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IMPACT OF DIABETES ON COVID–19 OUTCOME AND MORTALITY IN PATIENTS ADMITTED DURING APRIL 2021 TO OCTOBER 2021 IN A TERTIARY CARE CENTRE FROM NORTH WEST RAJASTHAN

General Medicine

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ABSTRACT

Introduction: Most people with COVID-19 have mild illnesses or asymptomatic, while approximately 14% develop severe disease that requires hospital admission and oxygen therapy, and 5% patients need an Intensive Care Unit (ICU) treatment. Objectives: To study the relationship between diabetes mellitus and severity of and outcome of COVID19 infections in patients. **Methodology:** 100 consecutive patients of RT-PCR positive COVID 19 patients admitted in dedicated COVID 19 hospital were taken in the study. **Results:** According to presenting complaint, most common presenting complaint was dyspnoea in 74 cases (74%), followed by cough in 69 cases (69%) and fever in 59 cases (59%). Other presenting complaints were fatigue in 48 cases, headache in 26 cases, nasal discharge in 25 cases, pain abdomen in 18 cases, sore throat in 59 cases and chest pain in 19 cases. Severity level among DM patients were higher showing 31.81% had mild disease, 47.72% moderate disease, 20.45% had severe disease. **Conclusion:** Outcome in DM patients showed mortality of 15.91% and compared to 7.14% in non DM patients.

KEYWORDS

COVID 19, Diabetes mellitus, Dyspnoea, Hyperglycemia, RT-PCR

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of corona virus-induced disease 19 (COVID-19) was first reported in December 2019, in Hubei Province, China, from where it spread rapidly to all over the Globe. COVID-19 was declared as a global pandemic in March 2020 by the world health organization (WHO).[1] In India first case of COVID-19 infection was reported from Kerala, on January 30, 2020.[2] Most people with COVID-19 have mild illnesses or asymptomatic, while approximately 14% develop severe disease that requires hospital admission and oxygen therapy, and 5% patients need an Intensive Care Unit (ICU) treatment.[3]

The COVID-19 pandemic has been raging across the globe since early January 2020. Various geographical regions have been experiencing multiple waves of upsurge of cases which are not matched temporally as well as in severity. A similar phenomenon was seen during the 1918 influenza pandemic.[4]

Now It is rapidly spreading in India, there is 719665 confirmed case of Covid19, and 20160 deaths occurred due to Covid till 7 July 2020 in India.[5] Although Covid-19 is pandemic for more than 6 months but clinical profile of covid19 is not fully understood yet.

Presentation of Covid-19 cases have reported to vary from asymptomatic to sudden death therefore this study is planned to evaluate the clinical profile of Covid-19 cases and there outcome.

COVID-19 patients have underlying risk factors associated with adverse outcome, including advanced age, male gender, and the presence of comorbidities including hypertension, diabetes mellitus, cardiovascular diseases, and cerebrovascular diseases.[6] It is notable that diabetes has been demonstrated as a potential risk factor for adverse outcome in COVID-19 infection.[7] Moreover, it is well known that patients with diabetes have higher risk of infections because of alterations in the immune response.[8] Nonetheless, it remains controversial whether diabetes could be considered an independent risk factor for greater severity of illness and death, with some studies showing a detrimental effect[9-11] and others a neutral influence[12-14], also depending on adjustment for confounding variables. Moreover, the vast majority of the published literature comes from China and western countries, and little is known in India.

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors. Depending on the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system.

Glucose tolerance is classified into three broad categories: normal glucose homeostasis, impaired glucose homeostasis, or DM.

Glucose tolerance can be assessed using the fasting plasma glucose (FPG), the response to oral glucose challenge, or the hemoglobin A1c (HbA1c). An FPG <5.6 mmol/L (100 mg/dL), a plasma glucose <7.9 mmol/L (140 mg/dL) following an oral glucose challenge, and an HbA1c <5.7% are considered to define normal glucose tolerance.

The International Expert Committee with members appointed by the ADA, the European Association for the Study of Diabetes, and the IDF have issued diagnostic criteria for DM based on the following premises: (1) the FPG, the response to an oral glucose challenge (oral glucose tolerance test [OGTT], and HbA1c differ among individuals, and (2) DM is defined as the level of glycemia at which diabetes-specific complications occur rather than deviation from a population-based mean. For example, the prevalence of retinopathy in Native Americans (Pima Indian population) begins to increase at an FPG >6.4 mmol/L (116 mg/dL).

Abnormal glucose homeostasis can be diagnosed by three distinct criteria. First, impaired fasting glucose (IFG) is defined as a fasting plasma glucose (FPG) value of 5.6–6.9 mmol/L (100–125 mg/dL). Second, impaired glucose tolerance (IGT) is defined as a plasma glucose level of 7.8–11 mmol/L (140–199 mg/dL) following an oral

glucose challenge. Third, an HbA1c of 5.7–6.4% reflects dysglycemia by all mechanisms. While an HbA1c of 5.7–6.4%, IFG, and IGT do not identify the same individuals (i.e., different biologic mechanisms involved), individuals in all three groups are at greater risk of progressing to type 2 DM, have an increased risk of cardiovascular disease, and should be counseled about ways to decrease these risks.

Some use the terms pre-diabetes, increased risk of diabetes, or intermediate hyperglycemia (World Health Organization) and slightly different metrics for this category.

In general, people with diabetes are at higher risk of developing complications because of infection, particularly viral one. The differences in response are likely the result of the degree of viral load, host immune response, age of the patient, and presence of comorbidities. The higher risk of mortality and complications among people with diabetes was similar in the two other recent coronavirus outbreaks, the SARS and the Middle East respiratory syndrome (MERS).[15] Type 2 diabetes is associated with low grade chronic inflammation induced by the excessive visceral adipose tissue. This inflammatory condition affects the homeostatic glucose regulation and peripheral insulin sensitivity. Chronic hyperglycemia and inflammation can determine an abnormal and ineffective immune response.[16]

Diabetic patients with COVID-19 are at higher risk of being in an excessively hypercoagulable state and uncontrolled inflammation responses, which may contribute to a poorer outcome. In particular, a known history of diabetes and a fasting plasma glucose ≥7.0 mmol/l before steroid treatment were independent predictors of death with an increased risk (odds ratio) of 3.0 and 3.3, respectively.[16]

Objectives

- To study the relationship between diabetes mellitus and severity and outcome of COVID 19 infection in patients.

METHODOLOGY

100 consecutive patients of RT-PCR positive COVID 19 patients admitted in dedicated COVID 19 hospital during April 2021- October 2021 in North western Rajasthan.

Procedures and Definitions: Using medical records, data was reviewed related to demographic variables (age, gender, and occupational status), previous medical history and comorbidities and prescription medications. Date of admission, total hospital length of stay, presenting symptoms (including fever, cough, dyspnoea, diarrhea and conjunctivitis), vitals, plasma and serum based biomarkers at the time of hospital admission. Routine laboratory examinations including a complete blood cell count, liver (aspartate aminotransferase, [AST] and alanine aminotransferase, [ALT] and renal function testing, c-reactive protein (CRP) were recorded. Medical comorbidities of interest include diabetes, hypertension, coronary artery disease (CAD), stroke, malignancy, chronic obstructive pulmonary disease (COPD), asthma, chronic kidney disease (CKD) and hematological disorders.

Inclusion Criteria

- RT-PCR positive COVID-19 patients.
- Adult patients >18 years
- Patients who gave consent to be part of the study.

Exclusion Criteria

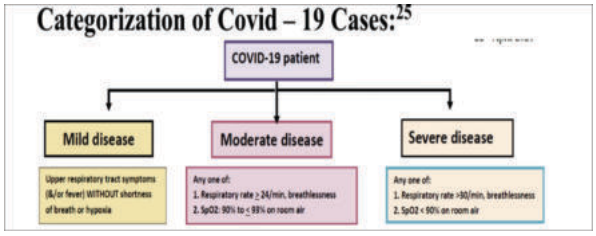
- Clinically ambiguous COVID-19 negative cases
- Patients age <18 years
- Those who did not give consent

Primary Predictors

Diabetes mellitus was diagnosed based on American Diabetes Association (ADA) criteria Patients were categorized into two groups: without diabetes and with diabetes.[13]

American Diabetes Association (ADA) Criteria:

- Symptoms of diabetes + random blood glucose concentration ≥ 200mg/dl
- Fasting plasma glucose ≥ 126mg/dl
- HbA1c level ≥ 6.5%
- 2 hours post prandial glucose ≥ 200mg/dl



Source : Ministry Of Health & Family Welfare, Govt. Of India.

Sample Collection

For all biochemical and hematological data of patient's blood samples were taken within 48 hours of admission. The thoracic imaging (chest radiographs and CT) of cases were reported by consultant radiologists. RT-PCR of a clinical specimen from nasopharyngeal swab was done for confirming the diagnosis of SARS-CoV-2 or COVID-19 infection. The decision to test was based on a clinical suspicion of COVID-19. The testing was performed either at the point of admission or as soon as possible afterwards.

Statistical Analysis

Differences in demographics and clinical characteristics were compared between two groups, using chi square test for categorical variables and ANOVA for continuous variables. All statistical analysis was performed using SPSS 16.0 software.

The study was approved by Institutional Review Board and informed consent was obtained from all patients prior to study entry.

RESULTS

This retrospective study was carried out on 100 cases of RT-PCR confirmed COVID-19 patients admitted during 2nd wave of COVID 19 pandemic during April 2021 to October 2021 in the dedicated COVID 19 hospital in the Department of Medicine, P.B.M. Associated Group of Hospitals and Sardar Patel Medical College, Bikaner.

Data reported in our study support the notion that diabetes should be considered as a risk factor not only for increased susceptibility to infection but also for a rapid progression and bad prognosis of COVID-19. Therefore, according to pathophysiological consideration, people with diabetes should be paid more intensive attention

This consideration argues for better glycemic control in patients with hyperglycemia at hospital admission. We know that blood glucose control is essential for patients with COVID-19 and those without the disease. Nevertheless, hyperglycemia is still a powerful predictor of the prognosis of hospitalized Covid-19 patients.

Salient features of our study are summarized as below:

- Out of total 100 cases there were 80 males and 20 were females.
- Mean age of females was 56.4±22.5years ranging 20-87 years and that of males was mean age 53.98±11.67 years ranging 21-80 years.
- Most females belonged to age group 61-80 years and most of the males belonged to age group 41-60 years.
- According to presenting complaint, most common presenting complaint was dyspnoea in 74 cases (74%), followed by cough in 69 cases (69%) and fever in 59 cases (59%). Other presenting complaints were fatigue in 48 cases, headache in 26 cases, nasal discharge in 25 cases, pain abdomen in 18 cases, sore throat in 59 cases and chest pain in 19 cases.
- DM was most common co-morbidity associated with covid-19. Overall 44 (44%) cases were having diabetes mellitus. Hypertension in 27, was 2nd most common comorbidity. CAD present in 14, COPD 11, CKD 8, CLD 8, CVA 7, Hypothyroid 6, SBP class 5, BA 5 and others were 16.
- Overall mortality rate in our study was 11.00%.
- Severity level among DM patients were higher showing 31.81% had mild disease, 47.72% moderate disease, 20.45% had severe disease.
- Outcome in DM patients showed mortality of 15.91% and compared to 7.14% in non DM patients.
- Severity among patients with HbA1c level >8.5 had 50% severe cases compared to 23.07% among patients with HbA1c level 7.5–8.5. With only 4.7% among patients HbA1c level <7.5.
- Mortality among patients with HbA1c level >8.5 was found to be

30% compared to 15.39% among patients with HbA1c level between 7.5–8.5 while showing 9.53% for patient with HbA1c level <7.5.

- Out of 89 recovered cases 94.38% cases had CRP level <100, 5.62% cases had CRP levels >100. Out of 11 died cases 36.36% had CRP levels <100 and 63.64% had CRP levels >100.

Figure 1: Distribution Of Cases According To Age And Gender

Age Group	Sex				Total	
	Male		Female			
	No.	%	No.	%	No.	%
20–40	12	15	6	30	18	18
41–60	45	56.25	4	20	49	49
61–80	23	28.75	7	35	30	30
>80	0	0	3	15	3	3
Total	80		20		100	
Mean	53.98		56.4			
SD	11.67		22.5			
Range	21-80		20-87			

Figure 2: Distribution Of Cases According To Comorbidities

Comorbidities	No. of cases	Percentage (n=100)
DM	44	44%
HTN	27	27%
CAD	14	14%
CVA	7	7%
CKD	8	8%
COPD	11	11%
BA	5	5%
CLD	8	8%
Malignancy	3	3%
Hypothyroid	6	6%
Other	16	16%

Figure 3: Distribution Of Cases According To Age Group In Relation To Hospital Stay

Age Group (In yrs.)	No. of cases		Hospital Stay (In days)					
			1 week		1-2 Weeks		> 2weeks	
	No.	%	No.	%	No.	%	No.	%
20–40	18	18	9	47.37	8	16.67	1	3.03
41–60	49	49	8	42.11	25	52.08	16	48.48
61–80	30	30	2	10.53	13	27.08	15	45.45
>80	3	3	0	0.00	2	4.17	1	3.03
Total	100		19		48		33	
p value	0.003							

Figure 4: Distribution Of Cases According To Presenting Symptoms

Symptoms	No. of cases	Percentage
Fever	59	59%
Fatigue	48	48%
Chest pain	19	19%
Anosmia	5	5%
Vomiting	12	12%
Altered Sensorium	18	18%
Cough	69	69%
Sore throat	59	59%
Dyspnoea	74	74%
Ageusia	3	3%
Loose stools	12	12%
Body ache	24	24%
Nasal discharge	25	25%
Headache	26	26%
Hemoptysis	2	2%
Pain abdomen	18	18%

Figure 5: Distribution Of Cases According To Present Symptoms And Their Outcome

Presenting complaints	No. of cases	Outcome			
		Survive (n=89)		Death (n=11)	
		No.	%	No.	%
Fever	59	49	10.99	10	11.49
Fatigue	48	42	9.42	6	6.90
Chest pain	19	16	3.59	3	3.45
Anosmia	5	65	14.57	0	0.00
Vomiting	12	11	2.47	1	1.15
Altered Sensorium	18	14	3.14	4	4.60
Cough	69	55	12.33	14	16.09
Sore throat	59	47	10.54	12	13.79
Dyspnoea	74	58	13.00	16	18.39
Ageusia	3	2	0.45	1	1.15
Loose stools	12	10	2.24	2	2.30
Body ache	24	20	4.48	4	4.60
Nasal discharge	25	20	4.48	5	5.75
Headache	26	20	4.48	6	6.90
Hemoptysis	2	2	0.45	0	0.00
Pain abdomen	18	15	3.36	3	3.45
Total	473	446		87	
p value	0.004				

Figure 6: Distribution Of Diabetic Cases According To HbA1c Level

Age Groups (In Yrs.)	HbA1c Level			Total
	<7.5	7.5–8.5	>8.5	
20–40	0	3	3	6
41–60	5	5	10	20
61–80	0	7	8	15
>80	0	0	3	3
Total	5	15	24	44

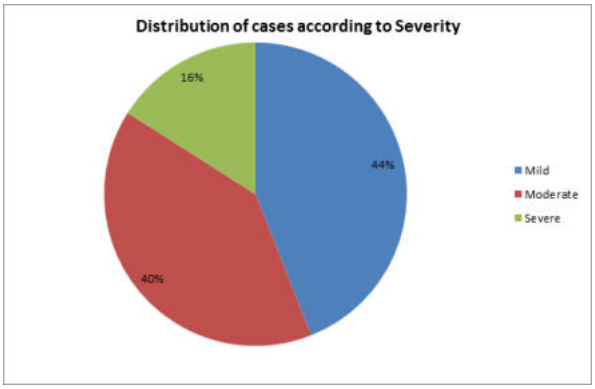


Figure 7

Figure 8: Distribution Of Severity According To HbA1c Level

Severity	HbA1c Level						Total
	<7.5		7.5–8.5		>8.5		
	No.	%	No.	%	No.	%	
Mild	8	38.09	4	30.76	2	20	14
Moderate	12	57.14	6	46.15	3	30	21
Severe	1	4.76	3	23.07	5	50	9
Total	21		13		10		44
x2	0.197						
P	0.04						

Figure 9: Distribution Of Outcome According To HbA1c Level

Outcome	HbA1c Level						Total
	<7.5		7.5–8.5		>8.5		
	No.	%	No.	%	No.	%	
Survive	19	90.47%	11	84.61%	7	70%	37
Death	2	9.53%	2	15.39	3	30%	7
Total	21		13		10		44
p value	0.04						

Table 10: Comparison Of Outcome In Relation With CRP Levels

CRP	No. of cases	Outcome			
		Recovered		Died	
		No.	%	No.	%
<100	70	84	94.38	4	36.36
>100	30	5	5.62	7	63.64
Total	100	89		11	
p value		0.03			

DISCUSSION

This was a retrospective cross sectional study conducted in Department of Medicine, Sardar Patel Medical College Bikaner on RT-PCR confirmed COVID 19 patient admitted in dedicated COVID 19

hospital from April 2021 to October 2021. A total 100 RT-PCR positive COVID cases were taken for this study.

In our study majority of the patients were male. There were 80 males i.e. 80% with mean age 53.98±11.67 years (ranging 21–80) and 20 females i.e. 20% with mean age 56.4±22.5 (ranging 20-87 years). We found male predominance M:F, 8:2

Maximum patients belongs to age group (41–60 years) i.e. 49% followed by older patients (61-80 years) 30%. While least patients belongs to age group >80 years. Similar finding were observed by Dave Mahesh et al47. They found in their study that maximum cases were in age group 15-49 years & 50-64 years which was 66.06 & 19.19% respectively.

100 cases 65 cases belonged to urban residential area i.e. (65%) and 35% cases were from rural residential area. Dave et al47 reported high prevalence of covid-19 in urban area.

Urban area is overcrowded as compared to rural area. Conditions in urban area favours rapid spread of COVID 19 infections.

In our study, out of 27 patients belonging to rural area had habits of smoking i.e. 44.44%, alcohol consumption i.e. 48.15% and 7.41% had tobacco users. Out of 36% of urban population 55.56% had habits of smoking, 36.11% had habits of alcohol consumption, 2.78% were opioid users, 5.56% were tobacco users.

In our study, 44 of patients had comorbidity of DM i.e 44%, 27 had HTN had 27%, 14 had CAD, 7had CVA, 8 had CKD, 11 had COPD, 5 had BA, 8 had CLD, 3 had malignancy, 6 had hypothyroidism. Similarly Hardeva Ram Nehra et al. (2022) found that diabetes mellitus (20.4%) and HTN (18.2%) were the most common comorbidities among COVID 19 patients, and 32.2% had more than one comorbidities. In a similar study, Djahruddin et al 202136 found the prevalent comorbidity was hypertension (42.31%), cardiovascular disease (30.77%), diabetes (28.21%), chronic kidney disease (23.08%), malignancy (15.38%), obesity (15.38%), chronic liver disease (7.69%), chronic respiratory disease (6.41%), immune related disease (3.85%), and non-traumatic cerebral infarction (3.85%). 41 (52.56%) patients reported having two or more comorbidities, and 37 (47.44%) only has one comorbidity.

Out of 100 cases, 48 people had their duration of illness 1-2 weeks following with 33 people >2 weeks and 19 were 1 week during their duration of illness. The mean of hospital stay was 10.4 ± 6.42 similar finding was observed by Faes C et al 202049 they found median time to symptom onset to hospital admission was 7 day (4-8) days.

In present study, in survived cases majority of patients have anosmia 14.37%, dyspnoea 13%, cough 12.33%, fever 1.99%, sore throat 10.54% and other presenting symptoms. In expired cases, majority of patient have dyspnoea 18.39%, cough 16.09%, fever 11.49% and other presenting symptoms. Similary Narendran Gopalan et al (2022) the distributions of symptoms were as follows: Fever 62.6%, dyspnoea 49.9%, cough 46.4%, gastrointestinal symptoms 10.9% in decreasing order of frequency.

Majority of cases i.e. 10 having higher HbA1c level (>8.5) are from 41-60 years of age group following with 8 were from 61-80 years of age group, 3 cases were from 20-40 years of age group and 3 cases from >80 years of age group respectively.

Out of the survived cases i.e. 37, 19 (51.35%) had HbA1c level <7.5 following with 11(29.73%) cases have HbA1c level between 7.5-8.5, in 7 (18.92%) cases have HbA1c level >8.5. In death cases, 3 (8.11%) cases have HbA1c >8.5, 2 (9.53%) have HbA1c between 7.5-8.5 and 2 (15.39%) have <7.5 HbA1c levels respectively.

In present study, severity according to HbA1c level among study population. In severity level, 21 cases having moderate, 14 were mild and 9 were severe. HbA1c as a clear predictor of COVID-19 severity. Pre-infection risk stratification is crucial to successfully manage this disease, efficiently allocate resources, and minimize the economic and social burden associated with an undiscriminating approach.

In our study, outcome according to type 2DM status among study population. In our study, out of 44 DM cases 37 survived and 7 died. Out of 56 non DM cases 52 survived and 4 died. In a similar study,

Out of 44 type 2DM cases, 21 had moderate disease, 14 had mild and 9 had severe disease. In non DM cases 30 had mild disease, 19 had moderate disease and 7 had severe disease. Among the diabetic patients 31.81% had mild disease, 47.72% had moderate disease and 20.45% had severe disease. Comparing with non diabetic patients 53.57% had mild disease, 33.92% had moderate disease and 12.5% had severe disease. p value (0.02) is statistically significant.

In our study, among the diabetic patients 84.04% patients survived and 15.91% died. Comparing with non dm patients 92.86% patients survived and 7.14% expired with (p value 0.006) which is statistically significant. Similarly Salman Hussain et al[10] (2020) found that mortality risk was significantly higher in COVID-19 patients with diabetes as compared to COVID-19 patients without diabetes with a pooled risk ratio of 1.61 (95% CI: 1.16–2.25%), (p = 0.005). He concluded that this meta-analysis found a high prevalence of diabetes and higher mortality among diabetic patients.

In our study, out of 89 recovered cases 84 (94.38%) cases had <100 CRP level, 5 (5.62%) cases had >100 CRP levels. Out of 11 expired cases 4 (36.36%) cases had <100 CRP level and 7 (63.64%) cases had CRP levels >100. Similarly, Mohammed Zaqaria et al (2022)52 he found that the mortality rate in the patients with CRP >100mg/l was 77.4% and compared with 22.6% for patients with CRP <100mg/l. The p value (0.03) is statistically significant.

CONCLUSION

COVID-19, due to its heterogeneity, can be considered a systemic disease as it is more than a single-organ disease. The association with diabetes makes the whole condition at a higher risk of poor outcomes. For this reason, from now on, diabetes care has to include a careful, holistic evaluation of all the patients affected by COVID-19.

Our study shows there are certain factors which can affect outcome in the cases of covid-19 like elderly age, co-morbidity and the duration of illness, raised CRP are the important factors associated with poor outcome. Early recognition and alertness is important to reduce morbidity and mortality. Patients should also be screened for multiple organ involvement at the time of hospitalization by laboratory test like CBC, RFT, LFT, CRP titre for early diagnosis of multiple organ involvement so as to treat appropriately to prevent multiple organ failure and mortality.

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