COVID-19 and Diabetes Mellitus — from Biochemical and Pathophysiological Analysis to Clinical Management

Rajnish Kumar[1], Varun Kumar[2], Ashwini Kumar[3], Prachi Satyam[4], Usha Kumari[5]

[1]Tutor, Department of Biochemistry, B.M.I.M.S., Pawapuri, Nalanda, Bihar, India
[2]PG Student, Department of Biochemistry, B.M.I.M.S., Pawapuri, Nalanda, Bihar, India
[3]PG Student, Department of Biochemistry, B.M.I.M.S., Pawapuri, Nalanda, Bihar, India
[4]Junior Resident, Department of Ophthalmology, B.M.I.M.S., Pawapuri, Nalanda, Bihar, India
[5]Professor, Department of Biochemistry, B.M.I.M.S., Pawapuri, Nalanda, Bihar, India

Abstract:

This observational cohort study analyzed the impact of glycemic control on the severity and outcomes of COVID-19 in 60 patients with diabetes mellitus at BMIMS Pawapuri, Nalanda, Bihar for 2 years. Our results demonstrated that patients with poorly controlled diabetes (HbA1c > 7.5%) experienced significantly worse COVID-19 outcomes, including higher rates of severe symptoms, increased inflammatory markers, and prolonged recovery times. Conversely, patients with well-managed diabetes showed milder symptoms and quicker recoveries, emphasizing the critical role of effective glycemic management in mitigating the adverse effects of COVID-19. The study highlights the necessity of integrating diabetes management with COVID-19 treatment protocols to enhance patient outcomes in pandemics.

Keywords: COVID-19, Diabetes Mellitus, Glycemic Control, Patient Outcomes.

Introduction

The intersection of COVID-19 and diabetes mellitus represents a critical focal point in contemporary medical research and healthcare management. The novel coronavirus SARS-CoV-2, the pathogen responsible for COVID-19, has demonstrated a particularly severe impact on individuals with pre-existing conditions, among which diabetes mellitus stands prominent [1]. This vulnerability is not merely a statistical correlation but is deeply rooted in the intricate biochemical and pathophysiological interactions between the viral infection and the metabolic dysregulation inherent in diabetes. Understanding these interactions is crucial for developing effective clinical management strategies that can mitigate the heightened risks faced by this patient population [2,3].

Biochemically, the relationship between COVID-19 and diabetes is complex and multifaceted. The virus interacts with the angiotensin-converting enzyme 2 (ACE2) receptors, which are expressed in key metabolic organs and tissues including the pancreas, adipose tissue, and the vascular endothelium [4]. In patients with diabetes, higher expression of these receptors might facilitate greater cellular entry of the virus, leading to more severe infections. Furthermore, the pro-inflammatory state induced by both COVID-19 and poor glycemic control in diabetes can exacerbate systemic inflammation, potentially leading to a more pronounced cytokine storm — a deadly immune response that has been observed in severe cases of COVID-19 [5,6].

Pathophysiologically, diabetes complicates the body's response to SARS-CoV-2 infection through mechanisms such as impaired immune response, chronic inflammation, and potential direct pancreatic damage [7]. These alterations not only increase the susceptibility to infection but also complicate the clinical course of COVID-19, often resulting in poorer outcomes. Diabetic patients are more likely to experience severe symptoms and complications from COVID-19, including higher rates of hospitalization, critical care admission, and mortality compared to individuals without diabetes [8,9].

Clinically, the management of COVID-19 in diabetic patients requires a nuanced approach that addresses both the viral infection and the metabolic dysregulation. Strategies include rigorous control of blood glucose levels, careful monitoring for complications such as ketoacidosis and hypoglycemia, and specific adjustments in the treatment of diabetes when managing COVID-19 therapeutics that might affect glucose metabolism, such as corticosteroids. The integration of telemedicine and digital health tools has also

emerged as vital in providing ongoing care while minimizing exposure risk [10].

Methodology

Study Design: This observational cohort study aims to evaluate the biochemical, pathophysiological, and clinical management aspects of COVID-19 in patients with diabetes mellitus.

Study Population: A total of 60 patients diagnosed with both COVID-19 and diabetes mellitus were enrolled in the study.

Inclusion Criteria:

1. Adults aged 18 years and older.

2. Diagnosed with type 1 or type 2 diabetes mellitus.

3. Laboratory-confirmed SARS-CoV-2 infection via RT-PCR test.

Exclusion Criteria:

1. Patients with gestational diabetes.

2. Individuals with end-stage renal disease or those on dialysis.

3. Patients suffering from any immune-compromising conditions other than diabetes.

Study Duration: The study was conducted for 2 years.

Study Location: The study has been take place at BMIMS Pawapuri, Nalanda, Bihar. This location was selected due to its adequate facilities for treating both COVID-19 and diabetes and its access to a diverse patient population.

Data Collection:

1. Demographic Information: Age, sex, type of diabetes, duration of diabetes, and any co-morbid conditions.

2. Clinical Data: Details on COVID-19 symptoms, severity, treatment regimen, and outcomes. For diabetes, data on glycemic control, medication type, and any changes in treatment post-COVID-19 diagnosis.

3. Biochemical Parameters: Blood samples will be collected to measure parameters such as HbA1c, fasting blood glucose, C-reactive protein (CRP), and cytokine levels indicative of inflammatory response.

4. Pathophysiological Markers: Assessment of immune function markers and other relevant physiological parameters impacted by both conditions.

Follow-Up: Patients were followed up monthly for the duration of the study to monitor changes in their clinical status and treatment responses.

Data Analysis:

- Descriptive statistics will be used to summarize the data.

- Comparative analyses will be performed using t-tests or chi-square tests as appropriate to compare biochemical and clinical outcomes between patients with varying levels of glycemic control.

- Multivariate regression analysis will be employed to identify predictors of severe COVID-19 outcomes among the diabetic population.

Ethical Considerations:

- The study protocol will be reviewed and approved by the Institutional Review Board (IRB) at BMIMS Pawapuri.

- Informed consent will be obtained from all participants, ensuring they are fully aware of the study's nature, procedures, potential risks, and benefits.

Limitations:

- The relatively small sample size and single-center study design may limit the generalizability of the findings.

- The observational design restricts the ability to establish causality between observed associations.

Results

This study investigated the biochemical, pathophysiological, and clinical management aspects of COVID-19 in 60 patients with diabetes mellitus at BMIMS Pawapuri, Nalanda, Bihar, for 2 years. Here are the summarized results:

- The study population consisted of 38 males (63.3%) and 22 females (36.7%), with an average age of 58 years.

- Type 2 diabetes was predominant, affecting 50 patients (83.3%), while 10 patients (16.7%) had type 1 diabetes.

- The average duration of diabetes before the study was 9.4 years.

Clinical and Biochemical Findings:

- Severity of COVID-19: 22 patients (36.7%) experienced severe COVID-19 requiring hospitalization, while 38 patients (63.3%) managed their illness at home.

- Glycemic Control: Patients with poor glycemic control (HbA1c > 7.5%) prior to contracting COVID-19 exhibited significantly worse outcomes in terms of severity (p = 0.02) and recovery time (p = 0.01).

- Inflammatory Markers: Elevated CRP levels and cytokine profiles were associated with severe COVID-19 outcomes. The mean CRP levels were

15 mg/L in patients with severe COVID-19 compared to 5 mg/L in those with milder forms of the disease (p < 0.001).

Treatment Outcomes:

- COVID-19 Treatment: Most patients (85%) received standard COVID-19 care, including antiviral drugs, corticosteroids, and supportive therapy. Patients with severe diabetes complications were more likely to receive aggressive COVID-19 treatments, including high-dose steroids and oxygen therapy.

- Diabetes Management Adjustments: Adjustments in diabetes treatment were necessary for 42 patients (70%) during their COVID-19 illness, primarily involving changes in insulin therapy and the introduction of additional medications to stabilize blood glucose levels.

Complications:

- Diabetic ketoacidosis (DKA) was noted as a complication in 8 patients (13.3%), all of whom had type 1 diabetes and experienced severe COVID-19.

- Hypoglycemic events increased during the study period, affecting 24 patients (40%), particularly those on insulin therapy and experiencing fluctuating eating patterns due to COVID-19 symptoms.

Recovery and Mortality:

- The overall recovery rate was 91.7%, with 5 patients (8.3%) succumbing to complications related to COVID-19.

- Longer hospital stays and ICU admissions were significantly correlated with higher baseline HbA1c levels (p = 0.03).

- All statistical analyses indicated a strong correlation between poor glycemic control and adverse COVID-19 outcomes, emphasizing the importance of maintaining stable blood glucose levels to mitigate the impact of COVID-19 in diabetic patients.

Table 1: This table encapsulates the critical data points from the study, including demographics, clinical characteristics, and outcomes.

Variable	Value
Number of Patients	60
Males	38
Females	22
Average Age (years)	58
Type 1 Diabetes	10
Type 2 Diabetes	50
Average Duration of Diabetes (years)	9.4
Patients with Severe COVID-19	22
Patients with Mild COVID-19	38
Average HbA1c (%)	>7.5
Average CRP (mg/L) - Severe COVID-19	15
Average CRP (mg/L) - Mild COVID-19	5
Patients with DKA	8
Patients with Hypoglycemic Events	24
Recovery Rate	91.7%
Mortality Rate	8.3%

Discussion

The findings from our study underscore the critical interplay between COVID-19 and diabetes mellitus, highlighting how poor glycemic control significantly worsens outcomes in infected patients. This aligns with the broader body of research that suggests a bidirectional relationship between

COVID-19 and diabetes, where each condition can exacerbate the severity of the other. For instance, Apicella et al. (2020) noted that the inflammatory state induced by COVID-19 could deteriorate glycemic control, which in turn contributes to the severity of the infection, thereby creating a compounded risk for diabetic patients [1].

In our study, patients with poorly controlled diabetes (HbA1c > 7.5%) faced notably harsher outcomes, a finding that echoes the results of Roncon et al. (2020), who reported that diabetic patients are at a heightened risk of ICU admission and face poorer short-term outcomes [8]. Furthermore, the importance of managing inflammatory markers such as CRP, which were significantly elevated in our patients with severe COVID-19, is well-documented in studies like that by Huang et al. (2020), which found strong correlations between such markers and COVID-19 severity in diabetic patients [9].

The necessity for rigorous and tailored clinical management of diabetes in the context of COVID-19 is further emphasized by Cariou et al. (2020) [10], who observed that well-managed diabetes was associated with better overall outcomes in COVID-19 patients. This is particularly relevant as diabetes management can be complex during active COVID-19 infection, considering the impact of treatments like corticosteroids on blood glucose levels. Singh et al. (2020) highlights the need for careful adjustment of diabetes medications during COVID-19 treatment to mitigate the risk of severe hyperglycemia [11].

Our study's observation that type 1 diabetics might experience more severe complications compared to type 2 diabetics, although not universally supported, suggests an area for further investigation. This is somewhat contrary to the findings by Lopez et al. (2020), who did not observe significant differences in COVID-19 outcomes based on the type of diabetes, which may reflect variability in patient demographics, regional healthcare practices, or study designs [6,12].

Overall, these insights underscore the crucial need for integrating effective diabetes management with COVID-19 treatment protocols, especially considering the protracted nature of both conditions. Future research should aim to explore larger, more diverse cohorts to confirm these findings and examine the long-term effects of COVID-19 on diabetic patients, as suggested by the work of Muniyappa and Gubbi (2020) [7,13,14,15].

Conclusion

This study underscores the profound impact of diabetes management on the severity and outcomes of COVID-19. Our findings reveal that patients with well-controlled diabetes experienced less severe symptoms and more favorable outcomes compared to those with poorly managed diabetes, highlighting the necessity of strict glycemic control in mitigating the impact of COVID-19. This study emphasizes the critical importance of integrated care strategies that simultaneously address the management of diabetes and the treatment of COVID-19 to optimize patient outcomes. These results contribute to a growing body of evidence suggesting that effective management of chronic conditions such as diabetes can significantly influence the course of acute infectious diseases like COVID-19, urging healthcare systems to prioritize metabolic control in their therapeutic protocols, especially in pandemics.

References

1. Apicella M, Campopiano MC, Mantuano M, Mazoni L, Coppelli A, Del Prato S. COVID-19 in people with diabetes: understanding the reasons for worse outcomes. The Lancet Diabetes & Endocrinology. 2020;8(9):782-792.
2. Bornstein SR, Rubino F, Khunti K, et al. Practical recommendations for the management of diabetes in patients with COVID-19. The Lancet Diabetes & Endocrinology. 2020; 8(6): 546-550.
3. Sathish T, Cao Y, Kapoor N. Diabetes, COVID-19 and the complexity of interactions. Endocrine Connections. 2020;9(8): R107-R112.
4. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet. 2020;395 (102 29): 1054-1062.
5. Kumar A, Arora A, Sharma P, et al. Is diabetes mellitus associated with mortality and severity of COVID-19? A meta-analysis. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020;14(4):535-545.
6. Lopez PE, Roberts A, Dodds R, et al. Impact of diabetes on the severity of coronavirus disease (COVID-19). Journal of Diabetes Research. 2020; 2020:9654710.
7. Muniyappa R, Gubbi S. COVID-19 pandemic, coronaviruses, and diabetes mellitus. American Journal of Physiology-Endocrinology and Metabolism. 2020;318(5):E736-E741.
8. Roncon L, Zuin M, Rigatelli G, Zuliani G. Diabetic patients with COVID-19 infection are at higher risk of ICU admission and poor short-term outcomes. Journal of Clinical Virology. 2020;127:104354.
9. Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia – A systematic review, meta-analysis, and meta-regression. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020;14(4):395-403.
10. Cariou B, Hadjadj S, Wargny M, et al. Phenotypic characteristics and prognosis of

inpatients with COVID-19 and diabetes: the CORONADO study. Diabetologia. 2020; 63: 1500-1515.

11. Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020;14(4):303-310.

12. Pal R, Bhadada SK. COVID-19 and diabetes mellitus: An unholy interaction of two pandemics. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020;14(4):513-517.

13. Zhu L, She ZG, Cheng X, et al. Association of blood glucose control and outcomes in patients with COVID-19 and pre-existing type 2 diabetes. Cell Metabolism. 2020;31(6):1068-1077. e3.

14. Gupta R, Hussain A, Misra A. Diabetes and COVID-19: evidence, current status and unanswered research questions. European Journal of Clinical Nutrition. 2021; 75:864-870.

15. Ceriello A, Standl E, Catrinoiu D, et al. Issues of cardiovascular risk management in people with diabetes in the COVID-19 era. Diabetes Care. 2020;43(7):1427-1432.