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New Onset of Diabetes in Adults with Post-Covid Infection in a Tertiary Care Hospital

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Aim/Scope: This study is aimed to investigate the incidence of diabetes after infection with the coronavirus (COVID-19). SARS COV2 is a rapidly spreading disease which causes morbidity and mortality. One of the most important complications associated with covid 19 is Diabetes Mellitus. **Materials & Methods:** This was a retrospective descriptive study of (50 diabetic and 50 non-diabetic) patients who had a previous history of covid-19 and who are infected during the second wave (Aug'21-Oct'21) at a tertiary care hospital, Hyderabad, India. Data collected including patient demographic and baseline characteristics like patient's age, sex and history of covid infection were analyzed using Statistical Package for Social Sciences (SPSS) software version 22.0. **Results:** In the study among covid infected(n=50) subjects who were tested diabetic after Long Covid, 28(56%) were hospitalized, 13(26%) were found to have ICU admissions and 9(18%) were discharged with mild covid symptoms and the subjects(n=50) who didn't have any symptoms of diabetes after Long Covid, majority 32(64%) were found to be discharged with mild covid symptoms, 5(10%) were found to have ICU admissions and 13 (26%)were found to be hospitalized with the critical covid condition. It was observed that patients hospitalized with critical covid conditions were susceptible to onset of diabetes (p-value: 0.10) **Conclusion:** This study showed a high incidence of complications in patients infected with COVID-19 with diabetes being the most common one. Patients with poor glycemic control should be routinely monitored and treated appropriately

Keywords: COVID 19, diabetes, HbA1c, SARS COV2

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Introduction

COVID-19 is caused by the SARS COV2 virus. It is the most recent and dreadful pandemic that affected millions of people across the globe. It can cause mild to severe upper respiratory tract infections. To gather information on people with diabetes linked to COVID-19, a new worldwide registry has been created. New research reveals that COVID-19 may potentially cause healthy individuals to develop diabetes. [1].

Similar to the first pandemic wave, about half of the infected individuals during the second wave have at least one comorbidity. Diabetes mellitus has been one of the characteristic co-morbidities that has persistently been linked to severe illness, acute respiratory distress syndrome, and death in COVID-19 from the start of the pandemic [2]. Diabetes has been implicated as the most important cause of mortality in COVID-19 hospitalized patients.

Additionally, COVID-19 has been linked to the emergence of newly developed diabetes (NOD) [3]. During the acute COVID-19 phase, also known as the "Long COVID," or during the post-acute COVID phase, new-onset diabetes might appear. In a retrospective cohort analysis of 47,780 COVID-19 patients in England who had been discharged, the rate of NOD was 29 / 1000 person-years with a mean follow-up of 4.6 months. The patients' median age was 65. [4] Yang et al. reported that patients with SARS (caused by SARS-CoV, the "cousin" of SARS-CoV-2) who had never received glucocorticoids had significantly higher fasting plasma glucose levels than patients with non-SARS pneumonia. Although any serious illness can be associated with stress-related hyperglycemia.

The present study aimed to find the association of diabetes as co-morbidity in post-COVID-infected patients.

Materials And Methods

Setting: The present study was carried out in the department of medicine at a tertiary health care centre. The study population were patients diagnosed with diabetes previously infected with covid infection.

Duration and type of the study: A single-centred retrospective descriptive study was carried out from January 2022 to June 2022 (6 months)

Sampling methods: The medical records of covid 19 patients who were hospitalized were obtained and reviewed to determine the patient's age, sex and history of diabetes development, HbA1c levels and severity of infection.

Sample size calculation: A total of 100 covid 19 patients (50 diabetics and 50 non-diabetic) were selected for this retrospective study.

Inclusion Criteria: Data of adult patients previously infected with COVID-19 between the age group 18-45 years were included in the study.

Exclusion Criteria: All the other means of diabetic onsets such as juvenile diabetes, gestational diabetes, and pediatric and geriatric populations with a history of covid were excluded from the study.

Data collection procedure: Data were collected into a Microsoft Excel sheet considering various factors like patient age, sex and history of covid 19 infection.

Statistical Analysis: Data were entered into a Microsoft Excel sheet and were analyzed using SPSS Software version 22.0(IBM SPSS statistics). Categorical data was represented in the form of frequencies and proportions in MS Excel and MS Word. The Chi-square test was used as a test of significance for qualitative data and a p-value <0.05 was considered statistically significant.

Results

Among Covid infected patients, the majority of subjects 16(32%) were in the age group 32-45 years, and among non-infected patients, the majority of subjects 19(38%) were in the age group 25-31 years. There was no significant difference in age distribution between covid infected and non-infected subjects.

Table 1: Profile of Subjects in the study

Demographic Variables		COVID-19 INFECTION						P-value
		Yes		No		Total		0.025
		Count	%	Count	%	Count	%	
Age (Years)	18-24	8	16%	7	14%	15	15%	
	25-31	17	34%	19	38%	36	36%	
	32-38	9	18%	11	22%	20	20%	
	39-45	16	32%	13	26%	29	29%	
Sex	Male	32	64%	29	58%	61	61%	0.061
	Female	18	36%	21	42%	39	39%	

Among the infected, 32(64%) were male and 18(36%) were female and among the non-infected 29(58%) were male and 21(42%) were females. There was no significant difference in sex distribution between infected and non-infected subjects.

In this study, among the subjects who were tested diabetic after Long Covid, 28(56%) were hospitalized, 13(26%) were found to be still in ICU and 9(18%) were discharged with mild covid symptoms. Of those who didn't have any symptoms of diabetes after Long Covid, the majority 32(64%) were found to be discharged with mild covid symptoms, 5(10%) were found to have ICU admissions and 13 (26%) were found to be hospitalized with the critical covid condition. There was no significant difference between the onset of diabetes in infected and non-infected individuals (with p-value-0.10)

Table 02: Prevalence of covid-induced diabetes in various stages of Infection

Hospital data Of subjects	Covid Induced Diabetes					
	YES		NO		TOTAL	
	Count	Percent (%)	Count	Percent (%)	Count	Percent (%)
Hospitalized (Critical covid)	28	56%	13	26%	41	41%
Still in ICU (severe covid)	13	26%	5	10%	18	18%
Discharged (mild covid)	9	18%	32	64%	41	41%
Total	50	100%	50	100%	100	100%

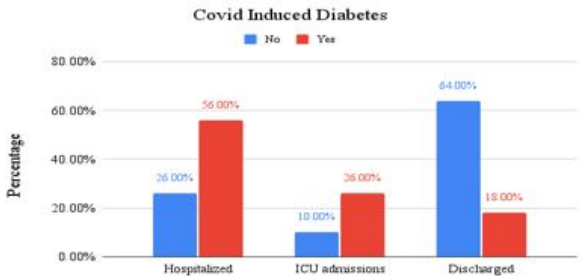

Figure- 03 Bar diagram showing onset of diabetes in different scenarios

Discussion

A difficult condition to manage in the COVID-19 pandemic is diabetes mellitus. Compared to non-exposed individuals, patients hospitalised in intensive care units for COVID-19 have a death rate that is at least twice as high and a two- to three-fold greater prevalence of diabetes [5].

Chronic inflammatory processes and increased susceptibility to infection in people with diabetes mellitus are both associated with hyperglycemia. Granulocytes, monocytes/macrophages, dendritic cells, natural killer (NK) cells, B cells, T cells, and cytokine signalling all exhibit defects in the innate response. [6]. Poor glycemic management has been linked to an increased risk of infections, and hyperglycemia can weaken the host's defences.

The association between covid 19 and diabetes is now recognised to include a complicated etiology. Infection with SARS-CoV-2 leads to increased reactive oxygen species (ROS) production. These effects lead to lung fibrosis, acute lung damage and acute respiratory distress syndrome (ARDS). Hyperglycemia and insulin resistance can result from the creation of ROS and viral renin-angiotensin-aldosterone system (RAAS) activation via increased angiotensin II expression. [7]. The pancreas expresses ACE2, and its mRNA levels are greater than those of the lungs. Both the islets and the exocrine pancreas have the expression of ACE2. Elevated blood amylase and/or lipase are signs of exocrine pancreatic damage in 1-2% and 17%, of individuals with non-severe and severe COVID-19 respectively.

They found that SARS-CoV-2 selectively infects human islet cells in vitro and infects human pancreatic cells in individuals who died from COVID-19. [9]. Only 30% of the COVID-19 patients had beta-cell ACE2 expression, despite 70% of the patients expressing ACE2 in the vasculature. Necroptotic cell death, immune cell infiltration, and SARS-CoV-2 viral infection of pancreatic beta-cells may all play a role in varying degrees of metabolic dysregulation in COVID-19 patients even in the absence of new-onset diabetes. [10].

COVID-19, like SARS-CoV-1 to enter the cell, uses ACE-2 as a receptor [11]. This receptor ACE-2 expresses in many locations such as the heart, renal tubular epithelium, endothelium, intestinal epithelium and pancreas apart from type 1 and type 2 epithelial alveolar cells in the lungs and upper respiratory tract. A conformational change in the S-glycoprotein is caused by the binding of S-glycoprotein to ACE-2 on the surface of COVID-19, which leads to proteolytic digestion by proteases such as TMPRSS2 and Furin that acts as host cell allowing the virion to be internalized [12].

These cellular entries of the virus produce interferon γ by triggering an inflammatory response with T helper cells, which further leads to other inflammatory cells causing a cytokine storm which eventually leads to organ damage and failure of multiple organs observed mainly in severe cases of infection.

Reiterer et al. discovered that among 4,102 U.S. hospitalised COVID-19 patients, those with ARDS had a higher prevalence of hyperglycemia with poor outcomes (85%) than those without ARDS (37%), which was suggested as the plausible mechanism behind the development of "acute diabetes" in patients with SARS [13]. They examined plasma samples for hormones that control glucose homeostasis and were able to discriminate between B-cell failure or insulin resistance associated with hyperglycemia [14].

Montefusco et al. Had similar insights about Covid 19 and insulin resistance and tested impaired glucose homeostasis in long run. Among 551 hospitalized Italian patients, 253 patients (46%) with no prior diabetes history exhibited new-onset hyperglycemia during acute COVID-19. Among this subset, 35% remained hyperglycemic 6 months after COVID-19 recovery while an additional 2% were diagnosed with T2D, indicating that new-onset hyperglycemia can predispose individuals to long-term glycemic abnormalities.[15].

Several published studies have reported that 12% to 22% of COVID-19 patients have comorbid diabetes, and a report of 72,314 patients with COVID-19 published by the Chinese Centre for Disease Control and Prevention found increased mortality in people with diabetes [16]. Zhou's research results also revealed that the risk of in-hospital death was 2.85 times higher in patients with diabetes than in those without diabetes. Obviously, the presence of diabetes is associated with increased mortality [17].

Numerous cytokines increase in SARS-CoV-2 disease. IL-6 plays a higher deleterious role in SARS-CoV-2 disease and it is increased in diabetes [18]. Monoclonal antibodies such as tocilizumab which inhibits IL-6 receptor is being tested in a trial in SARS-CoV-2[19].

As a result, lowering mortality depends greatly on how diabetes patients' blood glucose is managed. Therefore, blood glucose levels in patients should be closely monitored to lower diabetes-related complications and death.

Data on the relationship between blood glucose management and COVID-19 results are still few. It is still unknown if newly developed SARS-CoV-2-induced diabetes results from recognised pathways in T1D or T2D or instead reflects an unusual kind of diabetes due to the COVID-19 pandemic's changing nature.

Furthermore, it is yet unknown if COVID-19 individuals are still more likely to experience newly appearing diabetes or other associated issues after the virus has been cleared and recovered.[20].

Cases of new-onset diabetes following COVID-19 have been reported in India and other countries. SARS COV-2 gains entry into the cell using receptor Angiotensin Converting Enzyme-2 (ACE-2) present in pancreatic beta cells leading to the development of diabetes. [21].

A study shows that 6 out of 9 patients with COVID-19 and pancreatic injury were found to have raised blood glucose levels. This finding suggests that pancreatic injury after COVID-19 may be caused by 3 different mechanisms including the direct cytopathic effect of SARS-COV-2 replication, the indirect effect of systemic responses to respiratory failure or the harmful immune response induced by SARS-COV-2 and drug-related pancreatic injury in those who take acetaminophen before admission. [22].

Lockdown as a result of COVID-19 can cause movement restriction, sedentary lifestyle, improper diet, and stress which can worsen HbA1C and complications of diabetes mellitus. A sedentary lifestyle and the unavailability of healthy food can cause weight gain. Patients with obesity and COVID have worse outcomes, increasing both mortality and ventilation requirements. [23].

Patients who have COVID-19 along with raised pancreatic enzyme levels have significantly worse outcomes such as the need for hospital admission, ventilation and mortality. [24].Diabetes-specific risk factors worsen the outcome of COVID-19 and limited evidence indicates that patients with undiagnosed Type 2 diabetes mellitus have worse outcomes as compared to patients with diagnosed DM. [25].

Limitation

The major limitations of this study were the small sample size and the interpretation of the statistical significance of the mentioned data requires a lot of caution and skill.

Conclusion

The outbreak of the COVID-19 pandemic has caused a global health crisis of our time. A growing body of clinical evidence shows that patients with a previous history of COVID19 are highly susceptible to diabetes mellitus and its associated mortality rates. The exact mechanisms linking diabetes and COVID19 remain to be further elucidated, but our observations suggest that the risk of the onset of T2DM in patients exposed previously to Sars Cov2 infection is higher in exposed than non-exposed patients. The requirement for further studies involving a larger sample size needs to be considered to draw further conclusions.

Based on our observations in this study, it explains that the risk of new onset of T2DM is higher in patients previously hospitalized with Sars Cov2, however, the risk is still high in patients with any severity of covid 19 infection due to damage of beta islet cells of the pancreas caused by viral cytokine storm.

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