ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 09, 2023

Assessment Of Fatality Ratio In Covid19 Patients With Diabetes And Without Diabetes Mellitus: Comparative Retrospective Study in Waves One and Two of Covid-19

Dr. Mangala Sirsikar[1], Dr. Suhas Dhulipala[2], Dr. Shailaja Alapaty[3], Dr. Alamelu[4], Dr. Umalakshmi Annavarapu [5], Dr. Deepthi Mahendrakar[6] and Dr. Jyothi A Natikar[7]

[1]Associate professor Department of Biochemistry, Vydehi Institute of Medical Sciences and Research Centre is in Whitefield, Bangalore
[2]Junior resident Department of pulmonology, Vydehi Institute of Medical Sciences and Research Centre is in Whitefield, Bangalore
[3]Professor Department of Biochemistry, Vydehi Institute of Medical Sciences and Research Centre is in Whitefield, Bangalore
[4]Professor & HOD Department of Pulmonology, Vydehi Institute of Medical Sciences and Research Centre is in Whitefield, Bangalore
[5]Assistant professor Department of Biochemistry, Vydehi Institute of Medical Sciences and Research Centre is in Whitefield, Bangalore
[6]Assistant professor Department of Biochemistry, Vydehi Institute of Medical Sciences and Research Centre is in Whitefield, Bangalore
[7]Assistant professor, Department of Biochemistry, Vydehi Institute of Medical Sciences and Research Centre is in Whitefield, Bangalore

Corresponding author:
Dr Mangala Sirsikar
Email id: mangalans81@gmail.com

Abstract:
Background: An infection with the deadly COVID-19 virus is more likely to occur in people with type 2 diabetes mellitus. The virus itself causes an altered glycemic state by raising insulin resistance and lowering beta cell production. This leads to increased blood sugar levels. **Aims:** In order to make a comparison between the clinical outcomes of people who have diabetes and those who do not have diabetes in terms of survival, mortality, and fatality rates across various categories of clinical severity in both waves of the COVID-19 study. **Methods**: A tertiary care hospital served as the location for the execution of this retrospective investigation. The data on a total of 1773 participants were gathered from wave one and wave two of the ofCOVID-19 epidemic among diabetics and those who did not have diabetes. **Results**: In the first wave of the study, there were 1283 individuals who did not have diabetes, but 224 patients (14.9%) did have diabetes. During the second wave, there were 205 individuals, of whom 77 people did not have diabetes and 61 persons did have diabetes.During the first wave of the study, there were no verified fatalities among the non-diabetic participants who made up 1283 of the subjects who survived. Out of the diabetics, 199 (88.8%) made it through, while 25 (11.16%) did not. The number of non-diabetics who survived wave two was 192 (94%), whereas the number of diabetics who survived was 52 (81.88%). The death rate was determined to be 13 (6.34%) among non-diabetic individuals and 9 (14.75%) among diabetic individuals, respectively. First wave diabetes had a Case Fatality Rate (CFR) of 11.16 percent. The CFR was 14.75 percent in diabetics and 4.33 percent in non-diabetics, according to the second round of studies. **Conclusion:** The CFR was found to be high in both waves in diabetics, which suggests that increased glycated hemoglobin and poor blood sugar management both enhance the chance of severity. In wave two, the CFR indicated that non-diabetics were experiencing an enhanced cytokine storm.
Keywords: Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Cov-2), Hyperglycemia, Wave One. Wave, Two, Case Fatality Rate.

INTRODUCTION:

The city of Wuhan, which is in the Chinese province of Hubei, was the scene of the first confirmed cases of atypical pneumonia brought on by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) towards the end of December 2019.The World Health Organization (WHO) declared the 2019 coronavirus disease (COVID-19) to be pandemic on March 11, 2020 [1]. This happened as a direct effect of the virus' rapid global dissemination. An infection with Covid-19 may be asymptomatic, cause mild upper respiratory symptoms, cause abrupt respiratory failure requiring critical care, or any combination of these three outcomes [1]. In India, the first wave started in March of 2020 and peaked in the middle of September of the same year. The peak of the second wave was achieved in April 2021, and it persisted there until May of the same year[1]. Among the many other ways that the second wave of diabetes was different from the first, researchers found variations in the course of the illness [2]. This was only one of many ways the second wave of diabetes differed

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 09, 2023

from the first. Around the world, it was estimated that 463 million people had diabetes mellitus [2, 3], or 9.3 percent of the total population. One of the problems the world has was diabetes. Insufficient glucose metabolism as a consequence of either an absolute or relative insulin shortage and its usage characterizes diabetes mellitus, a challenging and chronic systemic disease [4]. One of the reasons why this was the case was because diabetes was a systemic illness that wreaked havoc on the body. When people with diabetes are exposed to COVID-19, a chronic inflammatory condition, their immune and inflammatory systems respond more strongly, which in turn encourages the production of cytokines and hyperglycemia [4]. This resulted in the development of hyperglycemia, which then produced advanced glycation end products, which in turn brought on oxidative stress and glucotoxicity in a range of tissues spread across the body [4]. As a result, it is likely that persistent inflammation and hyperglycemia are what interact to cause mortality and multi-organ failure [5].

One of the most significant independent risk variables for a severe COVID-19 course was poor glucose management.Higher levels of hyperglycemia in diabetics are a result of an abnormal glycosylation of the ACE2 receptor, which leads to insulin resistance and pancreatic cell dysfunction [6, 7].The World Health Organization (WHO) recommends high steroid dosages for patients with severe or critical COVID-19 since doing so considerably reduces the patient's risk of dying [8]. For a very long time, it had been known that steroid therapy would promote peripheral insulin resistance, which would eventually lead to the emergence of hyperglycemia. Stress had a significant role in the development of hyperglycemia. Acute diseases brought on by COVID-19 resulted in the release of cortisol, adrenaline, and glucagon into the system. This directly led to an increase in gluconeogenesis in the liver, which resulted in a brief surge in blood sugar [9,10]. These behaviors lead to hyperglycemia, which in turn is likely to cause glucose toxicity of b-cells, which further reduces the insulin secretory activity. Inflammatory cytokines and excessive steroid use both have the power to reduce the body's capacity to produce insulin [11]. People with COVID-19 may have glucose dysregulation, which may be a result of any one of the aforementioned routes or may be exacerbated by a combination of pathways. Numerous studies have shown that diabetes is associated with a high risk of serious to life-threatening illness (14%-32%). Patients with COVID-19 have a prevalence of diabetes that ranges from 5% to 20%, and they are at a much higher risk. Diabetes has been identified as a co-morbidity in both waves [12]. Further research is necessary to fully understand the similarities and differences between the two waves of diabetes and non-diabetics in terms of their characteristics. In order to compare survival and fatality rates across all levels of clinical severity and draw comparisons between the data from the two waves, it is important to perform a study of COVID-19 hospitalized patients in both diabetics and non-diabetics. We divided the total number of SARS-CoV-2 cases documented in the 10 days before to admission by the total number of COVID-19-related fatalities to arrive at the case fatality ratio [13]. because it often took 10 days or more between the onset of symptoms and admission to an intensive care unit (ICU) [13].

Understanding how COVID-19 patients with diabetes mellitus have poor blood glucose homeostasis may help in the early detection of diabetes complications and mortality. The development of diagnostic tools, potent medications, and vaccines, all of which contribute a significant deal to the decline in mortality, are primarily due to the case fatality rate. By comparing the overall number of deaths to the total number of confirmed cases of Covid-19 reported in Indian medical literature, the case fatality rate was calculated. The case fatality rate might be calculated thanks to this comparison. This was the first study to evaluate clinical outcomes between individuals with diabetes and those without the illness throughout the course of two research cycles and across a variety of diabetes severity levels. In India [14], where there is a shortage of knowledge on the problem, this was the first research to compare people with diabetes and those who did not. This was one of the first retrospective studies to compare the case fatality rate of people with diabetes to those without diabetes among the two waves of the COVID-19 trial.

MATERIAL AND METHODS:

Study design:

Inclusion Criteria

Patients who tested positive for SARS-CoV-2 using RT-PCR using nasal and oropharyngeal swabs and were older than 18 years of both sexes. Type II Diabetes Mellitus patients. The American Diabetic Association (ADA) used HbA1C and fasting blood glucose to diagnose diabetes in patients. Non-diabetics had normal fasting blood sugar levels and no prior history of DM. In this study, DM was defined as having HbA1c 6.5%, fasting glucose 200mg/dL, medical records suggesting a known case, and anti-DM medication usage. HbA1c 6.5, fasting glucose 70-100mg/dL, and no history of DM or anti-DM medicine use were considered to be non-DM [15].

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 09, 2023

Exclusion criteria:
Co morbid conditions, including but not limited to, cardiovascular disease, trauma, infection, burn, and chronic inflammatory diseases including lupus, vasculitis, rheumatoid arthritis, and inflammatory bowel disease, disqualified patients from participation in the experiment. Patients having symptoms compatible with COVID-19 who reported to the hospital but did not need hospitalization because their infection could not be confirmed by RT-PCR in the laboratory.

Data collection:
The portion of the health record from which the patient information was derived. The pandemic's first wave and second wave were both taken into account. Patients' ages, genders, dates of admission, and a number of other demographic information were noted.

During waves 1 and 2 of the COVID-19 trial, a total of 1773 data points were gathered due to the availability of fasting blood glucose and glycated hemoglobin on the day of admission. The analysis of the findings was built on these data points. Then, these data were split into two separate groups: the first group included individuals with diabetes mellitus, while the second group included those without the disease. In the first group, 223 people had diabetes, compared to 1283 participants without the condition. When the second wave of patients came, there were 61 individuals with diabetes and 205 persons without the disease. [15]

Depending on the severity of their clinical symptoms, participants were categorized as asymptomatic, mild, moderate, severe, or critically ill. When a patient tests positive for SARS-CoV-2 using a virologic test (such as a nucleic acid amplification test or an antigen test) but does not exhibit symptoms like COVID-19, the terms "asymptomatic" and "presymptomatic infection" are used to characterize them. The new criteria that the NIH has created for assessing the impact of the COVID-19 outbreak have only lately been made public by the Indian government. These recommendations were used to gauge the patient's sickness severity at the time of admission. More information on these criteria is given in the next paragraph [16].

Patients with COVID-19 symptoms (fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhoea, and loss of taste and smell) who don't also exhibit symptoms of more severe respiratory distress (such as shortness of breath, dyspnea, or abnormal chest imaging) are thought to have a mild illness. Like its name would imply, a mild sickness does not endanger life.

People with a mild form of the sickness are those whose oxygen saturation (SpO2) is less than 94% in room air at sea level and who demonstrate symptoms of lower respiratory disease on clinical examination or imaging.

A severe sickness is recognized when a patient's oxygen saturation (SpO2) on sea level room air is lower than 94%, their PaO2/FiO2 is lower than 300 mmHg, their respiratory rate is more than 30 breaths per minute, or their lung infiltrates are higher than 50%.

A severe sickness may cause a patient to have respiratory failure, septic shock, or organ dysfunction.

Participating in a Fasting Period A chemical analyzer (Beckman Coulter AU 700) was used to measure the levels of glucose in the blood. Fasting blood glucose levels were regarded as normal when they were between 70 and 100 mg/dL. [15]

As part of routine hospital practice, inflammatory laboratory blood markers including LDH, CRP, D-dimer, and serum Ferritin were assessed to see whether or not there was a relationship between the severity of the disease and the chance of death. The study's main finding was a comparison of clinically significant fatality rates and survival rates for hospitalized people with and without diabetes. By dividing the total number of COVID-19 cases among diabetes patients and non-diabetics by the number of confirmed COVID-19 deaths, we were able to calculate the overall case fatality ratio. As a result, we were able to contrast the intensity of the initial and second waves of the epidemic.

Statistical Analysis:
The data was then subjected to an SPSS version 22 analysis after being entered into an Excel spreadsheet. Counts and percentages were used to show how well each group was represented. The chi-square test was used to gauge the qualitative data's degree of significance. The continuous data were investigated for probable normality using the Shapiro-Wilk and Kolmogorov-Smirnov statistics. When reporting on continuous data, the mean and standard deviation are two statistics that are often utilized. To determine the standard deviation of the difference between the two quantitative variables, an independent t-test was performed. The median difference

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 09, 2023

between the two quantitative variables was determined using the Mann-Whitney U test as a significant test. Due to the skewed distributions of both quantitative variables, this was done. The quantitative data was subjected to Analysis of Variance (ANOVA) in order to identify which group's mean values were substantially different from those of the other groups. The mean difference between three or more groups was calculated using the Kruskal-Wallis test when the distribution of the quantitative data was skewed. When the test was run, this was the situation. A result was considered statistically significant if it had a p value of less than 0.05, which signifies the chance that the outcome is correct, after all relevant statistical testing processes had been carried out.

RESULTS:

Table1: Mean age comparison between 1st wave and 2nd wave wave of Covid with respect to Diabetics and Non-Diabetics

				Mean Age	SD	P value
Diseases status	Non-Diabetes	Wave	1st Wave	45.01	15.51	0.456
			2nd wave Wave	48.58	16.27	
	Diabetes	Wave	1st Wave	55.65	12.52	0.029*
			2nd wave	53.84	11.50	

Table 1: The average age of diabetics in Covid 1st wave was 55.65 ± 12.52 years, and in 2nd wave, 53.8 ± 11.50 years. Diabetics had a substantial mean age difference between waves (P=0.029*). Non-Diabetic individuals in Covid 1st wave had a mean age of 45.01 ± 15.51 years, and in 2nd wave, 48.58 ± 16.27 years. The mean age of non-diabetic patients did not alter across waves. 0.456 p-value.

Table 2: Comparisons of Gender between 1st wave and 2nd wave of Covid-19 with respect to Diabetics and Non-Diabetics.

Gender distribution among Diabetics versus Non-Diabetes in two waves					
1st wave	**Diabetics(N=224)**	**Male**	**155**	**69.19%**	**P < 0.0001***
		female	**69**	**30.8%**	
	Non-Diabetes(N=1283)	**Male**	**732**	**57.05%**	**P < 0.0001***
		female	**551**	**43%**	
2nd wave	**Diabetics(N=61)**	**Male**	**44**	**48%**	**P = 0.0234**
		female	**17**	**28%**	
	Non-Diabetes(N=205)	**Male**	**132**	**64.2%**	**P < 0.0001***
		female	**73**	**36%**	

P < 0.0001 statistically significant.

Table 2: In wave one, there were 69.1% men and 30.8% women who had diabetes, compared to 57% men and 43% women who did not. Statistically speaking, there was a substantial difference between the male and female groups (p 0.0001).*

In the second wave, there were 48% men and 28% women with diabetes, compared to 64.2% men and 36% women without diabetes. A statistically significant difference existed between the male and female groups (p 0.0001).

Table 3: Distribution of subjects with respect to Diabetes and Non-Diabetics in wave one and two among clinical severity

1st wave N=1507		**Clinical Severity**				**Total**
		Mild	**Moderate**	**Severe**	**Critical**	
Non Diabetic	**Count (%)**	**1028(89.9%)**	**228(72.2%)**	**21(58.3%)**	**6 (54.5%)**	**1283 (85.1%)**
Diabetic	**Count (%)**	**116 (10.1%)**	**88 (27.8%)**	**5 (45.5%)**	**15 (41.7%)**	**224 (14.9%)**
2nd wave N=266						
Non Diabetic	**Count (%)**	**147 (81.1%)**	**42 (66.7%)**	**8 (72.7%)**	**8(72.7%)**	**205 (77.0%)**
Diabetic	**Count (%)**	**34 (18.9%)**	**21 (33.3%)**	**3 (27.3%)**	**3 (27.3%)**	**61 (23.0%)**

#Kruskal Wallis test

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 09, 2023

Table 3: In wave one, 1283(85.1%) were Non-Diabetic and 224(14.9%) were diabetic. In 2nd wave, 204 (77.0%) were Non-Diabetic and 61 (23.3%) were diabetic.

Table 4: Comparisons of Fasting Blood Glucose, Glycated Hemoglobin with respect to Diabetes and Non-Diabetics in wave one and two

Wave one n=1507				
variables (Mean and SD)	Non Diabetic	Diabetic	95% CI	P-value
Fasting Blood Glucose mg/dL	107±33	391±80	277.84 to 290.15	P < 0.0001
Glycated hemoglobin %	5.2 ± 12	13.5±18	5.9 to 9.6	P < 0.0001
2nd wave N=266				
Fasting Blood Glucose mg/dL	110±23	449±76	327.06 to 350.9	P < 0.0001
Glycated hemoglobin %	5.2 ± 20	15.5± 25	4.19 to 16.40	P = 0.0001

Chi-square test,P < 0.0001* statistically significant.

Table 4: The 2nd wave mean and SD of Fasting Blood Glucose was 449±76, considerably higher than wave one (391±80) with P < 0.0001. Diabetic patients had substantially higher glycated hemoglobin in wave 2 (15.5±25) compared to wave 1 (13.5±18) with P = 0.0001. Non-Diabetics have no substantial fasting blood glucose-glycated hemoglobin differential.

Table 5: Distribution of Outcome of survival and death among Diabetics and Non-Diabetic in 1st wave Covid-19 in clinical Severity.

Out come	Wave one N=1507	Clinical Severity				Total	p Value
		Mild	Moderate	Severe	Critical		
Survival	Non Diabetics=1283	1028(80.12%)	228(17.77%)	21(1.63%)	6 (0.46%)	1283 (100%)	P < 0.0001
	Diabetic N=224	110(49%)	86(38.39%)	2 (0.89%)	1(0.4%)	199(88.8%)	
	Insulin therapy	08 (7.2%)	04(4.65%)	-	-	12(6.03%)	
	Oral hypoglycemic therapy	102(92.72)	82(95.34%	2(100%	1(100%	187(93.96%)	
Death	Non Diabetics=1283	NIL					P < 0.0001
	Diabetic N=224	6(2.6%)	2(0.89%)	3(1.3%)	14(6.25%)	25(11.16%)	
	Insulin therapy	5(83.3%)	1(50%)	3(100%)	13(92.9%)	22((88%)	
	Oral hypoglycemic therapy	1(16.6%	1(50%)	-	1(7.14%)	3(12%)	

significantly significant (P < 0.0001).The Kruskal Wallis test is shown in Table 5. In wave one, all 100% non-diabetic participants (1283) survived, whereas 88.8% diabetes subjects (199) survived with P values <0.0001. Significantly increased diabetic fatalities 25 (11.16%), 14 (6.25%) of which had severe respiratory failure, on ventilator, and 3 (1.3%) in ICU with oxygen assistance. Non-Diabetics had no recorded fatalities with P values <0.0001.In diabetics who lived, 12 (6.03%) were on insulin and 187 (93.96%) were on oral hypoglycemic medication. Those who died, 22 (88%) were on insulin and 3 (12%).

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 09, 2023

Table 6: Distribution of Outcome survival and death among Diabetics and Non-Diabetics in 2nd wave of Covid-19 in clinical Severity.

2nd wave N=266		Clinical Severity				Total	p- Value
		Mild	Moderate	Severe	Critical		
Survival	Non Diabetics=205	145(70.73%)	38(18.62%)	3(1.47%)	6(2.9%)	192(94%)	
	Diabetic n=61	31(50.81%)	18(16.08%)	2(3.27)	1(1.63%)	52((81.88%)	
	Insulin therapy	5(16.12%)	06(33.33%)	-	-	11(21.15%)	
	Oral hypoglycemic therapy	26(83.87	12(66.66%)	2(100%)	1(100%)	41(78.84%)	
Death	Non Diabetics=205	2(0.97%)	4(1.9%)	5(2.4%)	2(0.97%)	13(6.34%)	
	Diabetic n=61	3(4.9%)	3(4.9%)	1(1.63%)	2(3.27%)	9(14.75%)	
	Insulin therapy	2(66.66%)	2(66.66%)	1(100%)	2(100%)	7(77.77%)	
	Oral hypoglycemic therapy	1(33.33%)	1(33.33%)	-	-	2(22.22%)	

Table 6: In the second wave, 192 non-diabetics (94%) survived compared to 52 diabetics (81.88%).With P < 0.0001. Diabetes was associated with 9 (14.75%) deaths compared to 13 (6.3%) among non-Diabetics, with P values <0.000.1Diabetes patients who survived were 11(21.15%) on insulin therapy and 41(78.84%) on oral hypoglycemic medication, whereas those who died were 07(77.77%) and 2(22.22%).

Table7: Distribution of C-RP, LDH, D Dimer and Ferritin among Diabetics and Non-Diabetics among 1st and 2nd wave wave ofCOVID-19

	1st wave			2nd wave wave		
Parameters	Non Diabetes Mean ± SD	Diabetes mellitus Mean ± SD	P values	Non Diabetes Mean ± SD	Diabetes mellitus Mean ± SD	P values
CRP mg/dL	4.24 ± 5.7	7.24 ±6.85	<0.0001*	5.99 ±5.7	9.45 ±9.72	<0.0001*
LDH IU/L	263.55±179.3	274.86±114.32	<0.0001*	255.55 ±179.3	294.86 ±114.32	<0.0001*
D Dimer (mcg/mL)	488.79±971.3	755.96±1765.9	<0.0001*	450.59 ±871.3	865.23±1565.0	<0.0001*
Ferritin (µg/L)	324.27±337.2	388.43 ±288.94	<0.0001*	324.27±337.29	588.43 ±35094	<0.0001*

P < 0.0001 statistically significant.#Mann Whitney U

Table 7:In wave one, mean and SD of inflammatory markers in Diabetic were significantly high with CRP (7.24 ± 6.85), LDH (274 ±114.32),D Dimer (755± 1765.97), Ferritin (388.43± 288.94) compared to Non diabetic group with CRP (4.24±5.70),LDH (263.55±179.30),D Dimer(488.79±971.30),Ferritin(324 ±186.55).In 2nd wave mean and SD of inflammatory markers in Diabetic were CRP (9.45 ±9.72), LDH (294.86 ±114.32),D Dimer 865.23±1565.0), Ferritin (588.43 ±35094) were increased with statistically significant p values of <0.0001* compared to Non diabetic CRP (5.99 ±5.7),LDH (255.55 ±179.3),D Dimer(450.59 ±871.3),Ferritin(324.27 ±337.29).

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 09, 2023

Table 8: Case Fatality Ratio **among diabetic and non-diabetic deaths in wave one and 2nd wave**

	Total	Mild dead	Moderate dead	Severe dead	Critical dead	Fatality rate	P value
1st wave=1507							
Diabetic	224	6	2	3	14	11.16%	-
Non diabetic	1283	0	0	0	0	0	
2nd wave=266							
Diabetic	61	3	3	1	2	14.75%	
Non diabetic	205	2	4	5	2	4.3 %	**P** = 0.0072

Table 8: When compared with non-diabetics, diabetics had a case fatality ratio of 11.16% in the first wave of the study. In the second wave of the case fatality ratio study, the ratio for non-diabetics was 4.3%, while the ratio for diabetics was 14.75%, indicating that fatalities were seen in both categories.

DISCUSSION:

This retrospective cross-sectional study investigated 1773 COVID-19 patients, both diabetic and non-diabetic, at a tertiary hospital in ……. In wave one, 1283 were non-diabetic and 224 had diabetes from March to September 2020. In the 2nd wave, 204 were non-diabetic and 61 diabetic from January to May 2021. First wave had more subjects than second. The wave differences were unknown. Novel SARS-CoV-2 variant, enhanced illness information, laboratory COVID-19 testing, intensive care units for extreme severity, better treatment mode, and vaccination status are plausible causes [17]. Patients averaged 21–70 years old. The average age of diabetics in Covid Wave 1 was 55.65 ± 12.52 years, whereas in Wave 2 it was 53.84 ± 11.50 years. Diabetics' mean age varied greatly between waves. Non-Diabetics' average age in Covid 1st wave was 45.01 ± 15.51 years, and in 2nd wave, 48.58 ± 16.27 years. The mean age of non-diabetic patients did not change between waves.

In wave 1, 69.1% of diabetics were male and 30.8% female; 57% were male and 43% female. A significant difference existed between men and women in both groups ($p < 0.0001$). Jain, S. Paranjape, et al. found diabetes men over 60 were older [18].

In the second wave, diabetics comprised 48 percent of the population whereas non-diabetic individuals comprised 64.2 percent of the population. Significantly different between males and females from a statistical perspective (p less than 0.0001).The older population was disproportionately impacted by both the first and second COVID-19 pandemics that occurred in India [19], as seen in Tables 1 and 2. According to Iftimie et al. [20], more younger patients were hospitalized during wave two than during wave one.

SARS-CoV-2 may affect people of both sexes, although investigations conducted throughout the globe found that older males were more susceptible (more than 50%).Both putative androgen response elements (AREs) and oestrogen response elements (ORE) have an effect on innate immunity; as a result, males are more susceptible to infection [21]. According to a number of studies, men have a higher risk of contracting a viral infection and manufacture less antibodies than women do. When women have greater amounts of TRL7, this leads to increased levels of interferon- and an improvement in their innate immunity [22].

According to Uday Yanamandra et al. [23], 32% of individuals in wave one and 25% in wave two were diabetic, suggesting COVID-19 infections include younger guys with impaired glucose metabolism.

The major outcome was survival vs. mortality in diabetics and non-diabetics of varied clinical severity. Wave one of 1283 non-diabetic participants survived with 732 (57%) men and 55 (4.2%) women. No deaths recorded. Of 224 diabetics, 199 (88.3%) survived and 25 (11.6%) died. In the second wave, 192 (94%) of 266 non-diabetics survived while 13 (6.34%) perished. 52 diabetics (81.8%) survived, 9 (14.7%) died. Diabetics died 11% from COVID-19, compared to 1% for non-Diabetics. The ICU on ventilator killed 14 men and 8 women in wave one of critically ill diabetes. Gupta R, Ghosh A, Singh AK, and Misra et al.'s study was financed [24]. While non-diabetics had an average fasting blood glucose of 107±33 mg/dl and HbA1C of 5.2 ± 12, diabetics had 391±80 mg/dl in wave one and 449±76 in wave two The mean and SD HbA1C values in wave one were 13.5±25, and in wave two, 15.5±20. Increased blood sugar and Glycated hemoglobin associated to mortality in both waves. Bode et al. [25] showed that COVID-19 patients (n = 184) with uncontrolled hyperglycemia (defined as >2 blood glucose value, >180 mg/dl during any 24-hour period) had a greater death rate (41.7 vs. 14.8%, p 0.001). Diabetes patients died more in COVID-19 due to stress-induced blood glucose increases and

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 09, 2023

cytokine and endogenous steroid production. Hyperglycemia increases pancreatic beta cell ACE receptors, affects innate immunity, neutrophil dysfunction, inhibits complement and immunoglobulin activity, damages endothelial cells, and promotes coagulopathy, which increases cytokine release.[26]. Merzon E, Shpigelman M, Green I. Their investigation related increased glycated hemoglobin to hospitalization and hypercoagulability, as in the current study with fasting blood glucose over 449mg/dl and HbA1C of 15.5% in critically sick ventilator-dependent patients with raised CRP, LDH, and Ferritin. Tablel-7 reveals hypercoagulability with 1815.96 mcg/mL D Dimer [27].

Researchers Wu J., Zhang J., Sun X., and others showed that diabetes was a major factor in wave one mortality. In the COVID-19 study, those with diabetes had a mortality risk that was 2.95 times higher than non-diabetic people [28]. During the whole of the quarantine, it was difficult to get medication, insulin, needles, glucose strips, and other supplies [29]. The second wave of non-diabetics had a higher mortality rate. As a consequence of the recurrence of COVID-19, many hospitals stopped providing services in their outpatient departments, diabetes treatment suffered, and poor glucose control was the end outcome [30]. The second wave was more severe than the first, spread more quickly, and was highly contagious. Patients diagnosed with diabetes who had higher admission levels of CRP, LDH, Ferritin, and D dimer were more likely to pass away. Wave 2 was much higher in height than wave 1. Admission hyperglycemia, d-dimer levels, and CRP levels have all been linked to poor patient outcomes [30].

The secondary finding was that the diabetes CFR for wave one was 11.16%. Deaths due to causes other than diabetes: none. In the second wave, the death rate for those without diabetes was 4.3 percent, whereas the death rate for diabetics was 14.75%. In the second wave of the study, diabetic patients had higher levels of inflammatory markers as well as CFR, FBS, and glycated hemoglobin [31]. After the first wave, the COVID-19 clinical guidelines suggested administering intravenous steroids and antivirals. Before the improved severe illness intravenous steroid recommendations were implemented, the CFR was 3.53 times higher than it is now. The second wave observed an increase in CFR in diabetics as well as non-diabetics due to a highly transmissible form of SARS-CoV-2-B.1.617, low social distance among young people, and self-treatment. Even though there were many Covid-19 labs, only a small number of persons were tested. Patients with moderate to severe illness were not hospitalized during later phases of COVID-19, and only adults were vaccinated [32]. individuals who were treated with insulin had a greater COVID-19 mortality rate compared to individuals who were treated with metformin [33].

Limitations:
Despite producing some incredibly fascinating results, the study had its share of issues. First, it's possible that the study confounders' contributions to properly forecasting catastrophic occurrences were exaggerated. This is because the study was based on a small sample size and was done retrospectively from a single site. For the purpose of reporting and result analysis, only the outcome and mortality of diabetic patients with COVID-19 were taken into account. There were considerably fewer individuals with diabetes mellitus in the sample as compared to non-diabetics. Here, neither the duration of DM nor the course of therapy are considered. The second wave's immunization status was excluded due to the reduced sample size. The technique of therapy is not mentioned. A DM underestimation or data that were ignored. When there are people who have the sickness but aren't receiving a diagnosis, the CFR will overestimate the real risk of fatality. There were a sizable number of people who did not get a COVID-19 diagnosis. By comparing the overall number of fatalities brought on by COVID-19 to the total number of cases, the CFR rate was calculated. The total number of CFR Indians studied in this single-centered hospital research was underestimated since only a small subset of individuals with diabetes mellitus and non-diabetic members of the general population were evaluated.

CONCLUSION

The researchers came to the conclusion that more individuals were in wave one than in wave two based on the findings of the retrospective study comparison between participants with diabetes and subjects without diabetes. Men were affected by both waves of the pandemic, in contrast to women. Seniors often experienced the first wave of diabetes effect, but younger people saw the second wave of non-diabetic impact. When compared to those with diabetes, individuals without diabetes had greater survival rates. In wave one, only deaths among individuals with diabetes were documented, but no deaths among those without diabetes were found. Deaths during the second wave included both those with diabetes and people without the disease. First, as diabetes has the potential to cause severe COVID-19, it is essential to maintain appropriate blood glucose monitoring. The high death rate during wave one was mostly caused by the lack of knowledge on COVID-19's pathogenic role in diabetes mellitus. The fact that non-diabetic individuals passed away during the second wave while having stable blood sugar levels shows that the organ damage and cytokine storm were made worse. Despite the fact that mortality can be caused by a number of factors, including age, sex, hospitalization, laboratory biomarkers,

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 09, 2023

immune state on the day of admission, and treatment, this finding shows that elevated glycated hemoglobin and hyperglycemia in diabetes mellitus were possible risks or comorbidities for severity. As a result, COVID-19 has to be evaluated in diabetes mellitus with more care.

Conclusion: Whether or whether COVID-19 patients are already aware that they have diabetes, the blood glucose level upon admission is unquestionably a crucial signal for risk classification and guiding the therapeutic treatment of COVID-19 patients. As a result, it is crucial that all COVID-19 patients be closely watched for both acute and chronic types of hyperglycemia upon admission. This will guarantee that, should it be necessary, prompt and effective treatment can be started.

Author contributions

--------- supervised the acquisition of the data, analyzed and interpreted the data.---- and ---- assisted in collecting clinical information about the patients and helped to interpret the data. Established the manuscript by ----and --- critically reviewed the manuscript. All authors edited and approved the final version of this manuscript.

Acknowledgement: We would like to thank our Management who had given an opportunity to do the research work.

Funding

This study did not receive any funding.

Competing interests

The authors declare no competing interests.

Additional information

Correspondence and requests for materials should be addressed to -------.

REFERENCES:

1. WHO. WHO Director-General's opening remarks at the media briefing on COVID-19 – 11. (2020). Available online at: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-−11-march-2020
2. Jordan RE, Adab P, Cheng KK. Covid-19: Risk Factors for Severe Disease and Death. BMJ (2020); 368:1198.
3. Iglay K, Hannachi H, Joseph Howie P, Xu J, Li X, Engel SS, et al. Prevalence and Co-Prevalence of Comorbidities among Patients With Type 2 Diabetes Mellitus. Curr Med Res Opin 2016; 32(7):1243–52.
4. American Diabetes A. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2021. Diabetes Care 2021; 44(Suppl 1):S15–33.
5. Koh H, Moh AMC, Yeoh E, Lin Y, Low SKM, Ooi ST, et al. Diabetes predicts severity of COVID-19 infection in a retrospective cohort: a mediatory role of the inflammatory biomarker C-reactive protein. J Med Virol 2021;93:3023–3032
6. Yang JK, Lin SS, Ji XJ, Guo LM. Binding of SARS Coronavirus to Its Receptor Damages Islets and Causes Acute Diabetes. Acta Diabetol 2010; 47(3):193–9.
7. Šestan M, Marinović S, Kavazović I, Cekinović Đ, Wueest S, Turk Wensveen T, et al. Virus-Induced Interferon-γ Causes Insulin Resistance in Skeletal Muscle and Derails Glycemic Control in Obesity. Immunity. 2018 Jul 17; 49(1):164-177.
8. WHO. Corticosteroids for COVID-19 (2020). Available at: https://www.who. int/publications/i/item/WHO-2019-nCoV-Corticosteroids-2020.1 (Accessed December 30th).
9. Mifsud S, Schembri EL, Gruppetta M. Stress-Induced Hyperglycaemia. Br J Hosp Med (Lond) (2018) 79(11):634–9.
10. Kalhan SC, Adam PA. Inhibitory Effect of Prednisone on Insulin Secretion in Man: Model for Duplication of Blood Glucose Concentration. J Clin Endocrinol Metab .1975; 41(3):600–10.
11. Petersons CJ, Mangelsdorf BL, Jenkins AB, Poljak A, Smith MD, Greenfield JR,et al. Effects of Low-Dose Prednisolone on Hepatic and Peripheral Insulin Sensitivity, Insulin Secretion, and Abdominal Adiposity in Patients With Inflammatory Rheumatologic Disease. Diabetes Care.2013; 36(9):2822–9.
12. Robertson RP, Zhou H, Zhang T, Harmon JS. Chronic Oxidative Stress as a Mechanism for Glucose Toxicity of the Beta Cell in Type 2 Diabetes. Cell Biochem Biophysics. 2007 48(2):139–46.
13. Abu-Farha M, Al-Mulla F, Thanaraj TA, Kavalakatt S, Ali H, Ghani AM, et al. Impact of diabetes in patients diagnosed with COVID-19. Front Immunol. 2020; 11:576-818.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 09, 2023

14. Ge, Y., Sun, S., & Shen, Y. Estimation of case-fatality rate in COVID-19 patients with hypertension and diabetes mellitus in the New York state: A preliminary report. Epidemiology and Infection, 2021; 149, E14.
15. Addendum. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-*2021*. Diabetes Care 2021;44(Suppl. 1):S15–S33
16. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed
17. Outer S. Hoogenboom, Antoine Pham, Harnadar Anand, Roman Fleysher, Alexandra Buczek, et al.First and second COVID-19 waves in Japan: a comparison of disease severity and characteristics J Infect. 2021 Apr; 82(4): 84–123.
18. Jain A., Paranjape S. Prevalence of type 2 diabetes mellitus in elderly in a primary care facility: an ideal facility. *I*ndian J Endocrinol Metab. 2013; 17:S318–S322.
19. Y. Chen, S.L. Klein, B.T. Garibaldi, et al. Aging in COVID-19: vulnerability, immunity and intervention Ageing Res Rev, 2021; 65: 101205.
20. Iftimie S, Lopez-Azcona AF, Vallverdu I, Hernandez-Flix S, de Febrer G, Parra S, et al. First and second waves of coronavirus disease-19: A comparative study in hospitalized patients in Reus, Spain. PLoS One 2021; 16(3): e0248029.
21. Kumar, B., Mittal, M., Gopalakrishnan, M., Garg, M. K., & Misra, S. Effect of plasma glucose at admission on COVID-19 mortality: experience from a tertiary hospital, Endocrine Connections,2021; 10(6), 589-598
22. Baud D, Qi X, Nielsen-Saines K, Musso D, Pomar L, Favre G. Real estimates of mortality following COVID-19 infection. Lancet Infect Dis. 2020 Jul;20(7):773.
23. Yanamandra U, Rajagopal S, Aggarwal B, Kaur P, Singh A, Aggarwal N, et al., Case controlled study amongst severe COVID-19 for impact of diabetes mellitus on survival. Med J Armed Forces India. 2022 Aug 22. doi: 10.1016/j.mjafi.2022.06.010. Epub ahead of print.
24. Gupta R, Ghosh A, Singh AK, Misra A. Clinical considerations for patients with diabetes in times of COVID-19 epidemic. Diab Metab Syndr. 2020; 14(3):211–212.
25. Merzon E, Green I, Shpigelman M, Vinker S, Raz I, Golan-Cohen A et al., Haemoglobin A1c is a predictor of COVID-19 severity in patients with diabetes. Diabetes Metab Res Rev. 2021 Jul; 37(5):e3398.
26. Bode B, Garrett V, Messler J, McFarland R, Crowe J, Booth R,et al. Glycemic Characteristics and Clinical Outcomes of COVID-19 Patients Hospitalized in the United States. J Diabetes Sci Technol. 2020 Jul;14(4):813-821
27. Wu J, Zhang J, Sun X, Wang L, Xu Y, Zhang Y, Liu X, Dong C. Influence of diabetes mellitus on the severity and fatality of SARS-CoV-2 (COVID-19) infection. Diabetes Obes Metab. 2020 Oct; 22(10):1907-1914.
28. Verma A, Rajput R, Verma S, Balania VKB, Jangra B. Impact of lockdown inCOVID-19 on glycemic control in patients with type 1 Diabetes Mellitus. Diabetes Metab Syndr. 2020 Sep-Oct; 14(5):1213-1216.
29. Wang Z., Du Z., Zhu F. Glycosylated hemoglobin is associated with systemic inflammation, hypercoagulability, and prognosis of COVID-19 patients. Diabetes Res Clin Pract. 2020; 164:108-214.
30. Gao Y, Li T, Han M, Li X, Wu D, Xu Y, Zhu Y, Liu Y, Wang X, Wang L. Diagnostic utility of clinical laboratory data determinations for patients with the severe COVID-19. J Med Virol. 2020 Jul; 92(7):791-796.
31. Soumik Purkayastha, Ritoban Kundu, Ritwik Bhaduri, Daniel Barker, Michael Kleinsasser, Debashree Ray, et al. (2021). Estimating the wave 1 and wave 2 infection fatality rates from SARS-Co India BMC Res Notes 2021; 14: 262.
32. Prasad Bogam, Aparna Joshi, Sanket Nagarkar, Divyashri Jain, Nikhil Gupte, LS et al., Burden of COVID-19 and case fatality rate in Pune, India: an analysis of the first and second wave of the pandemic,IJID Regions, 2022;(2) :74-81.
33. Khunti K, Knighton P, Zaccardi F, Bakhai C, Barron E, Holman N, et al. Prescription of glucose-lowering therapies and risk of COVID-19 mortality in people with type 2 diabetes: A nationwide observational study in England. Lancet Diabetes Endocrinol (2021) 9(5):293–303. doi: 10.1016/S2213-8587(21) 00050-4