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Original Research Article

IMPACT OF DIABETES ON COVID 19 CLINICAL OUTCOMES -A COMPARATIVE STUDY

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Corresponding Author:
Dr. Muraly C.P,
Email: muralycp@gmail.com

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Anand T.R[1], Harine Shathyakumar[2], Renny Issac[3], Muraly C.P[4], Sudhiraj T.S[5]

[1]Senior Resident, Department of General Medicine, Govt. Medical College Thrissur, Kerala, India
[2]Resident Intern, Department of General Medicine, Govt. Medical College Thrissur, Kerala. India.
[3]Professor, Department of General Medicine, Govt. Medical College Thrissur, Kerala, India
[4]Associate Professor, Department of Pulmonary Medicine, Medical College Thrissur, Kerala, India
[5]Associate Professor, Department of Community Medicine, Govt. Medical College Thrissur, Kerala, India

ABSTRACT

Background: The COVID-19 pandemic, caused by SARS-CoV-2, has posed significant challenges to healthcare systems worldwide. Diabetes mellitus (DM), a chronic condition associated with increased susceptibility to infections, has been identified as a major risk factor for severe COVID-19 outcomes. This prospective cohort study aimed to evaluate the clinical outcomes of diabetic patients infected with COVID-19 and assess the incidence of newly onset diabetes in non-diabetic COVID-19 patients. **Materials and Methods & Result:** The present study enrolled 50 diabetic and 50 non-diabetic COVID-19 patients admitted to a tertiary care teaching hospital in South India , from April 2021 to March 2022. Patients were followed during their hospital stay, and their disease severity, complications, and clinical outcomes were compared. The study revealed that diabetic COVID-19 patients presented with higher disease severity, with 56% classified as Category C severe compared to 12% in the non-diabetic group. Diabetic patients experienced significantly higher rates of complications, including acute respiratory distress syndrome (64% vs. 12%), acute cardiac injury (16% vs. 0%), acute kidney injury (36% vs. 8%), and sepsis (36% vs. 4%). ICU admissions (52% vs. 12%) and mortality rates (36% vs. 8%) were also higher among diabetic patients. **Conclusion:** Diabetic COVID-19 patients consistently present with more severe disease compared to non-diabetic individuals, as demonstrated by higher rates of ICU admissions, increased mortality, and greater complications such as ARDS, acute cardiac injury, acute kidney injury, and sepsis. The need for antibiotics and steroids is markedly higher among diabetic patients, reflecting their vulnerability to secondary infections and escalated inflammation.

INTRODUCTION

Impact of Diabetes on Covid 19 clinical outcomes -A comparative study

The global outbreak of COVID-19, caused by the novel coronavirus SARS-CoV-2, has significantly affected public health, economies, and healthcare systems worldwide. While most individuals infected with the virus experience mild to moderate respiratory symptoms and recover without advanced treatment, certain populations face much greater risks. Among these vulnerable groups, individuals with diabetes mellitus stand out as particularly susceptible to severe disease and complications.[1]

Over the past two decades, diabetes has emerged as a major global health threat, and extensive evidence shows that diabetic patients are more prone to infections and poorer prognoses compared to non-diabetic individuals.[2,3] This heightened vulnerability was evident in previous coronavirus outbreaks, such as SARS in 2002, where diabetes was independently linked to adverse outcomes.[4] Similarly, during the COVID-19 pandemic, research indicates that diabetes is a common comorbidity among those with severe infections and higher ICU admissions. Reports from the Center for Disease Control and Prevention further highlight that patients with type 2 diabetes and metabolic syndrome may have a significantly increased risk of death if infected with COVID-19.[5]

Beyond direct cellular damage, COVID-19 infection can also result in the alteration of self-antigens, potentially triggering immune-mediated destruction of β-cells. Additionally, evidence suggests that in patients with pre-existing type 2 diabetes mellitus (T2DM), COVID-19 can further exacerbate insulin resistance, leading to worsening glycemic control.

Understanding these processes is critical because they explain how SARS-CoV-2 infection may cause new cases of diabetes and contribute to poorer outcomes in individuals already suffering from diabetes.

Abdullah Alshukry et al,[6] in their study titled "Clinical Characteristics and Outcomes of COVID-19 patients with diabetes mellitus in Kuwait", retrospectively studied 417 consecutive COVID-19 patients, and analyzed and compared disease severity, outcome, associated complications, and clinical laboratory findings between diabetic and non-diabetic COVID-19 patients. Similar Study done by Qiao Shi et al,[7] titled "Clinical Characteristics and Risk Factors for Mortality of COVID-19 Patients With Diabetes in Wuhan, China: A Two-Center, Retrospective Study described the characteristics and outcomes and analyzed the risk factors for in-hospital mortality of COVID-19 patients with diabetes. This study was performed at two tertiary hospitals in Wuhan, China involving confirmed COVID-19 patients with diabetes (N=53) who were discharged or died from 1 January 2020 to 8 March 2020 and they made into a conclusion that COVID-19 patients with diabetes had worse outcomes compared with the sex- and age-matched patients without diabetes.

context of the COVID-19 pandemic, optimizing glycaemia in hospitalized patients is of paramount importance and screening to detect undiagnosed cases of diabetes may be particularly relevant.

Lihua Zhu et al,[8] As the studies are very limited regarding this topic, the current study can fill the gap between the association of Diabetes and COVID 19 morbidity.

Given these findings, it is imperative to explore the clinical outcomes of COVID-19 among diabetic patients. Understanding how diabetes impacts disease severity and progression will be crucial for guiding future treatment strategies and improving patient outcomes.

Aims and objectives

To evaluate the clinical outcomes of diabetic patients infected with COVID-19:

This objective seeks to understand how pre-existing diabetes influences the severity, progression, and recovery rates in patients who contract COVID-19, providing valuable insights for optimizing care strategies and reducing adverse outcomes.

MATERIALS AND METHODS

This study was conducted in a teritiary care teaching hospital in South India during the Covid 19 pandemic. This was a coghort study of patients admitted with Covid 19 infection and diabetes mellitus. The data were compared with Non diabetic Covid 19 infected patients.

Inclusion Criteria

Consecutive patients who were admitted as COVID-19 POSITIVE, COVID Positive wards and ICU

Exclusion Criteria

Patients less than 18 years of age were excluded

Sample Size Calculation

Cohort Sample size is calculated using the formula :

n=2 $(Z\alpha 2+Z\beta)2$ $p(1-p)(p1-p2)2$

Reference study study conducted by Alshukry A et al (6)

$p1$=42.4 ; $p2$=6.6 In case of ARDS

Hence the minimum sample size needed was calculated to be 23 in each group with the total of 46. So the sample size is set as 100 (50 in each group)

Study Procedure

Consecutive patients satisfying the inclusion criteria were enrolled in the study. All the participants were subjected to thorough clinical examination and routine blood investigation. They were divided into 2 groups based on the diabetic status at the time of admission.

1. COVID Positive Patient with Diabetes
2. COVID Positive Patient without Diabetes

These patients were prospectively followed up during the hospital stay. Patients demographic details, severity and complications and clinical outcomes were compared between the two groups. Also the incidence of newly detected diabetes in non-diabetic Covid patients were also observed during the hospital stay. This study enrolled patients during April 2021 to March 2022.,

Operational definitions

Diagnosis of ARDS is determined based on Berlin Definition.[9]

Presence of Cardiac injury is established based on cardiac blood markers and ECG

Acute kidney injury is evaluated based on KDIGO definition.[10]

Sepsis is evaluated based on Sepsis III guidelines.[11]

The quantitative data were analysed in terms of mean, median and standard deviation. Qualitative data were expressed in proportion. Comparison between the groups of qualitative data was done using Chi Square test and $p<0.05$ was taken as significant.

RESULTS & DISCUSSION

In the present study, the study population is divided into 50 Diabetic COVID-19 patients and 50 Non Diabetic COVID-19 patients. Among Diabetic group, 28 (56.0%) were male and 22 (44.0%) were female. Whereas in Non-Diabetic group 36 (72.0%) were male and 14 (28.0%) were female. The p value showed that sex was comparable between groups. The mean age was 58.5 ± 16.1 in Diabetic group and 61.6 ± 10.9 in Non-Diabetic group. The p value showed that age was also comparable between the two groups. Majority of them were in the age group of 61 to 70 years. However a study conducted by Yingyu Chen et al,[12] showed, median age of the patients was 64 years which was similar to present study. In a study conducted by Abdullah Alshukry et al,[6] the mean age of the Non Diabetic group was 39.55 (±16.59) years and mean age of the Diabetic

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group was 56.44 (±11.64) which was also similar to the present study

When the duration of Diabetes in Diabetic group is taken into account, for 46 (92.0%) participants duration of diabetes was less than 10 years. Only 4 (8.0%) participants had duration of diabetes of more than 10 years.

The present study showed there is NO significant differences in other co-morbidities for diabetic Covid-19 patients versus non-diabetic patients, including hypertension (46.0% versus 36.0%, p=0.300), coronary artery disease (38.0% versus 40.0%, p=0.838), cerebrovascular disease (12.0% versus 8.0%) and chronic kidney disease (12.0% versus 4.0%). So these two groups are comparable in terms of "Presence of other previous co-morbidities" However, study conducted by Yingyu Chen et al,[12] showed significant differences in comorbidities for diabetic COVID-19 patients versus non-diabetic patients, including hypertension (58.3% vs. 31.3%, P < 0.001), coronary heart disease (17.7% vs. 8.0%, P = 0.035), and chronic renal disease (6.3%vs 0%, P = 0.007). In the study by Abdullah Alshukry,[6] the diabetic group had a higher prevalence of comorbidities hypertension, asthma, cardiovascular disease, and chronic renal disease.

In diabetic group majority of the participants presented as Category C severe 28 (56.0%), followed by Category B in 12 (24.0%) participants and 10 (20.0%) were Category C moderate. Whereas in non-diabetic group, majority of the participants were in the category B 40 (80.0%), followed by category C severe in 6 (12.0%) and 2 (4.0%) participants in each category A and category C moderate. The p value showed that diabetic covid-19 patients had higher severity of disease compared to non-diabetic group.

The present study showed significant differences in ARDS for diabetic Covid-19 group compared to non-diabetic group (64.0% versus 12.0%, p<0.01). The study by Wu et al,[13] also showed that diabetes was associated with a hazard ratio of 2.3 for ARDS. Study done by Qiao Shi et al also showed similar findings as the patients with diabetes were more likely to have ARDS (24.8% vs. 11.1%) compared to the Non Diabetic group

In diabetic Covid-19 group, 8 (16.0%) participant had developed acute cardiac injury whereas in non-diabetic group none of them developed acute cardiac injury. It was also statistically associated (p=0.003). In the Study done by Qiao Shi et al,[7] also it is found out that Patients with diabetes were more likely to have acute cardiac injury (30.7% vs. 17.0%) compared with patients without Diabetes (p=0.005) Abdullah Alshukry et al,[6] study also stated that compared to Non Diabetic group, Diabetic group had a considerably greater prevalence of Cardiac injury (19.4% Vs. 2.6%) (p value <0.001)

In diabetic Covid-19 group, 18 (36.0%) participants had developed acute kidney injury whereas in non-diabetic group only 4(8.0%) were developed acute kidney injury. The p value showed that acute kidney injury was significantly higher in diabetic covid-19 group compared to non-diabetic group (p<0.01). Study done by Qiao Shi et al also showed that patients with diabetes were more likely to have AKI (12.4% vs.3.3%) (p value=0.003) Abdullah Alshukry,[6] also showed similar statistically significant (p<0.001) findings and stated that Diabetic group had developed acute kidney injury than Non Diabetics (24.3% Vs.2.2%)

In diabetic Covid-19 group, 18 (36.0%) participants had developed sepsis whereas in non-diabetic group only 2 (4.0%) were developed sepsis. The p value showed that sepsis was significantly higher in diabetic covid-19 group compared to non-diabetic group (p<0.01). Similar findings are obtained in the study of Abdullah Alshukry,[6] where Diabetic group had a high prevalence of Sepsis (31% vs. 4.8%) compared to the Non Diabetic group (p <0.001)

In the present study, Invasive Mechanical Ventilation was initiated more in diabetic covid-19 patients than non-diabetic patients (32.0% versus 4.0%, p<0.01). However, Qiao Shi et al,[7] in their study demonstrated that among all of the treatment strategies, only non-invasive mechanical ventilation (13.7% vs.5.2%, P = 0.05) was applied more commonly in patients with diabetes. Yingyu Chen et al,[12] also showed Non-invasive mechanical ventilation was initiated in more diabetic patients than non-diabetic patients (4.2% vs. 1.8%, P = 0.306)

Under strict glycemic control measures, in the present study, diabetic Covid-19 group, 36 (72.0%) participants received steroids whereas in non-diabetic group 8 (16.0%) were received steroids. The p value showed that usage of steroids was significantly higher in diabetic covid-19 group compared to non-diabetic group (p<0.01). Also In diabetic Covid-19 group, 38 (76.0%) participants were received Antibiotics whereas in non-diabetic group 4 (8.0%) were received Antibiotics. The p value showed that usage of Antibiotics were significantly higher in diabetic covid-19 group compared to non-diabetic group (p<0.01).

In the present study, in diabetic Covid-19 group, 32 (64.0%) were discharged and 18 (36.0%) were died. Whereas in non-diabetic group 46 (92.0%) were discharged and 4 (8.0%) were died. The p value showed death rate was higher in diabetic covid-19 group compared to non-diabetic group (p<0.01). Similarly Abdullah Alshukry et al,[6] also found that the diabetes group had a significantly higher percentage of death as compared with the non-diabetic group (16.7% vs. 12.1%, p < 0.001; Qiao Shi et al.[7]

also made the finding as Death was more common in patients with diabetes (20.3% vs. 10.5%, P , 0.05) in their study. But Yingyu Chen et al,[12] in their study showed that among the patients with diabetes, a tendency toward severe prognosis was observed, even though there was no statistical significance in the clinical outcomes between the diabetic and non-diabetic groups such as discharge from hospital (84.8% vs 88.4%,P = 0.397), death (6.3% vs. 2.7%, P = 0.307).

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In diabetic Covid-19 patients have higher rates of need for intensive care unit 26 (52.0%) than non-diabetic group 6 (12.0%). It was statistically significant ($p<0.01$) According to the study by Abdullah Alshukry,[6] COVID-19 patients with diabetes had more ICU admission than non-diabetic COVID-19 patients (20.1% vs. 16.8%, $p<0.001$). Qiao Shi et al also similar results in their study which stated that Patients with diabetes were more likely to require intensive care unit (ICU) admission (17.6% vs.7.8%, P=0.05).

Out of 50 Non Diabetic participants, 10 (12.0%) were newly developed diabetes during Covid-19 infection during the hospital stay. In a retrospective cohort study conducted by Wolfgang Rathmann et al,[14] titled "Incidence of newly diagnosed after Covid-19", it is observed that COVID-19 confers an increased risk for new onset type 2 Diabetes compared with other acute upper respiratory infections (15.8 vs. 12.3 per 1000 person years) . The precise mechanisms behind the development of new-onset diagnosis in people with COVID-19 are not known, but it is likely that a number of complex, interrelated etiologies are responsible, including impairments in glucose disposal and insulin secretion, stress hyperglycemia and preadmission diabetes. Acute hyperglycemia with coronavirus infection has been linked to the binding of the coronavirus to the ACE2 receptor in the pancreatic islet cells. ACE2 expression has been shown to be higher in the pancreas than the lungs and expressed in both exocrine glands and the islets of the pancreas, including β-cells. Alternatively, the proinflammatory cytokines and acute-phase reactants due to COVID-19 could directly cause inflammation and damage to pancreatic β-cell. Another study reported that the SARS-CoV-2 receptor and ACE2 and related entry factors are expressed in the pancreatic β-cells, and in COVID-19 patients they infect β-cells, attenuate pancreatic insulin levels and secretion, and induce β-cell apoptosis.[15]

In general, the present study concluded that the patients with Diabetes had more severe COVID-19 outcomes than the patients without Diabetes, represented by the high proportion of Severe Covid Categories, ICU admissions and deaths. Results of the present study are in agreement with findings obtained from study conducted by Abdullah Alshukry in COVID 19 patients in Kuwait. Our results are also similar to the findings obtained from a Chinese COVID-19 cohort in which Diabetic patients had a 7.3% increased risk of mortality than 2.3% for the general population.[16] Moreover, British Cohort showed that COVID-19 patients with uncontrolled diabetes had a higher death risk than the other patients did.[17]

Present study also showed that the Diabetic COVID-19 patients had significant complications like ARDS, acute kidney injury, acute cardiac injury and sepsis when compared with the non-diabetic patients. Study of Abdullah Alshukry et al in COVID 19 patients in Kuwait also showed similar results.

Even recent Indian similar Studies done by Naveen Mittal et al,[18] & Viny Kantroo et al,[19] came to a conclusion that the presence of diabetes can be considered as a significant risk factor for mortality in patients with COVID-19. Lastly, to conclude aggressive treatment for diabetes mellitus must be considered in the management of hospitalized COVID-19 patients.

CONCLUSION

Diabetic COVID-19 patients consistently present with more severe disease compared to non-diabetic individuals, as demonstrated by higher rates of ICU admissions, increased mortality, and greater complications such as ARDS, acute cardiac injury, acute kidney injury, and sepsis. The need for antibiotics and steroids is markedly higher among diabetic patients, reflecting their vulnerability to secondary infections and escalated inflammation. Diabetes remains a substantial risk factor for poor outcomes and elevated mortality in the context of COVID-19, underscoring the necessity for prompt and aggressive management of glycemic status in hospitalized cases.

These findings highlight the critical importance of recognizing diabetes as a major modifier of COVID-19 severity and outcome, and call for rigorous monitoring, tailored treatment strategies, and heightened awareness of post-infection metabolic complications in this population.

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