average of 14 d. In patients >70 y it was shorter than in patients under 70 [25]. Fever, cough, tiredness are the most frequent symptoms of COVID-

19 onset, and diarrhea, headache, hemoptysis, and sputum are other symptoms [26-28].

Increased number of leukocytes, irregular respiratory observations, and increased plasma levels of proinflammatory cytokines were reported by patients infected with COVID-19. In one of the COVID-19 cases, a patient had a cough and a coarse lung coughing sound and a body temperature of 39.0 degrees Celsius at 5 d of fever [29].

### Risk factors

Patients which are at major risk for the progression of the disease, according to the researches it is confirmed that 87% of the people affected by COVID-19 were aged 30 to 79 y, almost half of such cases have one or more such severe health condition including diabetes, hypertension, cardiac diseases, and other such diseases condition which suppress the activity of immune system [22]. Smoking is assumed to generate adverse diseases related to the respiratory tract and also suppress the activity of the immune system [30]. Patients with hypertension as compared with healthy persons, have a higher affinity of facing severe conditions [31]. Patients suffering from diabetes mellitus have a greater risk of acquiring COVID-19. Type 2 diabetes is viewed as chronic, which leads to the imbalance of the immune system for a longer time, obesity with nutrient excess, or metabolic syndrome [32].

### Treatment

Radiological inspections are well known as essential in the early diagnosis and management of the coronavirus. Chest computed tomography can recognize the initial stage of lung poisoning and give rise to enormous citizen's health supervision and retaliation system [33-35]. The incorporation of chest computed tomography for detection ensued in 14,840 authenticated latest instances reported on February 13, 2020. Nowadays, Realtime reverse transcription polymerase-chain-reaction (RT-PCR) evaluation for the pathogen is evolved and applied in hospitals [18]. RT-PCR is of prominent attentiveness nowadays for the recognition of SARS-CoV-2 on accounts of its well-being as a determined and easy approximate analysis. Besides, real-time RT-PCR has sufficient responsiveness to assist us considerably in detecting premature contamination [36]. Even though RT-PCR remnants the attribution quality to produce a definition inspection of COVID contamination the big incorrect rejection grade and inconvenience of RT-PCR analysis in the premature phase of the outburst confined and give rise to the detection of diseased persons [37].

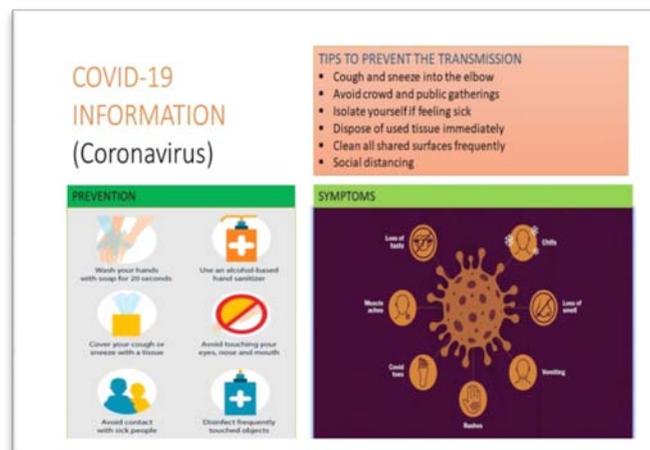
INF-alpha is an inclusive range antiviral agent that is mainly applied in the treatment of hepatitis however, it revealed to retard SARS-CoV breeding *in vitro* [38]. Ritonavir/lopinavir is a medicine that is used for the human immunodeficiency virus (HIV), generally given in amalgam along supplementary drugs to cure mature people and children above fourteen days of age those are suffering from HIV-1, it is also used in the SARS-CoV [39, 40]. Experts from China proposed that patients suffering from the virus pneumonia and not having a contraindication to chloroquine, be diagnosed with 500 mg two times a day for 10 d [41]. Hydroxychloroquine is illustrated as an anti-SARS-CoV effect *in vitro*. Its clinical assurance is preferable than that of chloroquine and permits a high daily dose and has little distress related to drug-drug interaction [42]. Chloroquine has vigorous anti-SARS-CoV outcomes *in vitro*, essentially referable to a deficiency at the surface of virus-cells in the glycosylation receptors, so that it may not be able to attach to the ACE 2 indicated in heart, lungs, kidneys, and intestines. SARS-CoV-2 uses the analogous surface receptor ACE 2 glycosylation and helps in the prevention of SARS-COV-2 binding to the targeted cells [43, 44]. As the anatomy and mode of action of chloroquine and hydroxychloroquine are quite similar, excluding an extra hydroxyl group at an end of hydroxychloroquine, both function on a weekly basis that can change acid intracellular organs' pH, like endosomes/lysosomes, which are important for the fusion of membrane [45]. Convalescent plasma (CP) treatment, a best compatible treatment for the immune has been sued to safeguard and to cure many contagious afflictions from surpassing 100 y. CP treatment may be an encouraging therapy choice in COVID-19 rescues. Sufferers who have recorded from coronavirus with an elevated counteract antibody titer might be an important contributor to CP [46]. Targeting the trimer spike (S) glycoprotein at the surface of SARS-CoV-2 that arbitrate entry into anchor cells can be counteracted by monoclonal antibodies [47]. The utilization of monoclonal antibodies is the latest period in contagious illness safeguards, which controls so many imperfections linked with serum treatment and intravenous immunoglobulin's preparation concerning individuality, clarity, moderate threat of bloodborne pathogen infections, and welfare [48].

### Vaccines

**Table 1: Provides the details about the list of vaccines for COVID-19**

Name	Characteristics of vaccine	Manufacturer	Current status	Reference
mRNA-1273	S protein-encoding for LNP-encapsulated mRNA vaccine	Moderna	Phase I (NCT04283461)	[49]
Ad5-nCoV	The S protein-expressing adenovirus type 5 vector.	CanSino biologicals	Phase I (NCT04313127)	[49]
INO-4800	S protein supplied by electroporation plasmid Encoding DNA	Inovio pharmaceuticals	Phase I (NCT04336410)	[49]
LV-SMENP-DC	Lentiviral vector modified DCs expressing synthetic minigenous on the basis of domains of selected viral proteins; administered with antigen-specific CTLs.	Shenzhen Geno-Immune Medical Institute	Phase I (NCT04276896)	[49]
Pathogen specific aAPC	Lentiviral Vector Modified aAPCs dependent on domains of selected viral proteins Synthetic Minigenes.	Shenzhen Geno-Immune Medical Institute	Phase I (NCT04299724)	[49]

S protein-SARS-CoV-2 spike protein; LNP-lipid nanoparticle; DC-dendritic cell; CTL-cytotoxic T lymphocyte; aAPC-artificial antigen-presenting cell.



**Fig. 1: Information about coronavirus**

## Prevention

COVID-19 infection is a zoonotically origin virus transmitted in human and also, it is a human-to-human transferrable disease, with an outbreak that is distributed all over the world. Patients which are affected by the virus should be isolated and the patient should be provided a single room for isolation. In severe medical conditions and to reduce the chance of contact with others, without late should refer to the clinical centers [50]. The patient should wear a proper mouth-covered mask and disposal of it properly. Maintaining distance socially by not having any type of physical contact may prevent the spread of diseases. For a stronger immune system by which we can prevent the coronavirus infection, we should consume healthy and nutritional food and should do regular exercise [51].

## Management of diabetes during this pandemic

Diabetes is one of the world's biggest death risk, with a dramatic spike in the age span in developed countries [52]. The international federation for diabetes records 415 million diabetes mellitus patients around the world [53]. Diabetes is a rapid procuring position of a developing pandemic in India; excess of sixty-two million patients of diabetes are presently suffering from the disease. India was in the top list in 2000 across the globe, followed by China and the US in terms of the highest diabetic patients [54]. The pancreas has two distinct components (i) acinar cells (ii) islets of Langerhans. There are at least four different types of cells in islets of Langerhans. Glucagon hormone is released from alpha cells. The beta cells release insulin. the secretion of insulin reduces the level of glucose in the blood, whereas secretion of glucagon increases it. Somatostatin secreted by delta cells, which hinders both glucagon and insulin [55]. Diabetes obtrudes a significant load to the community in the formation of inflated medical prices, previous productive capacity, transience, and ethereal prices in the form of a decreased grade of living [56]. Various pathogenic procedures are intricated in the expansion of diabetes. That ranges from autoimmune demolition of beta cells with successive insulin deficiencies to deformities that ensue obstruction in the action of insulin [57].

Diabetes is mainly of two types' diabetes insipidus and diabetes mellitus. Diabetes insipidus is associated with the injury of neurohypophysis or its afferent neurosecretory cells arising from the supraoptic and paraventricular nuclei of the hypothalamus. Deformity of ADH is normally received as being responsible for the polyuria and diabetes insipidus [58]. Diabetes mellitus is a class of metabolic problems designated by hyperglycemia evolved from faults in insulin action, insulin release, or both. Symptoms of hyperglycemia are renal disorders; weight loss sometimes blurred vision [59]. Diabetes mellitus is the principal form of disease attributing to at least 90% of all cases of diabetes mellitus and 382 million are affected by it across the globe as of 2013, and it is expected that it'll affect more than 592 million by 2035 [60]. Obesity is the crucial danger aspect for diabetes; still, researches are going on across India [54]. To minimize the problem load created by diabetes in India proper government purposes and collaborative attempts from contributors of the civilization are necessary [61].

Diabetes causes high septic course and serious pneumonia because of viral infection and happens in at least 20% of patients [62, 63]. Diabetes is supreme concurrent related to all 3 familiar people pathogenic coronavirus infection involving SARS-CoV-2. 20-50 percent of sufferers from COVID have had diabetes. Generally, people suffering from all types of diabetes are at prone risk of getting contaminated because of their faults in cell-mediated immunity, innate immunity affecting phagocytosis, and neutrophil chemotaxis, though large constancy of diabetes in severe instances of coronavirus can throwback the inflated generality of type 2 Diabetes Mellitus [64].

In this epidemic, "Corona Virus Disease 2019" an individual having diabetes is more prone to vital ICU acceptance. Regulation of diabetes in the Intensive Care Unit is all time confronting, although the condition becomes more serious when the patients suffering from coronavirus have diabetes [65]. Recent researches also showed that COVID-19 is related to hyperglycemia, especially in older people having non-insulin-dependent diabetes [66]. The patients with preexisting type 2 diabetes experienced remarkable additional

rigorous unified diagnosis to control indications of COVID-19 than the non-insulin-dependent diabetic issues [67]. Wuhan investigated in a review that on every side 10% of persons with type 2 diabetes and coronavirus always abided with a single part of hypoglycemia (<3.9 mmol/l) [68]. Diabetes mellitus is related to lessen assertion of ACE-2, an enzyme that is mostly articulated in the lungs, kidneys, intestines, and vascular endothelium [69]. Presymptomatic facts and fig. procured from reviewed established on previous SARS outburst (2003) suggested that COVID-19 may be accompanied to intensify management of glycemic in persons having diabetes mellitus that has generated due to stress of a serious disease [70]. Besides this, COVID-19 may cause inflamed insulin obstruction in humans with Type 2 Diabetes Mellitus and Type 1 Diabetes Mellitus. Gentle COVID-19 may produce a tendency to cause inflammation milieu as noticed by large numbers of Interleukin-6, Interleukin-1 beta, TNF-alpha, monocyte, and inducible protein-10 that may cause a lowering of insulin obstructions. Furthermore, obesity is mainly connected to type 2 diabetes mellitus, which provokes the cytokine reaction and thus causes inflamed insulin obstructions [71].

Tocilizumab is studied to enhance insulin obstructions and decrease HbA1C in persons suffering from diabetes mellitus and rheumatoid arthritis [72]. Camostat mesylate is commonly applied in the therapy of viral illness in opposition to COVID-19; the medicine was previously chased in the treatment of diabetes and it was observed to decrease levels of blood sugar in insulin-treated sufferers with diabetes [73]. Calcium channel blockers are observed to decline in the seriousness of disorders and transience in sufferers with pneumonia, likely to stop calcium reflux into the cell [74]. It is necessary to manage blood sugar levels in persons who are contaminated with the virus. Treatment of diabetes nowadays with the foundation on development is demanding; however, innovation like eHealth, telemedicine may be fruitful in this pandemic [75].

Diabetes management in this pandemic of Covid-19 can be controlled by keeping a few measures in mind. The former was to certify that primary diabetes facilities are procured and preserved in a period when there was a clepe for re-arrangement to maintain the necessity of common medical proficiency over secondary care facility. The latter was to give easy and secure diabetes guidelines to utilize by experts and non-expert's diagnosis patients having or suspected of COVID-19 contamination [76]. The existence of diabetes rapidly perched out as a crucial danger part of enlarged humanity and morbidity from COVID-19 in China. For example, it was revealed that person sufferings from both diseases were remarkably further promising for vital regulation in the ICU with mechanical ventilation and eventually lead to death from the disease in contrast to them with acute COVID-19 without diabetes [77]. As stated in various reviews, the generality of diabetes in persons contaminated with the virus is identical as in the common community, although relatively lesser. An Italian researched supervised in 146 patients with committed SARS-CoV-2 contamination at the University Hospital of Padova established a similar trend. The generality of diabetes in the patients was only 8.9 percent, while it was 11 percent between the age group of 55-75 from the same area in 2018 [78]. Diabetes is a metabolic condition that can be avoided by changes in lifestyle, nutrition, and overweight and obese regulation [79]. By the year 2030, its proportion will rise to 50% globally [80].

## CONCLUSION

Diabetes is among the rapidly-growing public health challenging diseases of the 21<sup>st</sup> century throughout the globe. Diabetes is generally growing very quickly in less-and middle earning countries than in high-earning countries. India is also known as the Diabetic capital of the world because of the high incidence of the disease. The current situation of the COVID-19 world pandemic gets worsens with each passing day. There is no vaccine developed for COVID-19 till now, so it's very important for people to boost their immunity and to take prevention. Early diagnosis can help diabetic patients to manage the disease. Diabetes is associated with the rising number and severity of COVID-19. For people suffering from both diseases, the morbidity is greater and those older significantly increased risk of death. It is necessary to maintain the blood sugar level of persons that are suffering from COVID-19.

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**AUTHORS CONTRIBUTIONS**

All the authors have contributed equally.

**CONFLICT OF INTERESTS**

Declared none

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