

## Original Articles

### Association of Diabetes Mellitus with Disease Severity and Outcome in Covid-19 Patients

Ravi J Shah\*, Rajkamal Chaudhari\*\*, Dhara B Roy\*\*\*, Ami Parikh\*\*\*\*

\*Resident, \*\*Associate Professor, \*\*\*Assistant Professor, \*\*\*\*Professor and Head of Department

Smt NHL Municipal Medical College, Ahmedabad.

**KEY WORDS** : Covid-19, Sars cov2, Diabets mellitus, Dm2, Hba1c

#### ABSTRACT

**Background:** The severity and mortality of covid 19 are linked to various comorbidities, Diabetes mellitus being one among them. Diabetes mellitus is an important comorbidity which is hypothesized to lead to worse outcomes in Covid 19

**Methods:** A retrospective observational study of all indoor patients admitted with covid-19 from 1 may to 7 may 2020 was conducted at a tertiary care hospital. Medical case records were searched for various parameters and data was collected on which statistical analysis was done by SPSS 25

**Results:** Increasing severity of diabetes was associated with worse radiological, clinical and biochemical characteristics. Higher hba1c was associated with increased O2 requirements

**Conclusion:** Severity of covid 19 is proportional to underlying severity of Diabetes in the above subset of patients.

#### INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease (COVID-19). The severity and mortality of covid 19 are hypothesized to be related to age and comorbidities including diabetes, hypertension, cardiovascular and cerebrovascular disease. World Health Organization (WHO) has declared the Coronavirus Disease 2019(Covid-19) as it has caused more than 500,000 deaths and spread to more than 200 countries<sup>[1][2][3]</sup>

Diabetes is an important comorbidity contributing to adverse outcome in covid 19 patients. There have also been reports of new onset of diabetes in covid 19 patients. We undertake following study to find out prevalence of diabetes in covid 19 patients and its association with disease severity and outcomes

India has a rising prevalence of diabetes. The overall prevalence of diabetes in all states of India was 7.3% (95% CI 7.0-7.5) as per a study from 017.<sup>[4]</sup> Patients with diabetes are more prone to a wide variety of secondary infections including bacterial, fungal, viral, etc. thus these patients might be at increased risk of covid 19.<sup>[5-10]</sup>

In this study we undertake a retrospective analysis of 328 patients with Covid-19 confirmed by a

nasopharyngeal swab and compare their hematological and biochemical parameters of disease severity and prognosis on admission and their peak values and in hospitalized outcomes of study population.<sup>[11]</sup>

#### MATERIALS AND METHODS

We conducted a retrospective observational study of all indoor patients admitted with covid-19 in a tertiary care hospital (SVP ISMR, Ahmedabad) from 1 May 2020 to 7 May 2020. A total of 328 patients were enrolled. All patients included in the study were diagnosed as per WHO guidelines.<sup>[5]</sup> The study was approved by Institutional ethics board of Smt NHL Municipal Medical College, Ahmedabad, Gujarat, India.

Medical case records were searched for following parameters :

1. Hba1c on admission
2. History of dm2
3. Disease category on admission (mild/moderate/severe) and any change in category post admission
4. Hematological and biochemical parameters of disease severity and prognosis on admission and their peak values
5. In hospitalized outcomes of study population

**Correspondence Address** : Dr. Ravi J. Shah  
1B Jay Jalaram Society, Vyaswadi, Nava Vadaj, Ahmedabad 380013  
Email : rjshah26395@gmail.com

6. To find correlation between diabetic control with derangement in lab parameters and in hospital worsening of clinical outcome

### 2.1 Statistical Analysis

Statistical analysis was done using SPSS 25.0 to arrive at aims and objectives as above. Continuous variables were shown as Median and Interquartile range(IQR) and compared by Kruskal wallis H test . Stepwise regression with forward and backward selection was used to determine association of diabetes with xray involvement in covid-19 and need for o2. Adjusted hazard ratio(aHR) with 95% confidence interval (CI) was presented as effect size. A p value  $p < 0.05$  was considered statistically significant.

### 2.2 Inclusion Criteria:

All indoor patients of covid 19 admitted in SVP ISMR from 1 May, 2020 to 7 May 2020 with age  $\geq 12$  years

### 2.3 Exclusion Criteria

### 2.4 Diagnostic criteria:

Covid 19 diagnosed by Sars-CoV 2 RT PCR nasopharyngeal and oropharyngeal swab

In hospital outcomes were categorized as

1. discharge on room air
2. discharge on o2
3. death

In hospital worsening was defined as shift from ward to ICU

Diabetes mellitus was defined as:[6]

1. Fasting plasma glucose  $\geq 126$  mg/dl\* or
2. 2 hour post prandial glucose  $\geq 200$  mg/dl\*\* or
3. Hba1c  $\geq 6.5\%$  or
4. Random plasma glucose  $\geq 200$ mg/dl with symptoms of hyperglycemia or hyperglycemic crisis

\*Fasting defined as no caloric intake for 8 hours atleast

\*\*OGTT performed as prescribed by WHO with a glucose load equivalent to 75 g anhydrous glucose

Classification of diabetes control was grouped as:

- 1:  $< 5.7$  or non diabetic as per FBS/PPBS/RBS
- 2: 5.7-6.4 - pre diabetic
- 3: 6.5-8.4 - mild diabetes
- 4:  $\geq 8.5$  - moderate-severe diabetes

## RESULTS AND DISCUSSION

### 3.1 Baseline demographics of patients of Covid 19

TABLE 1 : There were a total of 328 consecutive confirmed patients analyzed and 79 of those patient had diabetes. (24.08%). 87 patients had comorbidities other than diabetes with HTN (73,83.9%) being most common followed by Ischemic heart disease/Left ventricular dysfunction/Acute oronary syndrome/Valvular heart disease (12, 13.7%), hypothyroid(9,10.3%)

**Table 1 Comorbidities in Patients other than Diabetes**

HTN	73	0.8390804598
IHD/LVD/ACS	12	0.1379310345
HYPOTHYROID	9	0.1034482759
COPD/ASTHMA/TB	4	0.0459770114 9
CLD	3	0.0344827586 2
CKD	2	0.0229885057 5
CVA	2	0.0229885057 5
RA	1	0.0114942528 7
PSORIASIS	1	0.0114942528 7
ADDISON'S	1	0.0114942528 7

3.2 Hematological and Biochemical parameters in patients of Covid 19 on admission and their peak values

Significant difference were seen in CRP values on admission and peak( $p < 0.05$ ), NLR on admission and peak( $p < 0.05$ ), ferritin on admission and peak( $p < 0.05$ ), D dimer on admission and peak( $p < 0.05$ ), peak PCT value( $P < 0.05$ ) and peak NT pro BNP value( $p < 0.05$ ) with severity of diabetes( grouped as per hba1c)

3.3 Radiological parameters in patients of Covid 19 at peak involvement

Increasing severity of diabetes was associated with more severe radiological involvement as defined by maximum percentage of lung fields involved on chest xray. P value for involvement of xray and group of hba1c was found to be significant( $< 0.05$ ). [table 4]

**Table 2 : Radiological parameters in patients of Covid 19 at peak involvement**

GROUP OF HBA1C	SIGNIFICANT RADIOLOGICAL CHANGES		
	NO	<50%	>50%
1	65.90%(135)	31.70%(65)	2.40%(5)
2	32.60%(14)	51.20%(22)	16.30%(7)
3	24.50%(12)	55.10%(27)	20.40%(10)
4	20.00%(6)	56.70%(17)	23.30%(7)

P value 0

**Table 3 : Multivariate regression with O2 requirement as dependent variable and age, group, ct value, sex, comorbidities as independent variable**

	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
(Constant)	0.412	0.162		2.539	0.012
CT VALUE	0.013	0.005	0.179	2.713	0.007
GROUP OF HBA1C	0.138	0.034	0.315	4.079	0
COMORBIDITIES	0.131	0.073	0.134	1.791	0.075
SEX	-0.082	0.056	-0.096	-1.471	0.143
AGE	0.005	0.002	0.194	2.397	0.018
a Dependent Variable: O2					

**Table 4 : Peak O2 Requirement and Group of Diabetes**

GROUP	1	2	3	4	5	6	MEAN
1	92.2	5.853 659	0	0	0	2	1.1 56 1
2	67.4	14	2.3	2.3	0	14	1.9 76 74 4
3	51	30.6	6.1	0	0	12. 2	2.0 40 8
4	33.3	33.3	16.7	0	3.3	13. 3	2.4 66 66 7

We also performed a stepwise regression with forward and backward selection and found that age<sup>2</sup> (R square change= 0.192) and group of diabetes (R square change=0.026) were significantly associated with

radiological changes (p value< 0.05) while CT value, sex and comorbidities were not significantly associated with xray changes.[table 5,6]

#### 3.4 O2 Requirement in patients with covid 19

A stepwise regression with forward and backward selection was performed and found that group of diabetes ( R square change = 0.199) , age ( R square change= 0.053) and ct value ( r square change= 0.028) were significantly associated with patient of covid 19 requiring o2 while other comorbidities and sex were not significantly associated. [table 7,8]

#### KEY FOR PEAK O2 REQUIREMENT

1: RA	2: O2 UPTO 6L
3: O2 6-14L	4: HFNC
5: NIV	6: INTUBATED

#### 3.5 Analysis of deaths in covid-19

There were 21 deaths in this sample. The median age of patients succumbing to covid 19 was 67.5 (IQR 52.75-72.75). 75% were Male and 25% were female. 50% had other comorbidities while 50% did not have other comorbidities. The median CT value was 29(IQR 26-32.75). 20% belonged to group 1, 30% to group 2, 30% to group 3, 20% to group 4. Diabetes was statistically insignificant as a contributor to mortality.

#### CONCLUSION

Biochemical and radiological parameters were found to be proportionately worse in patients with increasing severity of diabetes.

Age and severity of diabetes were the only parameters found to be associated with severity of radiological changes. The viral load was not found to be associated with severity of radiological changes.

Age, severity of Diabetes and ct value were the parameters found to be associated with o2 requirements in Covid 19 patients. Thus, The outcomes were worse among diabetics as compared to non diabetics and even among diabetics they were associated with level of control of Diabetes. The population attributable risk for o2 requirements in diabetics was also high.

The sample size of the study was inadequate to comment regarding association of severity of diabetes and mortality in Covid-19 patients.

Thus, control of severity of diabetes is an important strategy to reduce severity of covid 19 cases.

#### REFERENCES

1. Yang, J., Zheng, Y., Gou, X., Pu, K., Chen, Z., Guo, Q., Ji, R., Wang, H., Wang, Y. and Zhou, Y., 2020. Prevalence Of Comorbidities And Its Effects In Patients Infected With SARS-Cov-2: A Systematic Review And Meta-Analysis.
2. Zhou F., Yu T., Du R. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020; 395:10229 :1054-1062
3. Clinical management of COVID-19. (n.d.). Retrieved August 13, 2020, from <https://www.who.int/publications/item/clinical-management-of-covid-19>
4. Anjana RM, Deepa M, Pradeepa R, et al. Prevalence of diabetes and prediabetes in 15 states of India: results from the ICMR-INDIAB population-based cross-sectional study [published correction appears in *Lancet Diabetes Endocrinol*. 2017 Aug;5(8):e5]. *Lancet Diabetes Endocrinol*. 2017;5(8):585-596. doi:10.1016/S2213-8587(17)30174-2
5. Hodgson K, Morris J, Bridson T, Govan B, Rush C, Ketheesan N. Immunological mechanisms contributing to the double burden of diabetes and intracellular bacterial infections. *Immunology*. 2015;144(2):171-185. doi:10.1111/imm.12394
6. American Diabetes Association. (2020, January 01). 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2020. Retrieved August 13, 2020, from <https://doi.org/10.2337/dc20-S002>
7. Lim S, Bae JH, Kwon HS, Nauck MA. COVID-19 and diabetes mellitus: from pathophysiology to clinical management. *Nat Rev Endocrinol*. 2021 Jan;17(1):11-30. doi : 10.1038/s41574-020-00435-4. Epub 2020 Nov 13. PMID: 33188364; PMCID: PMC7664589.
8. Carey IM, Critchley JA, Dewilde S, Harris T, Hosking FJ, Cook DG. Risk of infection in type 1 and type 2 diabetes compared with the general population: a matched cohort study. *Diabetes Care*. 2018;41(3):513-21.
9. Filardi T, Morano S. COVID-19: is there a link between the course of infection and pharmacological agents in diabetes? *J Endocrinol Invest*. 2020 Aug;43(8):1053-1060. doi : 10.1007/s40618-020-01318-1. Epub 2020 Jun 3. PMID: 32495299; PMCID: PMC7268955.
10. Mirjalili H, Dastgheib SA, Shaker SH, Bahrami R, Mazaheri M, Sadr-Bafghi SMH, Sadeghzadeh-Yazdi J, Neamatzadeh H. Proportion and mortality of Iranian diabetes mellitus, chronic kidney disease, hypertension and cardiovascular disease patients with COVID-19: a meta-analysis. *J Diabetes Metab Disord*. 2021 Feb 26:1-13. doi: 10.1007/s40200-021-00768-5. Epub ahead of print. PMID: 33654683; PMCID: PMC7907796.
11. España PP, Bilbao A, García-Gutiérrez S, Lafuente I, Anton-Ladislao A, Villanueva A, Uranga A, Legarreta MJ, Aguirre U, Quintana JM; COVID-19-Osakidetza Working group. Predictors of mortality of COVID-19 in the general population and nursing homes. *Intern Emerg Med*. 2021 Jan 5:1-10. doi: 10.1007/s11739-020-02594-8. Epub ahead of print. PMID: 33400164; PMCID: PMC7783294.