COVID-19 Infection, its Effects and Risk Assessment on Pre-existing Diabetes

Suchit Swaroop [1]*, Smita Raj Jaiswal [2], Naushad Ahmad Shah [3], Arti Yadav [1] and Asif Jafri *[4]

[1] Experimental and Public Health Lab, Department of Zoology, University of Lucknow, Lucknow- 226007, Uttar Pradesh, India.

[2] Department of Biochemistry, University of Lucknow, Lucknow- 226007, Uttar Pradesh, India.

[3] Department of Zoology, University of Lucknow, Lucknow- 226007, Uttar Pradesh, India.

[4] Department of Zoology, Khwaja Moinuddin Chishti Language University Lucknow, Lucknow- 226013, Uttar Pradesh, India.

Abstract- COVID-19 caused by SARS-CoV is known to be most emerging infectious disease that first originated from Wuhan, Hubei, China and quickly spread throughout the world, declaring it as pandemic by the WHO. Individuals with diabetes are at greater risk with any kind of viral, bacterial and fungal infection. Primarily, in several studies, it's been reported that diabetes is one of the most prevalent comorbidities in patients with severe COVID-19 infection. The present study briefly addresses the age group, risk, severity and recovery period associated with COVID-19 infection in the data of patients recorded and also found out the association between the risk factors involved with diabetic patients for getting infected with COVID-19. The trend associated with several demographic, clinical and health related complications were statistically analyzed. After interpretation the conclusion made is that the diabetes is an independent risk factor for prognosis of COVID-19. The patients with diabetes should be taken more care as comparedto non-diabetic one and proper treatment must be given.

***Keywords*-** SARS-CoV, COVID-19, diabetes, demographic complications, infection

Introduction

In both the animals as well as *Homo sapiens*, emerging infectious diseases (EIDs) causes major health, economic and lifestyle burden around the whole world and 75% of all the EIDs are zoonotic, of which many originate from wildlife (Jones et al., 2008). There has been an estimated report that a new human disease appears every four months, caused by mainly anthropogenic changes, consisting land-use change like urbanization, climate change, population growth and globalization. The most notable and significant EIDs during this era belong to the genus coronavirus (CoV). Traditionally, viruses were characterized and classified by culture, electron microscopy and serological studies. By using these phenotypic methods, coronaviruses are defined as a large family of enveloped viruses with a positive sense single-stranded RNA genome. Among all the known RNA viruses, one of the largest genomes is possessed by them consisting 26.4 kb - 31.7 kb approximately (Woo et al., 2010). The CoV derived from Latin word "crown" or "wreath" describes its characteristic appearance under electron microscope, with large, bulbous surface projections which is similar to crown. Coronavirus primarily infect the upper respiratory and gastrointestinal tracts of mammals and birds and disease severity varies significantly in human coronavirus (de et al., 2018). In 2002- 2003, a severe outbreak of severe acute respiratory syndrome (SARS) caused by coronavirus which was name as SARS CoV, started out in China. Following this, almost after a decade in 2012 the transmission and spread of Middle East Respiratory Syndrome coronavirus took place. In 2019, the very recent a new pandemic started out in China and spread globally which is caused by SARS-CoV-2 which ends up infecting more than 500,000,000 people. The origins of these zoonotic viruses seem to be bats, which is also home to many other coronaviruses. The amplifiers of SARS CoV-2 were seemed to small mammals sold at wet markets (Guarner et al., 2020, Hilgenfeld et al., 2013). The ACE2 (Angiotensin converting enzyme 2) enzyme seems to be receptor in host cells, which are found on many epithelial cells in the respiratory tract. The common symptoms could be seen in COVID-19 patients are fever, cough, fatigue and diarrhea and respiratory failure in critical cases.

More than two years have passed since the COVID-19 pandemic of 2019 and through various observational studies and clinical trials, poor outcomes have been identified. It's been observed that patients with little comorbidity are likely to suffer severely from COVID-19. Patients with any underlying diseases are found to have very high case of fatality rates which is around 73.3% (Guan et al., 2020). However, how these comorbidities affect the COVID-19 prognosis is not yet known. These comorbidities directly or indirectly favor the viruses. Either they accelerate the damage of target tissues or that they favor the virus life-cycle during a SARS CoV-2 infection. One of these comorbidities and risk factors diabetes, one of the most prevalent chronic metabolic diseases worldwide, with estimated prevalence of 9.3%, 463 million people suffering from it and mostly co-exists with other comorbidities.

Diabetes is a complex chronic metabolic disease which is characterized by abnormal regulation of glucose caused by an absolute or relative insulin deficiency. It includes various different types, type 1 diabetes

(T1D) and type 2 diabetes (T2D) as the most common subtypes. T1D is characterized by self-destruction of insulin producing pancreatic β-cells, while T2D caused by combination of β- cells secretory defect and insulin resistance (Landstra et al., 2021).

The relationship between Diabetes and COVID-19 is very complicated and bidirectional. On one hand diabetes mellitus is considered as one of the most important risk factors for severe cases of corona virus disease. One the other hand, treatment of severe COVID infection with steroids can have a specific negative impact on insulin target tissues and diabetes itself. Several factors that are present in diabetes are presumably to contribute the risk, such as pro-inflammatory and hypercoagulable state, older age, hyperglycaemia and underlying comorbidities. Treatment with steroids lead to the worsening of hyperglycaemia through increased insulin resistance and reduced β- cell regulatory function (Pranata et al., 2021). Worsening the increased glucose can, in turn and critically affect the course of COVID-19 and prognosis of it. The hyperglycaemic environment exist diabetes favors immune dysfunction through several pathways. Less production of interleukins in response to an infection, reduced chemotaxis and phagocytic activity and immobilization of polymorphonuclear leukocytes are the most underlying mechanism. Increased level of including the resulting glycosuria, also increases the virulence of certain pathogens. The enzymes ACE2 and DPP4 which leads the entry of SARS and SARS CoV-2 changes its expression pattern in diabetes, although in different ways, making the receptor proteins themselves an unlikely explanation for the elevated risk.

We adopted strategy of performing a study in an area of population to whom we can reach. In this study large numbers of people were included and the questions prepared were given to them, so that can answer accordingly and a conclusion can be made. Different demographic, clinical and health related analysis were done using SPSS (Statistical package for Social Sciences) software. These statistical approaches were applied to find out association and significant differences between different variables related to COVID-19 and between COVID-19 and Diabetes.

Corona Virus History

Over the course of last two decades, three corona viruses have periodically crossed animal species such as bats, transmitted to human and caused an ever-increasing outbreak of large-scale pandemic (Wang et al., 2020). The history of human coronaviruses began in 1965. It was first found in culture of human embryonic tracheal organ which was obtained from the respiratory tract of an adult with common cold. There are seven known human coronavirus and out of them four (HCoV-OC43, HCoV- HKU1, HCoV-229E, HCoV-NL63) cause mild to moderate symptoms of the common cold in humans and three can cause more serious even deadly disease. The three fatal coronaviruses are severe acute respiratory syndrome (SARS, caused by the SARS-CoV virus). Middle East respiratory syndrome (MERS, caused by MERS- CoV virus) and the most recent COVID-19 (caused by the SARS- CoV-2 virus). The COVID-19 causing SARS-CoV-2 share more than 80% identity in genetic sequence with SARS- CoV and 50% with

MERS-CoV (Lu et al., 2020, Zhou et al., 2020).

Corona Outbreak and Pandemic

In December 2019, a severe infectious pneumonia of unknown reason broke out in Wuhan, Hubei Province, China and quickly spread throughout the world. Deep sequencing analysis from lower respiratory tract samples indicated that this pneumonia causing pathogen was identified to be unique clade from the β- coronaviruses related to severe acute respiratory syndrome (SARS) and Middle East syndrome (MERS) and was given official name severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) (Shang et al., 2021). Although SARS CoV-2 has shown phylogenetic and clinical similarities with SARS CoV, the novel coronavirus has shown higher transmissibility and lowercase fatality rates. COVID-19 has a higher transmission rate and greater risk of mortality in comparison with influenza. A rapid global spread of the virus led the World Health Organization (WHO) to declare coronavirus disease 2019 (COVID-19) outbreak a Public Health Emergency of International Concern on 30 January 2020 and it was upgraded to pandemic from an epidemic on 11 March 2020. On 18 April 2020, SARS CoV-2 had caused approximately 84,000 confirmed cases and more than 4000 deaths in China. Globally, this virus has spread to more than 200 countries, including the India, United States, Italy, South Korea and Japan. The coronavirus pandemic has infected more than 500,000,000 people worldwide till 28 June 2022 and almost 6,000,000 people have died. In this the number of people infected in India is 43,420,608 and death numbers are 525,047 since the pandemic began. Everyday almost 14,000 new infections on averageare being added on the list.

Morphology of the Corona virus

Talking about the morphology of the coronaviruses, they are enveloped, positive single- stranded RNA viruses widely distributed in humans and animals worldwide. Most of the initial cases had a direct contact history with Chinese wildlife market, which suggests that the common source zoonotic exposure as the main mode of transmission. SARS CoV-2 and bat coronavirus might sharethe same ancestor but bats were not sold in those markets. They were might not sold there but may have infected live chickens or other animals sold out there. Later the cases which were reported among health workers and others without exposure history of wildlife which indicates human to human transmission. Currently it is considered that the virus can be mainly transmitted through air and water droplets, direct contacts and aerosols. Transmission through droplets may occur while sneezing and coughing etc. A person can also get infected when he/she touches the surface contaminated with virus and subsequently touching his/her mouth, nose or eyes. The infection period is not certain. The infection period is often assessed indirectly by deletion of viral RNA fromrespiratory specimens. Higher viral loads have been detected soon after symptoms onset, suggestingthe transmission may be more likely to occur in the earlier stages of infection. The duration of viral shedding seems to vary according to the disease severity. Negative viral RNA test on nasopharyngeal swabs has been observed in 90% of patients with milder symptoms while in the severe cases it remained positive for longer time in all cases. On the other hand, it has been reported that viral load in asymptomatic

patients was similar to symptomatic ones. Indeed, within the incubation period transmission from asymptomatic carriers or individuals have been described. Nevertheless, the extent to which this occurs remains to be determined.

The examination of infected cells observed after 3 days of infection. Electron microscopy shown that the virus particle sizes ranges from 70 to 90 nm of the corona-specific morphology of SARS- CoV-2 when observed under a wide variety of intracellular organelles, specifically in vesicles (Park et al., 2020). SARS CoV-2 speculated to be the same as SARS CoV due to high sequence similarity (Kumar et al., 2020). They are large pleomorphic spherical particles with bulbous surface projection over it. The envelope of the virus appears as a distinct pair of electron dense shells under electron micrographs. The viral envelope consists of a lipid bilayer where different proteins are embedded init namely membrane (M), envelope (E) and spike glycoproteins (S) which mediates the interaction with cell surface are various structural proteins that are anchored. The nucleocapsid which is formed from multiple copies of nucleocapsid protein are present in inside the envelope which are bound to positive sense single stranded RNA genome in continuous beads on the string type conformation (Figure 1)

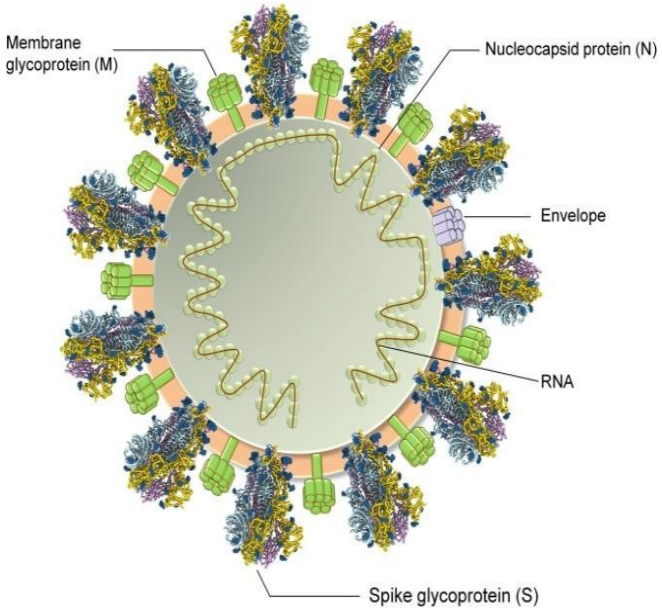


Figure 1- *Structure of SARS CoV-2 showing viral proteins, namely, spike glycoproteins (S), membrane protein (M) and envelope protein (E) are embedded in lipid bilayer membrane encapsulating the helical nucleocapsid comprising viral RNA (Adopted from Kumar et al., 2020).*

Clinical characteristics

All three human coronaviruses *viz.* SARS CoV, MERS CoV, SARS CoV-2 replicate in the lower respiratory tract and that leads to cause pneumonia, in severe cases leads to severe hypoxia, respiratory failure, shock and death (Tay et al., 2020). Through several studies it has been found thatFever and Cough are the most common symptoms (Kim et al., 2020, Pan et al., 2020, Zou et al.,

2020) and the age of most of the patients were between 30 and 79 and majority are male. The two-pattern severity increases with age and presenting symptoms broadly consistent with the epidemiology of SARS CoV and MERS CoV infections. Infection with SARS CoV-2 has been shown to reach a peak viral load 4-7 days after symptoms onset, this peak is earlier than SARS CoV which peaks at approximately 10 days after symptoms onset. Notably, SARS CoV-2 has been found in upper respiratory tract secretions of asymptomatic individuals (Ling et al., 2020).

Epidemiological studies related outbreaks have identified diabetes and other comorbidities illness such as hypertension and cardiovascular and cerebrovascular diseases as risk factors for severe or lethal infections (Badawi and Ryoo, 2016, Booth et al., 2003, Hui et al., 2018, Rivers et al., 2016, Yang et al., 2017, Fu et al., 2020). In the current pandemic with SARS CoV-2, clinical reports also show distinctive comorbidities with diabetes. Through several studies in hospitalized patients, it has been found that Diabetes (12.1%) was one of the most common morbidities after hypertension (30.0%) (Zhang et al., 2020). The patients in in ICU with diabetes were two fold higher than that without diabetes (Li et al., 2020). In some recent studies it's been found that individuals with diabetes need more medical interventions and significantly have higher mortality, well-controlled blood glucose levels were associated with improved outcomes. The hospitalizations in patients resulting from various types of infection in people with T1D and T2D were associated with poorly controlled glucose levels. Although, a large scale, independent, multicellular studies arerequired to understand the impact of pre-existing diabetes T1D or T2D on COVID-19 infection, well controlled blood glucose levels would correlate with improved outcomes (Erener S, 2020).

Pathogenesis and Mechanism for Increased SARS CoV-2 Infection Risk/Severity for Individuals with Diabetes.

Several studies have discovered diabetes as risk factor for many infections (Critchley et al., 2018). Diabetes was one of the leading comorbidities associated with infection severity in the COVID-19 pandemic. Other comorbidities which were thought to be found was being male, older age and underlying medical condition related lungs, cardiovascular diseases and hypertension.Late diabetes complications such as diabetic kidney disease and ischemic heart disease may complicate the situation for individuals with diabetes, making them frailer and further increasing the severity of COVID-19 disease, leading to kidney or heart failure. However, plasma glucose and diabetes were independent predictors for mortality and morbidity in patients with SARS. The mechanism by which diabetes can increase infection severity cannot be explained alone with associated comorbidities (Figure 2).

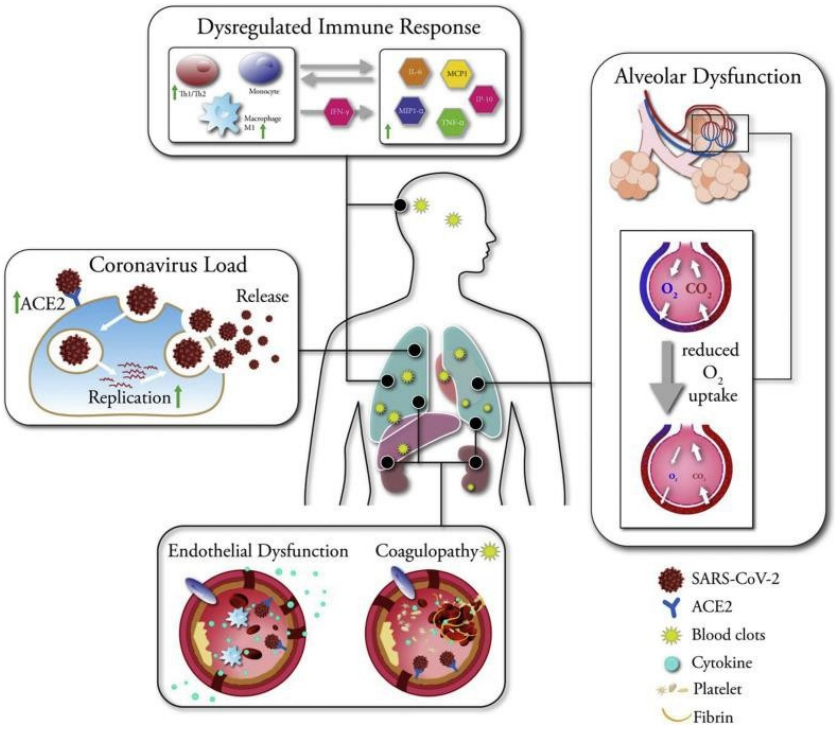


Figure 2- *Mechanism associated with increased COVID-19 severity in individuals with diabetes (Adopted from Erener S., 2020).*

Coronavirus Load: SARS CoV-2 infects the lung tissue via entry through ACE2 receptor. Increased ACE2 expression can be seen in individuals with diabetes. Medications such as ACE inhibitors, GLP-1 agonists and statins may increase ACE2 levels further. Increased glucose levels may allow SARS CoV-2 replication. **Dysregulated Immune Response:** Low chronic inflammation was seen in individual with diabetes, which exaggerated macrophage and monocyte and T-cell recruitment, promoting further inflammation in feedback loop. **Alveolar Dysfunction:** Numerous structural changes to the lungs are associated with Diabetes including augmented permeability of the vasculature and reduced gas exchange, causing an increased need for mechanical ventilation in diabetes patients. **Endothelial Dysfunction:** SARS CoV-2 directly infects the endothelial cells via the ACE2 receptors present on the endothelial cells. **Coagulopathy:** Individuals with diabetes have significant up regulation and fibrinolysis markers and increased platelet activity and adhesion to endothelial wall, constructing favorable environment for thromboembolic events to occur under hyperinflammatory conditions such as SARS CoV-2. Blood clots can be detected in multiple organs.

Viral Load

The efficient virus entry increases the viral load, which could be one of the possible mechanisms through which diabetes can enhance the infection risk. The entry receptor of ACE2 is expressed in various tissues including lung, heart and kidney tubules, the luminal surface of the small intestine and blood vessels

(Monteil et al., 2020). In mouse model of diabetes, the increased expression of ACE2 in lung, kidney, and heart was seen (Roca et al., 2017). Due to increased ACE2 receptor expression in multiple tissues in diabetes, the severity of COVID-19 might be higher. Elevation in blood glucose level can increase the concentration of glucose in airway secretions and exposure of epithelial cells to virus infection and replication (Philips et al., 2003). Although, it remains to be determined whether hyperglycemia increases coronavirus replication in vivo, this is a possible explanation of the prolonged recovery of COVID-19 patients with diabetes.

Dysregulated Immune Response and Cytokine Storm

In every infection, successful clearance of viral load heavily depends on the organized actions of theinnate and adaptive immune system. Elevated levels of glucose may also suppress the antiviral response (Reading et al.,1998). Individuals with diabetes have been described to have alterations in innate immune system components. For example- NK cell activity is reduced in the patients with diabetes and more pro-inflammatory M1 macrophages are present in T2D. Regardless of the involvement of endothelial cells, the initial interferon gamma response together with hyperinflammatory response in individuals with diabetes may exceeds the “cytokine storm” and elevate COVID-19 severity.

Alveolar Dysfunction

In recent case study in New York, patients who died, those with diabetes were more likely to have received invasive mechanical ventilation in the intensive care than those without diabetes. This observation suggests that people with T2D may have impairments in their alveolar functions. Indeed, earlier studies have shown that pulmonary functions such as such as forced viral capacity, alveolar membrane permeability and alveolar gas exchange were reduced in the individual with diabetes (Ananda Lakshmi et al., 2013). Impaired respiratory function present in the individuals with diabetes, in conjunction with the tendency of SARS Cov-2 to infect lung tissue cells may aggravate pulmonary complications of COVID-19.

Endothelial Dysfunction

In all pathologies observed due to SARS, MERS, and COVID-19 damage was not confined to lung only and occurred in multiple organs including the heart and kidneys, suggesting that SARS CoV-2 can infect vascular endothelial and can circulate to other organs (Wang et al., 2020). In patients with diabetes endothelial dysfunction is a consistent finding and precedes microvascular disease (Avogaro et al., 2006). Endothelial dysfunction observed in individuals with diabetes may play role in cytokine storm and pulmonary lesions. Whether cytokine production from endothelial cells contributes to pulmonary lesions in COVID-19 patients this is exasperate in individuals with diabetes remains to be investigated.

Coagulopathy

More recent data indicate that significant number of COVID-19 patients in intensive care units slow hypercoagulation in multiple organs with elevated D-dimer levels and fibrinogen/fibrin degradation

products which are associated with overall survival rates (Zhou et al., 2020, Wang et al., 2020, Tang et al., 2020). Severity in COVID-19 infection has also been associated with a significantly increasedrisk for developing deep vein thrombosis and pulmonary embolism (Cui et al., 2020, Klok et al., 2020). Hypercoagulation may occur due to profound inflammatory response, probably due to cytokine storm observed in some COVID-19 patients. Since patients with diabetes have an increased risk for more inflammatory response, they may be at a greater risk to suffer.

Methodology

The main aim of present study was to find the trend of COVID-19 infection and to find that if there isany link between the patients with pre-existing diabetes. Also, the study has been done to see that there are any inter-connecting factors which may worsen the infection or recovery of the patients.

Selection of the Subject

Between 10 April 2022 and 10 June 2022, a comprehensive and elaborative study was conducted in which people above age 18 were chosen and they were required to fill a questionnaire form. This questionnaire form was made, consisting of details regarding their general and clinical data. The form was given to some people randomly which were our classmates, family members and neighbors. Some people were included in the survey on purpose with our concerned disease. The data has been collected by visiting the diabetes OPD of hospitals viz. Balrampur Hospital, Lucknow, Ram Manohar Lohia Hospital, Lucknow and Medanta Hospital, Lucknow by distributing the forms or asking and interviewing them with the questions present in the form. The survey form was circulated offline as well as online through various social media platforms in the mode of Google forms. The subjects' general information data, socio-demographic, clinical and health related details like COVID-19 related queries, diabetic related queries were taken.

Questionnaire and Data Collection

The study was conducted for the duration of two months between April and June. The study consisted questions like name, age, gender, weight, height socio-economic status. It also has questions related to COVID-19 and its vaccination and diabetic related issues. The questionnaire was categorized in different parts; in order get optimal data so that an effective study can be done.

Demographic Information

The people were asked about their name, age, gender, height weight, residence, occupation, religion.

Diabetes Related Information

The people were asked about diabetes related issues like whether they are having diabetes, any family history of diabetes, types of diet they consume, sign and symptoms they have related with diabetes, smoking and alcoholic habits, and exercising patterns.

COVID-19 related Information

The people were asked about COVID-19 related information, if they had contracted COVID-19, in which they were infected, types of treatment they opted, their recovery period, vaccination, wave in which they were infected.

Statistical analysis:

The data that was collected through this study was analysed anonymously by us. There were a total 420 individuals who filled up the questionnaire, out of which 210 were the number of people who had contracted COVID 19. 84 were the number of people who had any diabetic condition and 42 were the number of people who had been inflicted by both, COVID-19 and diabetes.

About 252 people were considered to be eligible for the statistical analysis by us. These people were considered to be eligible because they had qualified the minimum criteria of having either COVID-19 or diabetes, or had both of these disorders at one point of time. The data of these people underwent various statistical tests in order to find the trend in COVID-19 patients and if there is any association between the individual contracting COVID-19 and the pre-existing diabetic condition. The various individual that suffered from diabetic symptoms, were analyzed with the individual contracting COVID-19 in order to figure out if these symptoms somehow increased the subject's susceptibility to contract COVID-19. The data that was collected from this study; the data that belonged to the 252 people who were found to be eligible for the study; was copied on MS Excel (on an excel sheet) and was run under the SPSS version 20.0.

Results

Demographic and Clinical Characteristics

A total number of 420 people were included in the respective study. The data has been extracted and analyzed. Out of 420 people, only 252 people were related with our concerned problem that is COVID-19 and Diabetes. The people those were included in the study was divided into the groupsas stated by that whether they were infected with COVID-19, they are suffering from Diabetes or they had both. For analyzing and reaching to the conclusion different tables have been made.

The Descriptive Tables that were made for analysis are as follows

Unhealthy	Frequency	Percent
No	42	16.7
Yes	210	83.3
Total	252	100.0

Table 1- *Data showing frequency and percentage of unhealthy people.*

Table 1 shows that whether the people were infected with COVID-19 or not. Out of 252 unhealthy people 210 (83.3) were infected with COVID-19 and 42(16.7) were not infected with COVID-19

but they were diabetic.

Gender	Frequency	Percent
Male	114	45.2
Female	138	54.8
Total	252	100.0

Table 2*- Data showing classification of unhealthy individuals on the basis of gender.*

Table 2 depict that 114 out of 252 were male and 138 were female. The percentage was 45.2 and 54.8 of male and female respectively. This indicates that the males are more prone than females to any kind of infection or diseases.

Residence	Frequency	Percent
Urban	165	65.5
Rural	87	34.4
Total	252	100.0

Table 3- *Data showing classification of people on the basis of their residence.*

Table 3 shows that the out of 252 unhealthy people, 165 that is 65.5 % were residents of urban and 87% were from rural area. This depict that people who are residents of urban area are likely to get more infected comparatively who lives in rural area.

Exercise	Frequency	Percent
Yes	131	52
No	121	48
Total	252	100.0

Table 4*- Data showing classifications of people on the basis of their exercising habits.*

Table 4 shows that out of 252, who were Diabetic or COVID-19 infected, 131 were involved in some kind of exercises or yoga making it 52% of unhealthy population and 121 were not involved in any kind of physical activities or exercises.

BMI	Frequency	Percent
Underweight	11	4.4
Normal	192	76.2
Overweight	40	15.9
Obese	9	3.6
Total	252	100.0

Table 5- *Data showing categorisation of people on the basis of BMI.*

Table 5 showing the categorisation of people on the basis of BMI calculated from the height and weight of the people who have taken part in the study. 11 out of 252 people who were associated with any disease either COVID-19 or diabetes were underweight which comprises of 4.4% of total population. 192 out 252 were of normal weight making it 76.2% of the population. 40 people that is 15.9% were overweight and 9 people were obese comprising 3.6% of the population.

Age Range	Frequency	Percent
20 – 30	48	22.85
30 - 40	24	11.42
40 - 50	63	30
50 - 60	36	17.14
60 - 70	39	18.57
Total	210	100.0

Table 6 – *Data showing people with different age range who had contracted COVID-19.*

Table 6 shows the prevalence of COVID-19 infection in people of different age range who were included in the study. Out of 420 people who took part in study, 210 were infected with COVID-19 in any of the three waves. The highest infected group with COVID-19 was found to be in the middle age range i.e., 40-50. 63 out of 210 COVID-19 patients were from age range 40-50. This makes about 30% of total number of people in the study. About 22.85 % of people were between age range of 20-30, 11.42% of people were between age group 30-40, about 17.5% of total people were from 50-60 age range and at last the rest of 18.6% of people were infected was in the age group of older ones that is 60-70. This above data clearly signifies that no age group was remained untouched from COVID-19. Every age range of adult ones were infected with coronavirus.

Age range	Frequency	Percent
20-30	6	7.14
30-40	12	14.28
40-50	12	14.28
50-60	24	28.56
60-70	30	35.8
Total	84	100.0

Table 7- *Data showing people with different age range who had diabetes.*

Table 7 shows the number of people with different age range who were diabetic. 84 out of total 420 people were having diabetes. The age group having highest number of diabetic patients were between age range 60-70- which makes up about 35.8% of population of study. About 7.14% of the people were between age group 20-30, and the age range 30-40 and 40-50, each were having 14.28% and 14.28% of total number of people in the study. And lastly 28.56% of total number people were in age group 50-60.

Gender	Frequency	Percent
Male	99	47.1
Female	111	52.8
Total	210	100.0

Table 8*- Data showing the classification of number of people infected with COVID-19 on the basis of gender.*

Table 8 shows the classification of COVID-19 patients on the basis of gender. Out of 210 people who were infected with COVID-19, 111 out of them were female making it 52.8% of the total population and rest 99 that is 47.1% of people were male. This data clearly signifies that the

COVID-19 was more prevalent in females than males.

Gender	Frequency	Percent
Male	48	57.14
Female	36	42.85
Total	84	100.0

Table 9*- Data showing classification of number of people suffering from Diabetes on the basis of gender.*

Table 9 shows the classification of diabetic patients on the basis of gender. 48 out 84 people suffering from diabetes were male and 36 out of 84 were female. This data shows that the total number of people who had diabetes, highest number was found to be male and lesser number was of female.

Wave	Frequency	Percent
First	54	25
Second	114	55.0
Third	42	20
Total	210	100

Table 10*- Data showing number of people infected with covid in all the three waves.*

Table 10 shows the number of people infected with COVID-19 in each wave. 114 Out of 210 people were infected in Second wave, which was highest. This makes up about 55% of total people in the study. In the first wave 54 out of 210 were infected making it around 25% and 42 people got infected in the third wave that is 20% of the total infected population.

Age range	Frequency	Percent
20-30	1	2.3
30-40	3	7.14
40-50	3	7.14
50-60	19	45.5
60-70	16	38.09
Total	42	100.0

Table 11- *Data showing number of Diabetic patients infected with COVID-19.*

Table 11 shows the number of diabetic patients infected with COVID-19 in any of the three waves. The total of 42 patients who were diabetic contracted COVID-19. The greatest number of diabetic patients who contracted COVID-19 were in the range of above middle age 50-60, making 45.5% of total people in the survey. Only 1 person was there between age 20-30 who had diabetes and also contracted COVID. Each of age range 30-40 and 40-50 had 3 people with Diabetes and COVID-19 which makes up 7.14% of total population in the study.

Age range	Asymptomatic	Moderate	Severe
20 – 30	22	14	4
30 - 40	7	6	3
40 - 50	16	10	5
50 - 60	12	10	6

60 - 70	18	20	15
Total	75	60	33

Table 12- *Data showing severity of COVID-19 in different age range of people without diabetes.*

Table 12 shows the severity of COVID-19 patients who were not having diabetes, either they were asymptomatic, having moderate infection or severely infected in different age range. Out of 168 COVID patients 40 were in the age range of 20-30 in which 22 were asymptomatic, 14 were having moderate infection and 4 were severely infected. In the age range 30-40, 7 people were asymptomatic, 6 were moderately infected and 3 had severe infection out of total 16 infected people in that age range. Out of 31 people in age range 40-50 who got infected 16 were asymptomatic, 10 were having moderate symptoms and 5 had severe infection. In the age group 50-60, 12 infected people were symptomatic, 10 were having moderate infection and 6 got severe infection. And lastly the age group 60-70 was having 18 people were asymptomatic 20 were moderately infected and 15 were severely infected. Severity among different age groups varying differently, constituting 10% in age group 20-30, about 19% in age group 30-40, 16.12% in age range 40-50, around 21.5 % in 50-60. The age range 60-70 constitute about 28.03% of people who were severely infected among this age group, which is highest of all. This clearly signifies the oldest of all the age group were more severely infected.

Age range	Asymptomatic	Moderate	Severe
20 – 30	0	1	0
30 - 40	2	0	1
40 - 50	1	1	1
50 - 60	2	10	4
60 - 70	4	6	9
Total	9	18	15

Table 13- *Data showing severity of COVID-19 in different age range in patients with diabetes.*

Table 13 shows the severity of COVID-19 patients who were also suffering from diabetes, either they were asymptomatic, moderately infected or had severe infection in different age range. The only person who was diabetic and also contracted COVID-19 was moderately infected. The diabetic patients who were infected in the age range 30-40, 2 were asymptomatic, no one was moderately infected and only one was having severe infection. In the age group 40-50, 1 person was asymptomatic, 1 diabetic patient was having moderate infection and 1 was severely infected. 2 were asymptomatic, 10 were moderately infected and 4 patients were severely infected with COVID-19. In the oldest age group of diabetic patients 4 were asymptomatic, 6 patients were moderately infected and 9 of them were severely infected which is highest of all. Severity among different age range was comprised of 0% in 20-30 age group, 33.33% in 30-40 age range, about 33.33% in age group 40-50, 25% were severely infected in age range 50-60. And lastly in the oldest age group 60-

70, about 47% were having severe infection, which is highest among all.

Recovery period (In days)	Frequency	Percent
10 - 20	49	29.16
20 - 30	89	53.0
30 - 40	18	11.0
40 - 50	8	4.7
50-60	4	2.3
Total	168	100.0

Table 9- *Data showing Recovery period of number of people who were infected with COVID-19 but were non-diabetic.*

Table 9 shows the recovery period of COVID-19 infected people in the form of number of days. While analysing the data of people who took part in study, the result came out as the people took more than 10 days to recover from the infection. Few who were severely infected, even took more than two months to get fully recovered. 49 people out of 168 COVID infected patients who were non- diabetic which comprises 29.16% of the total people in the study took around 10-20 days to get recovered completely, about 89 people which is approximately 53% of people got fully recovered in around 20-30 days. Number of people who got fully recovered in 30-40 days were 18 which makes up to 11% of population in the study, 8 people took around 40-50 days to recover comprising 4.74% of people. And at last, 4 people took more than two months to recover comprising 2.38% of population.

Recovery period (In days)	Frequency	Percent
10 - 20	4	9.52
20 - 30	5	11.9
30 - 40	10	23.8
40 - 50	15	35.74
50-60	8	19.04
Total	42	100.0

Table 10- *Data showing Recovery period of number of people who were infected with COVID-19 and were diabetic.*

Table 10 shows the number of days in which diabetic patients who were infected with COVID-19 took to recover completely from the infection. 10-20 days have been taken by 4 people to recover which makes up to 9.52%, 5 diabetic patients took around 20-30 days to get recovered completely comprising 11.90% of total people in the study, 10 patients took around 30-40 days to get fully recovered making it 23.8%, 40-50 days have been taken by 15 patients constituting to get recover from the infection. And lastly 8 patients took more than two months to recover completely from infection.

Treatment	Frequency	Percent
Self-isolation	112	66.66
Hospitalization	56	33.33
Total	168	100.0

Table 11- *Data showing non- diabetic people infected with COVID-19, whether they were self-isolated or hospitalized.*

Table 11 shows the treatment, the infected people without diabetes opt for recovery, whether they were remained at home or say self-isolated or they got hospitalized. Out of 168 people 112 were self-isolated comprising 66.66% of total people in the study. And rest of 56 people got hospitalized that makes up to 33.33% of total population of the study. This clearly signifies that more than 50% of people without diabetes who were infected got recovered without getting hospitalized and got treated with self-isolation.

Treatment	Frequency	Percent
Self-Isolation	23	54.7
Hospitalization	19	45.3
Total	421	100.0

Table 12- *Data showing diabetic patients infected with COVID-19, whether they were self-isolated or hospitalized.*

Table 12 shows the type of treatment diabetic patients who contracted COVID-19 got. Out of 42 diabetic patients 25 got self-isolated and 17 out of them were hospitalized. That represent around 54.7% of patients were self-isolated and rest 45.3% patients got hospitalized. This signifies here in the case of diabetic patients too; the self-isolation percentage was more than hospitalization but less than the percentage in non- diabetic ones.

Signs and Symptoms	Frequency	Percent
Fever	63	67.4
Cough	51	54.9
Fatigue	48	51.6

Table 13*- Data showing non-diabetic people infected with COVID-19 having different sign and symptoms.*

Table 13 shows the most common sign and symptoms among the infected patients without diabetes. Out of 168 COVID patients without diabetes only 93 were having symptoms and rest were asymptomatic. The most common symptoms observed were Fever, Cough and Fatigue. 63 people out of 93 were having fever which comprises 67.4% of the total people in the study, 51 people were having cough, comprising 54.9% of total people. And lastly 48 people had symptoms of fatigue comprising 51.6% of the people in the study.

Signs and Symptoms	Frequency	Percent
Fever	30	71.42
Cough	27	64.42

Fatigue	38	90.5

Table 14*- Data showing diabetic patients infected with COVID-19 having different signs and symptoms.*

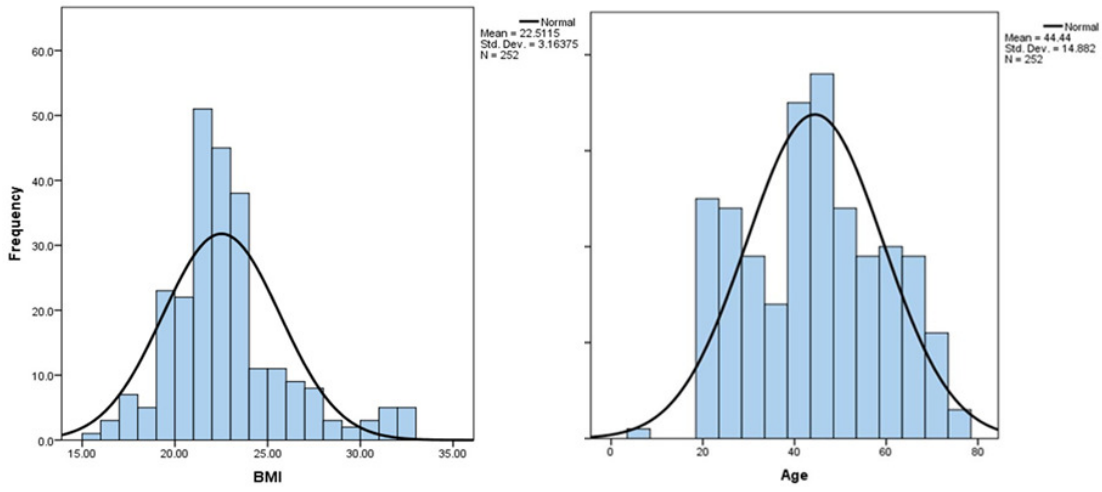
Table 14 shows the data of most common symptoms in diabetic patients after contracting COVID-19. The symptoms were same as they were in non-diabetic patients, but the percentage is quite different. Out of 42 patients, 30 were suffered from fever comprising 71.42%, 27 out of them were having cough making up to 64.28% of total population and 38 people out of 42 were having fatigue which comprises 90.5% of people in the study which is the highest percentage of symptoms people had.

Frequencies (Age and BMI)

Statistics		
	Age	**BMI**
Mean	44.44	22.5115
Median	44.00	22.0000
Std. Deviation	14.882	3.16375
Minimum	6	15.00
Maximum	76	32.50
Interquartile Range	23	2.2

Table 15*- Frequencies of continuous variables.*

Table 15 depicts different frequencies i.e., Mean, Median, Standard deviation and Interquartile range of continuous variables viz Age and BMI.



Discussion and Conclusion

Diabetes is defined as chronic inflammatory disease characterized by multiple macrovascular and microvascular abnormalities that can affect our body's response to pathogens (Knapp S, 2013). The association between diabetes and infection has always been an important concern of medicos.

In this retrospective study, we analyzed data from segregating 252 patients out of 420 people related to the concerned problem that they were either infected with COVID-19 or diabetes or with both.
Out of 252 individuals 210 individuals were infected with COVID-19 and 84 out of them were diabetic and 42 people had both conditions i.e., they were diabetic and got infected with COVID-19 in either of the three waves. The results are obtained after several descriptive and statistical test analysis. We compared the differences in demographic, clinical characteristics and underlying health conditions related to the diseases. The results indicate that there is no significant association between gender and COVID-19 infection. But according recent studies the males are more likely to get infected. It's been found that the elderly patients are more prone to get infected with COVID-19 (p= 0.044) and develop severity (0.026) as gets older. Aging is associated with declines in adaptive and innate immunity, so it in increases the risk factors. However, no age group remains untouched with infection. Also, it has been found that the wave in which the people are infected are associated with age (p= <0.001). Several studies have also confirmed that age is associated with wave of infection; the patients in the second wave were younger comparing to the first and third wave. Also,the severity of infection in all the three waves were different (p=<0.001). Furthermore, analysis concluded that COVID-19 infection is strongly associated with BMI (0.044) and comorbidities (Diabetes and Blood Pressure, p=<0.00, p= <0.00, respectively) present in the individuals. It's beenfound that the wave in which the individual got infected is also associated with recovery period (<0.001) In previous studies also it has been depicted that the in the first wave recovery period was more as compared to the second wave because in the second wave the younger people were more infected. The analysis also concluded that the COVID-19 infection is not significantly associated with residence (p= 0.859) to which the individual belongs and exercising habits (p=0.693).

After analyzing the groups having both the conditions COVID-19 infection and diabetes. The results indicatethat, the proportion of elderly patients in the diabetes group is significantly higher than that of non- diabetic one (p= <0.001). It is well known that diabetes in an ageing disease and various previous studies have depicted that aging is one of the important risk factors affecting prognosis of COVID-19. Therefore, a high number of elderly patients might suggest a poor clinical outcome. Moreover, analyzing the very prevailing comorbidity associated with diabetes i.e., Blood pressure also have theassociation with the infection of COVID-19 (<0.001) in diabetes patients. Analyzing the wave of infection and diabetes patients with Covid-19 infection the substantial relation has been found. Additionally, analyzing the symptoms of the patients it has been seen that diabetic patients are more likely to have symptoms of fever, cough and fatigue, out of which fever is the more prevalent symptoms which was found in almost 90% percent of the patients. According to the criteria in the methodology, evaluation has been done that severity of the infection in the patients were very high

(p= <0.001) that means that the patients in diabetic group very critically ill. This suggests that the diabetic people are more likely to progress to severe condition after the infection. The results also show that the BMI which plays very important role in the diabetes patients also have the significant association with severity of the infection in the patients of diabetes. Considering the severity, it's been also depicted that the treatment opted by the diabetic group were more of the hospital stay than self-isolation comparing to the non-diabetic one. The recovery period was also found to be substantially associated and found that the period was longer in the diabetic individuals due to the fact, of their older age and might be because of the severe inflammatory responses. The vaccination status cannot be set as the criteria for analysis, because during first wave the vaccination was given to few individuals only and in second and third wave a quite no. of people was vaccinated, so the comparison cannot be done.

These results suggest that more attention and care should be paid to the patients with older age,people lying in the range of higher BMI and diabetes patients as they are more prone to the infection.

It is very difficult to predict the future prospects of the COVID- 19 infection as we cannot think when (short and medium term) and how the virus can disappear. New variants may also appear, and vaccination may predictably will go longer until a large number of populations get protected.
Currently, the India has passed the third wave and still a large number people are getting infected. Our study indicates that the characteristics of the infection may vary over the time and the conclusions of our work suggest that we must remain observant in the constant study of the characteristics of the infection. And if necessary, modified treatment and care could be given to the people.

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