

ORIGINAL RESEARCH**To study the effect of Diabetes on inflammatory markers (CRP, D- Dimer, Serum Ferritin) and Mortality in Covid -19****¹Dr. Sneha Malik, ²Dr. Vikrant, ³Dr. Arvind Kumar**¹Assistant Professor, ²Junior Resident, ³Professor, Department of Medicine, LLRM Medical College, Meerut, Uttar Pradesh, India**Corresponding Author**

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Abstract**Aims and objectives of this study:**

1. To study the effect of Diabetes on inflammatory markers (CRP, D-dimer, Serum Ferritin) in Covid -19
2. To study the effect of Diabetes on Mortality in Covid -19

Material and Method: The study was done on patients with COVID- 19 admitted in second wave of covid 19 in super-speciality block of LLRM Medical College, Meerut. Diabetic (Cases) and non- diabetic (control) covid 19 patients were taken according to inclusion and exclusion criteria and they were followed for 6 months.**Result:** The present study states that the levels of inflammatory markers (D-Dimer, C-Reactive Protein , Serum Ferritin) and mortality was more in diabetic Covid -19 patients than the non- diabetic Covid 19 patients.**Conclusion:** With this study we can conclude that diabetes increases the severity as well as mortality in patients with covid 19 disease.**Keywords:** Covid 19, Diabetes, Inflammatory markers**Introduction**

Corona virus disease 2019 (COVID-19) is an infectious disease developed by severe acute respiratory syndrome *coronavirus-2 (SARS-CoV-2)*. Adults with some underlying medical conditions, such as cancer, heart conditions, chronic lung diseases, and diabetes, are more likely than others to become severely ill if infected with COVID-19. Among patients hospitalized with severe COVID-19 complications, 39.7% also had diabetes as an underlying medical condition.²

Patients with diabetes are known to have an increased risk of infections, which is partly attributed to hyperglycemia causing immune dysfunction, among other effects . On the other hand, severe SARS-CoV-2 infection and its associated hyper inflammation contribute to hyperglycemia through an indirect negative effect on insulin target tissues and a potential direct negative effect on pancreatic β -cells . The resulting hyperglycemia can, in turn, worsen the prognosis of COVID-19. The hyperglycemic environment present in diabetes favours immune dysfunction through several pathways. The most important underlying mechanisms are a decreased production of interleukins in response to an infection, reduced chemotaxis and phagocytic activity, and immobilization of polymorphonuclear leukocyte. The China Center for Disease Control and Prevention reported a diabetes prevalence of 5.3% among all

44,672 COVID-19 cases, but 19.7% among non-survivors, with a case fatality rate of 2.3% vs 7.3%, respectively³

Materials and Methodology

It was a comparative study done at LLRM Medical College, Meerut on patients with diabetes mellitus admitted in the second wave of covid 19 disease.

Sample Size

50 Diabetic Covid 19 patients (cases) and 50 Non- Diabetic Covid 19 patients (control)

Inclusion Criteria

1. Patients of type 2 diabetes
2. COVID -19 positive by RTPCR.
- 3.

Exclusion criteria

1. Immunocompromised patients
2. Malignancy, active immunological diseases.
3. Evidence of clinical cerebrovascular or cardiovascular disease.
4. Age >65 yrs and age <18 yrs,
5. Chronic diseases like chronic obstructive pulmonary disease, chronic liver disease, chronic kidney disease.

Criteria for diagnosis of Diabetics¹

1. Symptoms of diabetes and casual plasma glucose ≥ 200 mg/dl (11.1 mmol/l). Casual is defined as any time of day without regard to time since last meal. The classic symptoms of diabetes include polyuria, polydipsia and unexplained weight loss.
OR
2. FPG ≥ 126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h
OR
3. 2-h plasma glucose ≥ 200 mg/dl (11.1 mmol/l) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water
OR
4. HBA1C $\geq 6.5\%$

Observations and Results

Table1: Mean age of patients

Non-diabetic		Diabetic	
Mean	SD	Mean	SD
46.80	10.79	47.48	10.07

As per the table 2. Mean age of patients in non- diabetic group was 46.7 with standard deviation of 10.79 and mean age of patients in diabetic group was 47.5 with a standard deviation of 10.07

Table 2: Sex wise distribution of patients

Sex	Non-diabetic	Non-diabetic (%)	Diabetic	Diabetic (%)	Total
F	20	40.0%	22	44.0%	42
M	30	60.0%	28	56.0%	58
Total	50	100.0%	50	100.0%	100

From table 2. It can be interpreted that percentage of males in non-diabetic group were 60% and percentage of females in non diabetic group were 40%. . In Diabetic group males were 56% and females were 44 %

Table 3: D-dimer ($\mu\text{g/ml}$) in Non - diabetic and diabetic patients

Non-diabetic		Diabetic		Z	p-value
Mean	SD	Mean	SD		
0.77	0.41	1.46	1.01	-4.350	0.001

From table 3, it was observed that mean D -dimer ($\mu\text{g/ml}$) in non – diabetic patients was 0.77 ± 0.41 and in diabetic patient was 1.46 ± 1.01 .

By using Mann Whitney U test we found out that difference between the D-dimer of diabetic and non diabetic group was found to be statistically significant($p < 0.05$).

Table 4: C -Reactive protein(mg/dl) in Non diabetic and Diabetic patients

Non-diabetic		Diabetic		Z	p-value
Mean	SD	Mean	SD		
18.38	20.06	26.72	22.25	-2.485	0.013

Table 4 shows that mean C -Reactive protein(mg/dl) in non-diabetic patients was 18.38 ± 20.06 and in diabetic patient was 26.72 ± 22.25 .

This difference of C- reactive protein was found to be statistically significant by using Mann Whitney U test ($p < 0.05$)

Table 5: Serum ferritin (ng/dl) in non-diabetic and diabetic patients

Non-diabetic		Diabetic		Z	p-value
Mean	SD	Mean	SD		
307.52	129.67	637.08	173.38	-10.763	0.001

With the help of table 5 it is seen that in the non-diabetic group mean Serum ferritin(ng/dl) was 307.52 ± 129.67 and in diabetic group was 637.08 ± 173.38 .

The difference between the Serum Ferritin of both the groups was found to be statistically significant using Mann Whitney U test ($p < 0.05$)

Table 6: CT-severity score in non-diabetic and diabetic patients

Non-diabetic		Diabetic		Z	p-value
Mean	SD	Mean	SD		
14.82	4.78	16.58	4.39	-2.505	0.012

Table 6 shows that mean CT-severity score in non- diabetic patients was 14.82 ± 4.78 and in diabetic patient was 16.58 ± 4.39 .

By using Mann whitney test we found out that difference between the CT-severity score of diabetic and non diabetic group was statistically significant ($p < 0.05$)

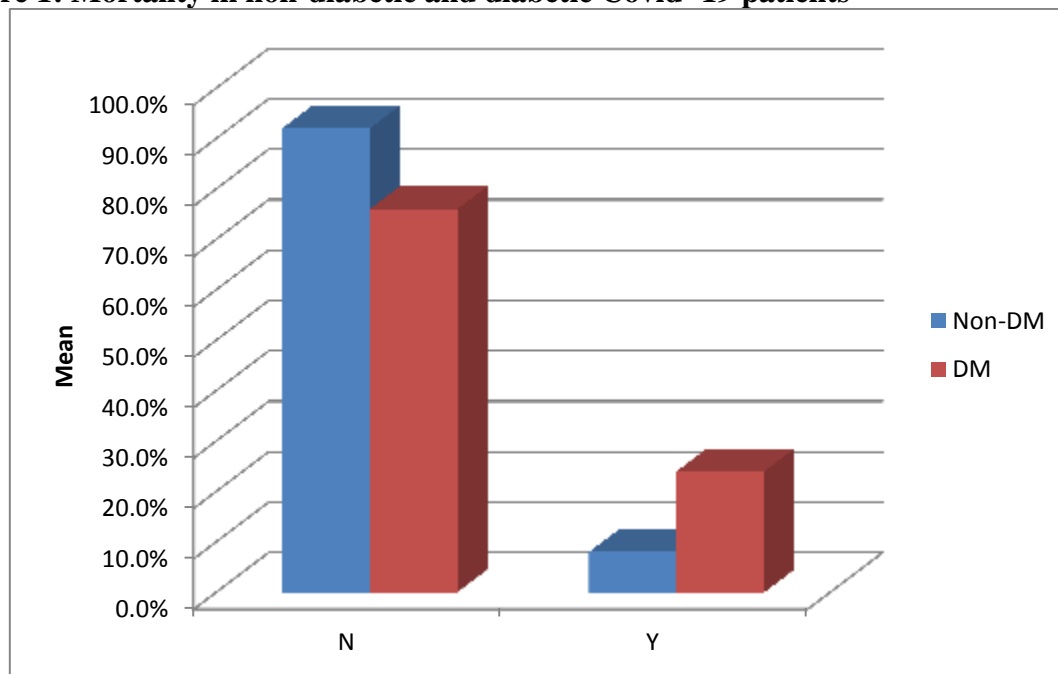
Table 7: Mortality during Covid-19 in non-diabetic and diabetic patients

Mortality	Non-diabetic	Non-diabetic(%)	Diabetic	Diabetic	Total	p-value
N	46	92.0%	38	76.0%	84	
Y	4	8.0%	12	24.0%	16	
Total	50	100.0%	50	100.0%	100	0.029

From table 7. It can be observed that mortality in non-diabetic patients was 4 and in diabetic patients was 12.

By using Chi square test we found out that difference between the Mortality of diabetic and non diabetic group was statistically significant ($p < 0.05$)

Figure 1: Mortality in non-diabetic and diabetic Covid -19 patients



Discussion

In our present study, we have compared inflammatory markers like D-Dimer, CRP, Serum Ferritin, mortality between non diabetic and diabetic Covid 19 positive by real time reverse transcription polymerase chain reaction test. The present study represent that the mean of D-Dimer (ug/dl) in non diabetic group and diabetic group was 0.77 and 1.46 respectively with a p value of 0.001 which was statistically significant. These values were comparable to studies of Yogendra Mishra and Basant Kumar Pathak in which mean D-dimer levels were 1509 in people with diabetes and 515 in patients without diabetes These values are also comparable to studies of Ibrahim Hashim and Ibrahim Elbashir, Yumeng Yao, Chaymae Miri.⁴ Patients with diabetes had higher D-dimer levels which were statistically significant. These values are also comparable to studies of Ibrahim Hashim and Ibrahim Elbashir, Yumeng Yao, Chaymae Miri.⁵

The present study represent that the mean of C-Reactive Protein (md/dl) in non diabetic group and diabetic group was 18.38 and 26.72 respectively with a p value of 0.013 which was statistically significant. These values were comparable to studies of Hoimonti Debi, Mahmoud Sadeghi-Haddad-Zavareh.⁶

The present study represent that the mean of Serum Ferritin (ng/dl) in non diabetic group and diabetic group was 307.52 and 637.02 respectively with a p value of 0.001 which was statistically significant. These values were comparable to studies of Nerea Pérez-García, Sibtain ahmed, Mukesh Kumar.⁷

The present study also represent that the mortality in non diabetic group and diabetic group was 4 and 12 respectively with a p value of 0.029 which is statistically significant. These values were comparable to studies of Rodrigo Esaki Tamura.⁸

Conclusion

In this study 50 diabetic and 50 non diabetic COVID -19 positive patients were taken and their inflammatory markers and mortality were compared. The mean age of diabetic patients 47.4 was and mean age of non- diabetic was 46.8

The mean of D- dimer (ug/dl) in non diabetic group and diabetic group was 0.77 and 1.46 respectively with a p value of 0.001, the mean of C-Reactive protein (ug/dl) in non diabetic group and diabetic group was 18.38 and 26.72 respectively with a p value of 0.013 and the mean of C-Reactive protein (ug/dl) in non diabetic group and diabetic group was 18.38 and 26.72 respectively with a p value of 0.013 which were statistically significant. The Mortality in COVID -19 non- diabetic patients was and diabetic patients was 4 and 12 respectively with a p value of 0.029 which was statistically significant.

Bibliography

1. American Diabetes Association (January 2014). "2. Classification and Diagnosis of Diabetes". *Diabetes Care*. 40 : S11–S24
2. <https://www.cdc.gov/diabetes/library/reports/reportcard/diabetes-and-covid19.html>
3. <https://www.frontiersin.org/articles/10.3389/fendo.2021.649525/full>
4. Relation of D-dimer levels of COVID-19 patients with diabetes mellitus. Mishra Y, Pathak BK, Mohakuda SS, Tilak TVSVGK, Sen S, P H, Singh R, Singh AR. *Diabetes Metab Syndr*. 2020 Nov-Dec;14(6):1927-1930. doi: 10.1016/j.dsx.2020.09.035. Epub 2020 Oct 1. PMID: 33035824
5. Comparison between D-dimer levels in diabetic and non-diabetic positive COVID-19 adult patients: A hospital-based study. Hashim Ibrahim Elbashir I, Kamal Ali Mohamed H, Adam Essa ME, Seri A. *Endocrinol Diabetes Metab*. 2022 Jul;5(4):e349. doi: 10.1002/edm2.349. Epub 2022 May 25. PMID: 35614558
6. Sadeghi-Haddad-Zavareh M, Bayani M, Shokri M, Ebrahimpour S, Babazadeh A, Mehraeen R, Moudi E, Rostami A, Barary M, Hosseini A, Bijani A, Javanian M. C-Reactive Protein as a Prognostic Indicator in COVID-19 Patients. *Interdiscip Perspect Infect Dis*. 2021 Apr 23;2021:5557582. doi: 10.1155/2021/5557582. PMID: 33968148; PMCID: PMC8083820.
7. Pérez-García N, García-González J, Requena-Mullor M, Rodríguez-Maresca MÁ, Alarcón-Rodríguez R. Comparison of Analytical Values D-Dimer, Glucose, Ferritin and C-Reactive Protein of Symptomatic and Asymptomatic COVID-19 Patients. *Int J Environ Res Public Health*. 2022 Apr 28;19(9):5354. doi: 10.3390/ijerph19095354. PMID: 35564749; PMCID: PMC9102188.
8. Tamura RE, Said SM, de Freitas LM, Rubio IGS. Outcome and death risk of diabetes patients with Covid-19 receiving pre-hospital and in-hospital metformin therapies. *Diabetol Metab Syndr*. 2021 Jul 13;13(1):76. doi: 10.1186/s13098-021-00695-8. PMID: 34256824; PMCID: PMC8275913.