



STUDY OF CLINICAL AND INVESTIGATION PROFILE OF COVID POSITIVE PATIENTS WITH TYPE 2 DIABETES MELLITUS IN MYH AND ASSOCIATED HOSPITALS

Dr Piyush Gupta*	MBBS PGT (M.D.), in Department of Medicine, Mahatma Gandhi Memorial medical college and Maharaja Yashwant Rao and associated group of hospitals, Indore, MP, India *Corresponding Author
Dr Dharmendra Jhavar	MD, DNB Medicine, Professor, Department of Medicine, Mahatma Gandhi Memorial medical college and Maharaja Yashwant Rao and associated group of hospitals, Indore, MP, India
Dr Karuna Thakur	MD Medicine, Associate Professor, Department of Medicine, Mahatma Gandhi Memorial medical college and Maharaja Yashwant Rao and associated group of hospitals, Indore, MP, India
Dr Mohit Gothwal	MBBS PGT (M.D.), in Department of Medicine, Mahatma Gandhi Memorial medical college and Maharaja Yashwant Rao and associated group of hospitals, Indore, MP, India
Dr Ved Prakash Pandey	MD Medicine, Professor and head, Department of Medicine, Mahatma Gandhi Memorial medical college and Maharaja Yashwant Rao and associated group of hospitals, Indore, MP, India

ABSTRACT

Background- COVID-19 disease in diabetic patients may provoke excessive stress and increased secretion of hormones such as catecholamine and glucocorticoid. Insulin resistance and hyperglycemia encourages production of oxidative stress. The severity of COVID-19 in diabetics could be due to the dysfunctional immune system, with increased susceptibility to viral infection and an exaggerated immune response like cytokine storm. Uncontrolled glycemic status weakens the immunity and provides a favorable condition for viral survival and longer recovery duration in diabetics. Therefore, we selected covid-19 patients with type 2 diabetes mellitus to study their clinical and investigation profile. **Methods-** 200 COVID-19-infected patients with T2DM in age group 30-60 years admitted in our 500 bedded covid dedicated hospitals associated with Maharaja Yashwantrao hospital, Indore, were observed for their clinical profile, complications, laboratory parameters, inflammatory markers, radiological parameters and outcome etc. Patients were divided into two study groups i.e. controlled diabetes group and uncontrolled diabetes group. **Results-** COVID-19 patients with uncontrolled diabetes status presented with more serious symptoms (predominantly shortness of breath), with significant fall in oxygen saturation, had prolonged hospital stay, with deranged laboratory parameters and markedly raised inflammatory markers, along with high chest CT severity score, required frequent clinical monitoring and higher attention regarding pharmacological treatment like strict glycemic controls, steroids, remdesivir, tocilizumab, immunoglobulins and supportive treatment like oxygen support, non-invasive ventilation, ICU care than those with controlled diabetes group. Patients in uncontrolled diabetes group developed significantly more complications (such as ARDS, DKA, Sepsis with MODS or Shock) and developed severe Covid-19 infection as compare to patients in controlled diabetes. Because of frequent monitoring, higher clinical attention and strict glycemic control of diabetes, there was no significant difference in outcome between both the study groups. **Conclusion-** HbA1c more than 7% in patients with diabetes mellitus should be considered a risk factor for an overall higher susceptibility for COVID-19 infection and severity in terms of symptomatic presentation, inflammatory cytokine storm, rapid and extensive lung involvement, requirement of more intensive care. Frequent monitoring of clinical, biochemical, radiological parameters resulted in good outcome equal to that of controlled diabetes group. Hence, some extreme measures for preventing COVID-19 in people with underlying DM are advisable beside an intensive care in already infected individuals.

KEYWORDS : covid-19, diabetes, severity, clinical, biochemical, inflammatory markers

INTRODUCTION

There is a two-way relationship between Covid-19 & diabetes. Diabetes is linked with an increased risk of severe Covid-19. whereas, severe metabolic complications of pre-existing diabetes, including diabetic ketoacidosis & hyperosmolality for which higher doses of insulin are required, have been seen in patients with Covid-19[1-3]. These manifestations of diabetes pose challenges in clinical management & suggest a complex pathophysiology of Covid-19 related diabetes.

Severe acute respiratory syndrome corona virus 2 (SARS - CoV-2), the virus that causes Covid-19, binds to angiotensin converting enzyme 2 (ACE2) receptors, which are expressed in key metabolic organs & tissues, including pancreatic beta cells, adipose tissue, the small intestine, & the kidneys [4]. Thus, it is likely that SARS-CoV-2 may cause alterations of glucose metabolism that could complicate the pathophysiology of pre-existing diabetes or lead to new mechanisms of disease.

The clinical spectrum of SARS-CoV-2 infection ranges from mild to critically ill cases, manifesting as asymptomatic infection, mild upper respiratory tract illness, & severe viral pneumonia with respiratory failure & even death.

Although most infected people are thought to have a favourable prognosis, chronic diseases commonly seen in elderly people, such as hypertension, diabetes mellitus, cerebral vascular disease, & their susceptibility conditions, may lead to poor clinical outcomes.

Case Study

In present study, out of total 200 covid-19 positive patients with type 2 DM of age group 30-60 years, 60(30%) patients had controlled diabetes (HbA1c level \leq 7%*) and 140(70%) patients had Uncontrolled diabetes (HbA1c level $>$ 7%*) reflecting their glycemic status of preceding 3 months. (* controlled diabetes status based on HbA1c levels- As per ADA guidelines).

Table No.1: Severity of COVID-19

Severity of COVID-19	Controlled Diabetes (n=60) (%)	Uncontrolled Diabetes (n=140) (%)	Total (n=200) (%)
Mild	15(25%)	7(5%)	22(11%)
Moderate	28(46.6%)	35(25%)	63(31.5%)
Severe	17(28.3%)	98(70%)	115(57.5%)

Chi Square value = 34.2131; p-value = 0.00001 Significant

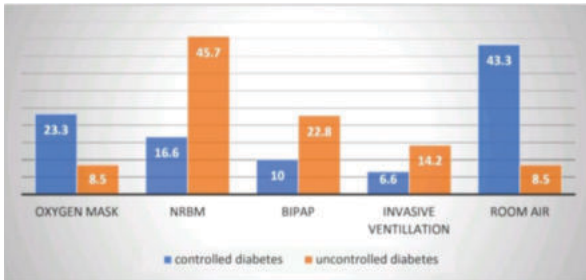


Figure 1 (Bar diagram): Modes of Oxygen delivery used by study groups

Table 2: Comparison of Mean values of lab parameters (hematological, biochemical, inflammatory, radiological) according to the study groups

Lab parameters	Controlled Diabetes n=60	Uncontrolled Diabetes n=140	Total n=200	P Value
Hb (g/dl)	12.5 ± 2.2	11.7 ± 2.2	11.9	0.0159*
TLC (cumm)	9238.8 ± 3605.0	11639.8 ± 6646.8	10919.5	0.0001*
NLR	4.3 ± 2.0	6.1 ± 2.0	5.5	0.0001*
Creatinine (mg/dl)	1.2 ± 1.0	1.4 ± 0.8	1.3	0.0569
Bilirubin (mg/dl)	0.8 ± 0.9	1.02 ± 0.7	0.9	0.1137
SGOT (U/L)	81.6 ± 167.5	116.2 ± 163.5	105.8	0.1750
SGPT (U/L)	79.8 ± 171.6	105.2 ± 158.3	97.6	0.3110
Na ⁺ (meq/L)	138.3 ± 4.3	138.0 ± 5.8	138.1	0.6686
K ⁺ (meq/L)	4.2 ± 0.7	4.1 ± 0.7	4.1	0.3270
HbA1c (%)	6.9 ± 0.2	9.5 ± 2.0	8.7	0.0001*
CRP	38.2 ± 33.9	74.6 ± 38.5	63.7	0.0001*
LDH	356 ± 82.8	428.5 ± 85.8	406.7	0.0001*
D Dimer	1.3 ± 0.8	2.7 ± 1.0	2.3	0.0001*
CT severity score (out of 25)	10.9 ± 5.7	16.8 ± 5.0	15.0	0.0001*

*p-value < 0.05; statistically significant

16% patients were in age group 30-40, 39% patients were in age group 41-50 and 45% patients were in age group 51-60 years. 64.5% patients were Male and 35.5% patients were Female. Most of the patients (72.5%) had diabetes within 10 years duration.

Clinical presentation-

Shortness of breath was reported by 172(86%) patients followed by cough- 164(82%), fever- 155(77.5%). Other symptoms like sore throat, headache, chest pain, generalized weakness, vomiting, diarrhea, joint pains were reported by less than 10% patients. Mean duration of hospitalization of uncontrolled diabetes group was significantly higher as compare to that of controlled diabetes group. (Duration of Hospitalization: controlled diabetes v/s uncontrolled diabetes Group: 5.9 ± 4.3 v/s 9.1 ± 5.1; p=0.0001).

Laboratory findings-

Mean Hb of uncontrolled diabetes group was significantly lower as compare to that of controlled diabetes group. (Hb: controlled diabetes v/s uncontrolled diabetes Group: 12.5 ± 2.2 v/s 11.7 ± 2.2; p=0.0159). Mean NLR of uncontrolled diabetes group was significantly higher as compare to that of controlled diabetes group. (NLR: controlled diabetes v/s uncontrolled diabetes Group: 4.3 ± 2.0 v/s 6.1 ± 2.0; p=0.0001). Mean HbA1c of uncontrolled diabetes group was significantly higher as compare to that of controlled diabetes group. (HbA1c: controlled diabetes v/s uncontrolled diabetes Group: 6.9 ± 0.2 v/s 9.5 ± 2.0; p=0.0001). No significant difference was observed in mean creatinine, bilirubin, SGOT, SGPT, Na⁺, K⁺ of both Study groups. Mean CRP of uncontrolled diabetes group was significantly higher as compare to that of controlled diabetes group. (CRP: controlled diabetes v/s uncontrolled diabetes Group: 38.2 ± 33.9 v/s 74.6 ± 38.5; p=0.0001). Mean LDH of uncontrolled diabetes group

was significantly higher as compare to that of controlled diabetes group. (LDH: controlled diabetes v/s uncontrolled diabetes Group: 356 ± 82.8 v/s 428.5 ± 85.8; p=0.0001). Mean D-Dimer of uncontrolled diabetes group was significantly higher as compare to that of controlled diabetes group. (D-dimer: controlled diabetes v/s uncontrolled diabetes Group: 1.3 ± 0.8 v/s 2.7 ± 1.0; p=0.0001).

Radiological findings-

Mean chest CT severity score of uncontrolled diabetes group was significantly higher as compare to that of controlled diabetes group. (CTSS: controlled diabetes v/s uncontrolled diabetes Group: 10.9 ± 5.7 v/s 16.8 ± 5.0; p=0.0001).

Diabetic complications-

Patients in uncontrolled diabetes group develop significantly more complications as compare to patients in controlled diabetes group. Controlled diabetes group develop ARDS-6(10%) followed by sepsis with MODS-4(6.6%), Diabetes keto acidosis- 2(3.3%), Shock- 2(3.3%). Uncontrolled diabetes group develop ARDS- 50(35.7%) followed by sepsis with MODS-30(21.4%), Diabetes keto acidosis- 25(17.8%), Shock-7(5%). No complication occurred in 112(56%) of total patients.

Analysis of severity, management and treatment-

Significantly higher number of patients in uncontrolled diabetes group developed Severe Covid-19 infection as compare to patients in controlled diabetes group. Controlled diabetes group develop Moderate covid-19 infection - 28(46.6%) followed by severe -17(28.3%), mild - 15(25%). Uncontrolled diabetes group develop severe covid-19 infection - 98(70%) followed by moderate -35(25%), mild - 7(5%). Requirement of oxygen was significantly higher in uncontrolled diabetes group (Requirement of oxygen: controlled diabetes v/s uncontrolled diabetes Group: 56.6% v/s 91.4%; p=0.00001). Requirement of ICU care was significantly higher in uncontrolled diabetes group (Requirement of ICU care: controlled diabetes v/s uncontrolled diabetes Group: 28.3% v/s 70%; p=0.00001). Oxygen mask was used by 14(23.3%) patients in controlled diabetes group as compare to 12(8.5%) patients in uncontrolled diabetes group. NRBM mask was used by 10(16.6%) patients in controlled diabetes group as compare to 64(45.7%) patients in uncontrolled diabetes group. BiPAP was used by 6(10%) patients in controlled diabetes group as compare to 32(22.8%) patients in uncontrolled diabetes group. Invasive ventilation was used by 4(6.6%) patients in controlled diabetes group as compare to 20(14.2%) patients in uncontrolled diabetes group. 86.5% patients required insulin whereas only 13.5% patients were treated on OHA. 92.5% patients were given antibiotics, 88% patients were given Steroids. Remdesivir was given to 69.5% patients, IVIG was given to 11% patients and tocilizumab was given to 21.5% of patients.

Outcome-

There was no significant difference in outcome between both the study groups. In Controlled diabetes group - 53(88.3%) were recovered and 1(1.6%) was LAMA. 6(10%) patients died. In Uncontrolled diabetes group- 110(78.5%) were recovered and 5(2.5%) were LAMA. 32(16%) patients died.

CONCLUSIONS

In the current study, we have considered 200 COVID-19-infected patients with T2DM in age group 30-60 years and considered their clinical, biochemical, inflammatory, radiological, and other required parameters. From the different observations, it can be concluded that poorly controlled diabetes mellitus can predispose an individual to a severe COVID-19 infection. Patients with uncontrolled diabetes status presented with more serious symptoms (predominantly shortness of breath), with significant fall in oxygen saturation, had prolonged hospital stay, with

deranged laboratory parameters and markedly raised inflammatory markers, along with high chest CT severity score. The severity of COVID-19 in diabetics could be due to the dysfunctional immune system, with increased susceptibility to viral infection and an exaggerated immune response like cytokine storm. Uncontrolled glycemic status weakens the immunity and provides a favorable condition for viral survival and longer recovery duration in diabetics. COVID-19 patients with uncontrolled diabetes required frequent clinical monitoring and higher attention regarding pharmacological and supportive treatment like oxygen support, non-invasive ventilation, ICU care than those with controlled diabetes group. Patients in uncontrolled diabetes group developed significantly more complications (such as ARDS, DKA, Sepsis with MODS or Shock) as compare to patients in controlled diabetes. Significantly higher number of patients in uncontrolled diabetes group developed Severe Covid-19 infection as compare to patients in controlled diabetes group. Because of frequent monitoring, higher clinical attention and strict glycemic control of diabetes, there was no significant difference in outcome between both the study groups. A large proportion of population is susceptible to COVID-19 and its complications due to a high prevalence of Type 2 DM in India. HbA1c more than 7% in patients with diabetes mellitus should be considered a risk factor for an overall higher susceptibility for COVID-19 infection and severity in terms of symptomatic presentation, inflammatory cytokine storm, rapid and extensive lung involvement, requirement of more intensive care. Frequent monitoring of clinical, biochemical, radiological parameters resulted in good outcome equal to that of controlled diabetes group. Hence, some extreme measures for preventing COVID-19 in people with underlying DM are advisable beside an intensive care in already infected individuals.

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