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Original Article

Internal Medicine Section

Comparative Study of Clinical and Radiological Profile and Outcome of COVID-19 Patients with and without Co-morbidities: A Cross-sectional Study

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ABSTRACT

Introduction: Coronavirus Disease-2019 (COVID-19) had devastating effects on the healthcare and economic sector worldwide. India stands second in the list of most number of COVID-19 cases. Most of the deaths due to COVID-19 were seen in patients with associated co-morbidities like hypertension, diabetes, chronic kidney disease and obesity. This study would like to examine specific co-morbidities in relation to the COVID-19 disease progression and outcomes.

Aim: To compare the clinicoradiological profile and outcome of COVID-19 in patients with and without co-morbidities (diabetes and hypertension).

Materials and Methods: The present observational, cross-sectional study was conducted at Jawaharlal Nehru Medical College, Aligarh, Uttar Pradesh between June 2020 to September 2020, after obtaining Institutional Ethics Committee (IEC) approval. A total of 148 patients with COVID-19 were included in the study. The COVID-19 patients admitted in the hospital were divided into four groups as those having only diabetes, only hypertension, both diabetes and hypertension, and those without any co-morbidities. Those with any other co-morbidity were excluded from the study. The general clinical characteristics, laboratory parameters, disease severity, morbidity and mortality were compared among various groups and the data was analysed. Categorical data were analysed using the Chi-square test.

Results: A total of 148 patients with COVID-19 were included in the study, of which 26 patients were diabetic, 36 were hypertensive, 24 were both hypertensive and diabetic and 62 patients did not had any significant co-morbidity. Severe COVID-19 disease was most commonly observed in those with diabetes 14 (53.8%). The highest proportion of patients requiring oxygen (84.6%) and Non Invasive Ventilator (NIV) support (46.1%) was also seen among diabetics. The presence of diabetes, severe disease and leukocytosis at presentation increased the risk of mortality. The association of hypertension with COVID-19 does not seem to affect the in-hospital mortality.

Conclusion: The COVID-19 in diabetics is associated with both increased risk of severe disease and increased odds of death. In diabetics, those with uncontrolled diabetes were more prone to severe disease and death than those with good glycaemic control. Hypertension, on the other hand, showed no association.

Keywords: Coronavirus disease-2019, Intensive care unit admission, Mechanical ventilation, Non invasive ventilation, Oxygen requirement

INTRODUCTION

The COVID-19, which was first diagnosed in Wuhan, China in December 2019, has now spread to more than 200 countries around the world, and it's unlike any other pandemic that we have seen in almost a century. With all the advancements in the health sector that is witnessed in the last decade or so, that has made almost all the impossible of the medical science possible, this pandemic has brought even the most advanced nations to its knees. India is one of the worst affected countries by the coronavirus. It is third in the list of the total number of patients in a country, behind only the United States and Brazil, and with almost 95000 new cases daily, it is well on track to lead the list [1].

Many of the published studies have identified the presence of co-morbidities, especially diabetes and hypertension, as associated with poor prognosis and clinical outcome. The study conducted by Albitar O et al., among 828 patients of COVID-19 identified that males, advanced age, hypertension, diabetes mellitus patients and patients located in America were the independent risk factors of death among COVID-19 patients. This study reported odds ratio of 12.234 for diabetes and 3.576 for hypertension [2]. Holman N et al., did a population based cohort study in 2020 to establish the association of COVID-19 mortality and diabetes mellitus. As per this study, mortality in people with type 1 and type 2 diabetes rose sharply during the initial COVID-19 pandemic in England. Compared to people with an HbA1c of 48-53 mmol/mol (6.5-7.0%), people with an HbA1c of 86 mmol/mol (10.0%) or higher, had significantly higher COVID-19-related deaths (hazard ratio [HR] 2.23 in type 1 diabetes and 1.61 in type 2 diabetes). In addition, in people with type 2 diabetes, COVID-19-related mortality was significantly higher in those with an HbA1c of 59 mmol/mol (7.6%). The mortality rate increased with higher values of HbA1C as it was found that hazard ratio of 1.22 for those with an HbA1c of 59-74 mmol/mol (7.6-8.9%) and 1.36 for 75-85 mmol/mol (9.0-9.9%) [3]. Mantovani A et al., did a meta-analysis of 83 observational studies to detect diabetes as a risk factor for COVID-19 severity and mortality. It concluded that pre-existing diabetes (in most cases type 2 diabetes mellitus) significantly increased the rate of COVID-19 associated mortality as well as the risk of incidence of severe/critical illness [4].

India is the diabetes capital of the world. The prevalence of diabetics in India has increased remarkably from 26 million in 1990 to a staggering 65 million in 2016 [5]. The same is the case with the prevalence of hypertension in India. According to one study, one in every three adults in India suffers from hypertension [6]. Thus, with India leading in both diabetes and hypertension along with COVID-19, it can be a worrisome and dreadful combination as there are evidences from multiple studies that both diabetes and hypertension

pose significant risk to the COVID-19 severity and mortality. The aim of present study was to compare the profile of COVID-19 patients having diabetes and/or hypertension than those without any co-morbidity and see how they are based on clinical profile, disease severity, laboratory parameters, and outcome.

MATERIALS AND METHODS

The present study was an observational, cross-sectional, hospital-based study, done between June 2020 to September 2020 at Jawaharlal Nehru Medical College, Aligarh, which is a tertiary care centre in Uttar Pradesh, India which was a Level-2 COVID Hospital. The Institutional Ethics Committee approved the study (letter no: 94/20/FM/AMU).

Inclusion criteria: All adult patients diagnosed with COVID-19 based on positive Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) of the nasopharyngeal swab and were admitted to the hospital were included in the study after obtaining written informed consent.

Exclusion criteria: Those patients with any other co-morbidity apart from diabetes and hypertension like coronary artery disease, cancer, chronic kidney disease, hypothyroidism, stroke, chronic lung diseases like COPD, bronchial asthma, etc were excluded from the study. Any patients below 18 years were also excluded.

Study Procedure

A total of 148 patients of COVID-19 were included in the study. They were divided into four groups, based on whether they were having only diabetes (n=26), only hypertension (n=36), both diabetes and hypertension (n=24), and none of these (n=62). These patients were assessed every day from the day of admission till the day of discharge/death with necessary clinical and laboratory investigations. All the patients were followed for a minimum of 30 days from the day of presenting to the hospital.

The COVID-19 was diagnosed by RT-PCR/Rapid antigen testing and classified according to severity into mild, moderate, and severe based on tachypnoea and/or decreased oxygen saturation as measured by pulse oximetry [7].

Mild cases had a upper respiratory tract symptoms and/or fever without shortness of breath or hypoxia, respiratory rate below 24/min and oxygen saturation (SpO_2) ≥94%. Moderate cases had respiratory rate between 24-30/min and/or oxygen saturation between 90% to ≤93% on room air. Severe cases had their respiratory rate above 30/min and/or oxygen saturation below 90% on room air [7].

The diagnosis of diabetes was based on past history or raised blood glucose levels during admission, according to the American Diabetes Association (ADA) guidelines [8]. Systemic hypertension was diagnosed based on the past history of taking antihypertensive medications for a period of more than six months or raised systolic and/or diastolic blood pressure according to American Heart Association (AHA) guidelines [9]. Chest X-ray finding was classified as being normal, mild to moderately involved, and extensively involved. Mild to moderate involvement was defined as having basal peripheral shadows and extensive involvement as having approximately more than 50% of the lung involvements bilaterally [10].

Data collection was done using a patient proforma to document clinical data. It included demographic factors like age and sex, symptoms and signs like fever, sore throat, cough, myalgia, dyspnoea, diarrhoea, headache and anosmia. The proforma also noted the presence/absence of any co-morbidities like diabetes, hypertension, clinical and radiological severity (mentioned above), and outcome in terms of improvement/deterioration/death. Laboratory investigations like Complete Blood Count (CBC), blood urea, serum creatinine, HbA1C, Random Blood Sugar (RBS), D-Dimer and Arterial Blood Gas (ABG) analysis were done for all subjects.

STATISTICAL ANALYSIS

All the data were collected, tabulated, and analysed using Statistical Package for the Social Sciences (SPSS) version 23.0. Continuous data was expressed as median with Interquartile Range (IQR). Non parametric Kruskal-Wallis test was used to compare the distribution of continuous variables that were not normally distributed. Categorical data were expressed as percentage and were analysed using the Chi-square test. The risk factors associated with mortality were examined with a multivariable binary logistic regression model. The odds ratio was used for evaluating the association between risk factors and mortality. Receiver Operating Characteristic (ROC) Curve was also used to test the regression model predicting mortality. All reported p-values were two tailed, p-value of <0.05 was considered significant.

RESULTS

A total of 148 patients of COVID-19 were included in the study. The mean age of the study subjects was 52.86±15.05 years. The oldest population was in the group with only hypertension while the youngest group was the one without any co-morbidity, the mean age being 61.28±8.3 years and 47.1±18.1 years, respectively. The difference between age among various groups was statistically significant. The majority of the patients were males (63.5%). The most common symptom in present study was fever (95.3%), followed by cough (68.9%) and dyspnoea (63.5%). Those with either diabetes alone or with both diabetes and hypertension had a significantly higher proportion of patients presenting with dyspnoea when compared to the other two groups. The median heart rate and respiratory rate were highest in the diabetes group, with the value being 96.0 and 20.0, respectively. None of the patients were in shock at the time of presentation. The median SpO_2 was lowest in the diabetes only group (85%), followed by those with only hypertension (88%). The proportion of patients having the severe disease was highest in the diabetes only group (53.8%), followed by those with only hypertension (50%). The chest X-ray was normal in 38 (25.7%) of the patients whereas extensive involvement was observed in 50 (33.8%) of the patients. About 14 (53.8%) of the patients in the diabetes only group had extensive involvement on chest X-ray [Table/Fig-1].

The baseline laboratory parameters of the study groups have been shown in [Table/Fig-2]. A significant difference in distribution was observed in the values of serum creatinine, blood urea nitrogen (BUN), D-dimer, lactate, and pO_2 levels among the four groups. The median serum creatinine and BUN levels were highest in patient group with both diabetes and hypertension, probably because such patients have greater risk of developing acute kidney injury. The median D-dimer value was highest in the diabetes group followed by those with both diabetes and hypertension, and the median pO_2 was lowest in the diabetes group.

Of the total patients, 62.1% required additional oxygen support was statistically significant (p=0.049). The highest proportion of patients requiring oxygen support were from the diabetes group (84.6%) followed by those having both hypertension and diabetes (66.7%). Patients required oxygen for a median of 7.5 days. There was no significant difference between the groups in their duration of oxygen requirement. (p=0.441) [Table/Fig-3].

Of the total patients, 22.9% required support of NIV in addition to oxygen inhalation. The highest proportion of patients requiring NIV was again among the diabetes only group (46.1%) followed by those having both hypertension and diabetes (33.4%). The difference was statistically significant (p=0.001). The median duration of NIV support was 6.5 days. There was no significant difference in the duration of NIV support between the groups. Invasive ventilation was required in 10.8% of the patients, the maximum proportion again being the diabetes only group (30.7%) [Table/Fig-3].

Patient characteristic	With only diabetes (n=26)	With only hypertension (n=36)	Both diabetes and hypertension (n=24)	Without any co-morbidity (n=62)	Total patients (n=148)	p-value
Age (in years)	50.54±12.12	61.28±8.3	57.67±8.65	47.1±18.1	52.86±15.05	<0.001
Sex						
Male	16 (61.5%)	14 (38.9%)	20 (83.3%)	44 (71%)	94 (63.5%)	0.002
Female	10 (38.5%)	22 (61.1%)	4 (16.7%)	18 (29%)	54 (36.5%)	
Symptoms						
Fever	26 (100%)	31 (86.1%)	24 (100%)	60 (96.8%)	141 (95.3%)	0.07
Sore throat	8 (30.8%)	8 (22.2%)	4 (16.7%)	20 (32.3%)	40 (27%)	0.428
Cough	24 (92.3%)	20 (55.6%)	16 (66.7%)	42 (67.7%)	102 (68.9%)	0.021
Myalgia	10 (38.5%)	14 (38.9%)	8 (33.3%)	28 (45.2%)	60 (40.5%)	0.764
Dyspnoea	24 (92.3%)	18 (50%)	16 (66.7%)	36 (58.1%)	94 (63.5%)	0.005
Diarrhoea	0	0	0	10 (16.1%)	10 (6.8%)	0.002
Headache	2 (7.7%)	2 (5.6%)	0	12 (19.4%)	16 (10.8%)	0.031
Anosmia and dysgeusia	2 (7.7%)	2 (5.6%)	0	0	4 (2.7%)	0.113
Vitals						
Blood pressure systolic {median (IQR)}	114.0 (110.0-19.0)	140.0 (128.0-150.0)	142.8 (130.0-154.0)	122.0 (112.0-130.0)	126.0 (114.0-138.0)	<0.001
Blood pressure diastolic {median (IQR)}	72.0 (70.0-80.5)	80.0 (80.0-88.0)	84.0 (80.0-88.0)	76.0 (70.0-80.0)	90.0 (70.0-84.0)	0.131
Heart rate {median (IQR)}	96.0 (89.5-104.25)	87.0 (82.0-88.0)	84.0 (82.0-85.0	88.0 (84.0-98.0)	88.0 (84.0-96.0)	<0.001
Respiratory rate {median (IQR)}	20.0 (19.5-22.0)	18.0 (16.0-22.0)	18.0 (17.0-20.0)	18.0 (16.0-20.0)	18.0 (16.0-22.0)	0.016
SpO_2 {median (IQR)}	85.0 (69.0-91.25)	88 (80.0-98.0)	92.0 (70.5-96.0)	93.0 (80.0-97.0)	91.0 (78.0-96.0)	0.005
Disease severity						
Mild	4 (15.4%)	16 (44.4%)	8 (33.3%)	26 (41.9%)	54 (36.5%)	0.076
Moderate	8 (30.8%)	2 (5.6%)	6 (25%)	12 (19.4%)	28 (18.9%)	
Severe	14 (53.8%)	18 (50%)	10 (41.7%)	24 (38.7%)	66 (44.6%)	
Chest x-ray						
Normal	2 (7.6%)	14 (38.8%)	4 (16.7%)	18 (29%)	38 (25.7%)	0.069
Mild-moderate involvement	10 (38.8%)	12 (33.3%)	12 (50%)	26 (41.9%)	60 (40.5%)	
Extensive involvement	14 (53.8%)	10 (27.8%)	8 (33.3%)	18 (29%)	50 (33.8%)	

[Table/Fig-1]: Baseline characteristics of patients.
Non parametric Kruskal Wallis test used for continuous variables; Chi-square test used for categorical data

Parameters	With only diabetes Median (IQR)	With only hypertension Median (IQR)	With both diabetes and hypertension Median (IQR)	Without any co-morbidity Median (IQR)	Total patients Median (IQR)	p-value
Total leukocytes count ($\times 10^9$/L)	8.8 (6.9-13.3)	7.2 (5.7-11.6)	7.3 (5.9-13.8)	10.1 (6.5-14.1)	8.3 (6.4-13.6)	0.26
Haemoglobin (mg/dL)	11.7 (18.85-12.8)	11.65 (11.0-12.7)	12.1 (9.3-12.8)	12.9 (10.0-14.1)	11.8 (10.5-13.0)	0.312
Serum creatinine (mg/dL)	0.72 (0.59-0.91)	0.79 (.59-1.10)	1.95 (1.01-3.73)	0.70 (.50-0.90)	0.8 (0.6-1.1)	<0.001
Blood urea nitrogen (mg/dL)	21.0 (12.7-30.3)	19.5 (14.0-23.0)	25.0 (19.0-38.0)	16.0 (14.0-25.0)	20.0 (14-28)	0.008
Random blood sugar (mg/dL)	321 (276.5-338.6)	111 (104-157)	242 (152-385)	101 (96-122)	120.5 (102-225)	<0.001
HbA1c (%)	9.7 (8.5-10.9)	5.9 (5.5-6.1)	8.4 (7.9-10.3)	5.7 (5.6-5.9)	5.9 (5.7-8.2)	<0.001
D-dimer (ng/mL)	970 (813.2-1208.3)	564.5 (372.0-818.0)	604.5 (373.5-1129.0)	503.0 (300.0-1102.0)	672 (345-1048)	0.002
Arterial blood gas						
pH	7.43 (7.41-7.44)	7.40 (7.37-7.43)	7.43 (7.40-7.47)	7.41 (7.39-7.45)	7.42 (7.39-7.44)	0.115
pO_2 (mmHg)	52 (47.25-62.5)	57.5 (49.0-78.0)	58 (56-83.7)	65 (54.0—85.0)	60 (51-79)	0.005
pCO_2 (mmHg)	36 (31-39.0)	40 (37.0-44.0)	36.5 (31.75-38.75)	40 (33-42)	38 (32-41)	0.015
Lactate (mmol/L)	1.9 (1.58-2.88)	2.1 (1.4-2.7)	1.5 (1.3-1.8)	1.6 (1.1-2.3)	1.7 (1.3-2.5)	0.001
Bicarbonate (mmol/L)	22.1 (20.95-25.90)	22.4 (21.8-25.4)	22.5 (21.0-25.25)	22.8 (21.3-26.00)	22.55 (21.1-25.6)	0.021
Haematocrit (%)	46 (43-48.25)	48 (43.0-51.0)	47.5 (42.0-50.5)	48.0 (45.0-52.0)	48 (44-51)	0.057
Sodium (mmol/L)	132 (131-135.25)	133.5 (131-137)	131 (128.5-135.5)	136 (132-139)	134 (131-137)	0.003
Potassium (mmol/L)	4.0 (3.65-4.27)	3.8 (3.2-4.0)	3.9 (3.53-4.10)	3.9 (3.6-4.10)	3.9 (3.6-4.1)	0.287

[Table/Fig-2]: Laboratory parameters of the patients.
Non parametric Kruskal Wallis test used for continuous variables

About 66.2% of the patients were discharged from the isolation ward, 25.6% of the patients had to be shifted to the ICU due to symptoms like dyspnoea and/or oxygen requirement or additional ventilation support. The mortality in the isolation ward stood at 8.1%, whereas the total mortality at the end of 30 days was 16.2%. The highest proportion of patients who died in the isolation ward, as well as the 30-day mortality, was highest in the diabetes only group (30.7%). The mean time to COVID RT-PCR negative conversion was 11.44 days. There was a significant difference between the groups (p=0.015), with the highest time to conversion observed in the diabetes group [Table/Fig-3].

A multivariate binary logistic regression model was applied on 148 patients to examine the risk factors associated with 30 days mortality using the variables shown in [Table/Fig-4]. Presence of diabetes,

Variables	Only diabeties	Only hypertension	With both hypertension and diabetes	Without any co-morbidity	Total patients	p-value
Need for oxygen	22 (84.6%)	20 (55.5%)	16 (66.7%)	34 (54.8%)	92 (62.1%)	0.049
Duration of oxygen (range)	8 (3-15)	8 (3-20)	6 (1-16)	7 (3-20)	7.5 (1-20)	0.441
Need for non invasive ventilation	12 (46.1%)	8 (22.2%)	8 (33.4%)	6 (9.6%)	34 (22.9%)	0.001
Duration of non invasive ventilation (days) (range)	5 (1-6)	3.5 (1-10)	7.5 (4-16)	5 (1-6)	6.5 (1-16)	0.254
Need for invasive ventilation	8 (30.7%)	4 (11.1%)	2 (8.3%)	2 (3.2%)	16 (10.8%)	<0.001
Outcome						
Discharged (if asymptomatic for 3 days)	12 (46.1%)	26 (72.2%)	14 (58.3%)	46 (74.1%)	98 (66.2%)	<0.001
Shifted to ICU (if there was clinicoradiological deterioration)	6 (23.2%)	8 (22.2%)	10 (41.1%)	14 (22.5%)	38 (25.6%)	0.001
Expired in the isolation ward	8 (30.7%)	2 (5.5%)	0 (0.0%)	2 (3.2%)	12 (8.1%)	0.001
Total mortality at 30 days	10 (38.4%)	4 (11.1%)	4 (16.6%)	6 (9.6%)	24 (16.2%)	0.007
Time to negative COVID RT-PCR conversion (days with range in brackets)	12.0 (11.0-14.25)	12.0 (10.0-13.0)	10.5 9.0-13.5)	10.5 (10.0-12.0)	11.44 (10.0-13.0)	0.015

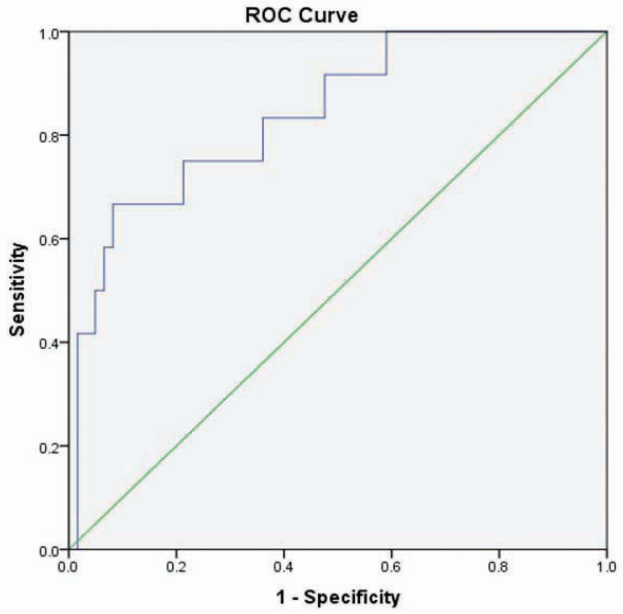
[Table/Fig-3]: The need for oxygen and ventilatory support and outcome.
Non parametric Kruskal Wallis test used for continuous variables; Chi-square test used for categorical data

Variables	p-value	OR (95% CI)
Age	0.517	1.019 (0.962-1.079)
Pulse rate	0.940	0.998 (0.942-1.056)
Respiratory rate	0.059	1.311 (0.990-1.736)
Diabetes	**0.016**	5.026 (1.346-18.763)
Hypertension	0.403	0.597 (0.178-2.001)
Total leukocytes count increased	**0.012**	1.201 (1.000-1.000)
Lactate	0.109	1.451 (0.921-2.286)
D-dimer	0.504	1.000 (1.111-1.001)
COVID Severity (moderate)	0.327	2.083 (0.480-9.051)
COVID Severity (severe)	**0.020**	4.000 (1.249-12.087)
Need for oxygen	0.157	0.261 (0.041-1.677)

[Table/Fig-4]: Multivariate analysis of independent risk factors associated with 30 days mortality.

high total leukocytes count at presentation, severe disease at the time of presentation were associated with increased odds of death. The presence of hypertension and raised D-Dimer levels did not increase the odds of death.

[Table/Fig-5] shows the ROC curve constructed for the binary regression model predicting 30 day mortality in COVID-19 patients admitted to the isolation ward. The Area Under Curve (AUC) was 0.840 which means that our logistic regression model has a good diagnostic ability.



[Table/Fig-5]: ROC curve for the model predicting 30-day mortality in COVID-19 patients admitted to the COVID isolation ward. Area under curve (AUC)=0.840.

DISCUSSION

The impact of the COVID-19 pandemic has been enormous and unprecedented. The total number of cases daily has been mind-boggling and thus, leading to the saturation of the healthcare system and infrastructure. So, it becomes imperative to identify those with increased risk of mortality and morbidity, various factors that can predict these risks early and thus, help us identify these patients so that early intervention can be made and help us with saving as many lives as possible [11].

Many studies have identified older age as a risk factor for mortality in COVID-19 patients [2,11,12]. The mean age of patients who expired in present study was 56.17±15.006 years while among survivors, it was 52.23±15.032 years. Older patients have a weaker immune system and are also more likely to be having lifestyle diseases which would further put them at a risk. The oldest group in the present study was those with hypertension followed by those having both hypertension and diabetes. Although the difference between the mean age of survivors and non survivors was not statistically significant in the study, it did increase the odds ratio for mortality in the multivariate regression analysis (OR=1.019). The most likely cause for the age difference being non significant would be that the centre under consideration was a level 2 referral centre where only sick, old age patients are admitted and very few patients with mild disease were admitted (mostly healthcare workers from the same hospital) which would result in the data being biased since the majority are sick patients.

The presence of diabetes is being constantly documented as a risk factor for mortality among COVID-19 patients in many studies [3,4,13,14]. In this study, of those who expired, 14 (58.3%) had diabetes. Diabetes significantly increased the odds of death (OR=5.026).

The data on hypertension as a risk factor in COVID-19 patients is conflicting. In the study done by Li G et al., [14], they did not find hypertension to increase the risk of death among COVID-19 patients while in the study done by Albitar O et al., [2] they found hypertension as an independent risk factor for mortality among COVID-19 patients. As per this study, hypertension did not increase the risk of mortality among COVID-19 patients (OR=0.597).

Also, according to this study, those having both diabetes and hypertension fared better when compared to those having only diabetes indicating that hypertension neither alone nor in diabetics, increased the risk of mortality among COVID-19 patients. As far as these patients being diabetics and faring better when compared to those having only diabetes is considered, the probable reason would be that the former group was having better glycaemic control compared to the latter group (mean HbA1c=8.6 vs 9.7). In the study done by Holman N et al., [3], they found that diabetics with HbA1c of

>7.6% were at significantly higher risk of mortality than those having HbA1c as <7.0%. Therefore, those having well-controlled diabetes are relatively protected than those with poor diabetes control.

A high total leukocyte count at the time of admission was also independently associated with increased odds of death in the present study. Similar results have been found in other studies as well [15]. A correlation has been found between high total leukocyte count and high Interleukin-6 levels in some studies, which would indicate higher levels of tissue inflammation, thus explaining increased morbidity and mortality in these patients [16]. Thus, in resource-limited settings, an increased total leukocyte count at admission can be taken as a surrogate marker for increased tissue inflammation and IL-6 levels. Also, a superadded bacterial infection, which is a known complication of viral pneumonia, maybe the reason for increased mortality in these patients.

Disease severity at the time of presentation was also an independent risk factor predicting mortality in the present study. Moderate and severe disease increased the odds for death by a factor of 2.083 and 4.000, respectively. Those with severe disease were more prone for post COVID lung fibrosis which may lead to increased morbidity and mortality. In the study done by Ojo AS et al., they found that disease severity, old age, history of smoking and alchoholism, prolonged stay in ICU and the need for mechanical ventilation as predictors of lung fibrosis in COVID-19 patients [17].

The 30-day mortality in the present study was 16.2% (24/148). A higher percentage of mortality seen in this study was probably because the hospital where the study was done catered mostly moderate and severe patients only. An important finding of this particular study was that a significant number of patients (12/24), expired after becoming COVID negative but within 30 days. They were all having severe disease at the time of presentation. Therefore, post-COVID-19 sequelae in those with severe disease and Acute Respiratory Distress Syndrome (ARDS) leading to lung fibrosis is also an important aspect associated with both morbidity and mortality in these patients that cannot be ignored.

Limitation(s)

Echocardiogram and autopsy was not performed in every patient to ascertain the cause of death. A multicentre study with a larger number of subjects would allow for a better co-relation of COVID-19 with co-morbidities and risk factors predicting mortality.

CONCLUSION(S)

The COVID-19 in diabetics results in both increased chances of severe disease and mortality. Those with uncontrolled diabetes fare poorly when compared with those having better glycaemic control. Hypertension did not seem to increase the risk of death among these pateints. Also, disease severity and increased leukocyte count at the time of presentation increased the odds of death among these patients. Furthermore, this study can be used as a source of reference as well as guide to anticipate prognosis and implement better management strategies in patients with co-morbidities in case of newer waves of COVID-19 or even in later pandemics.

REFERENCES

[1] Coronavirus Disease (COVID-19) Situation Reports. [cited 2020 Sep 26]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports.last access date: 2020 Oct 1.
[2] Albitar O, Ballouze R, Ooi JP, Ghadzi SM. Risk factors for mortality among COVID-19 patients. Diabetes Res Clin Pract. 2020;166:108293.
[3] Holman N, Knighton P, Kar P, O'Keefe J, Curley M, Weaver A, et al. Risk factors for COVID-19-related mortality in people with type 1 and type 2 diabetes in England: A population-based cohort study. The Lancet Diabetes & Endocrinology. 2020;8(10):823-33.
[4] Mantovani A, Byrne CD, Zheng MH, Targher G. Diabetes as a risk factor for greater COVID-19 severity and in-hospital death: A meta-analysis of observational studies. Nutr Metab Cardiovasc Dis. 2020;30(8):1236-48.
[5] Tandon N, Anjana RM, Mohan V, Kaur T, Afshin A, Ong K, et al. The increasing burden of diabetes and variations among the states of India: The Global Burden of Disease Study 1990-2016. The Lancet Global Health. 2018;6(12):e1352-62.
[6] Ramakrishnan S, Zachariah G, Gupta K, Rao JS, Mohanan PP, Venugopal K, et al. Prevalence of hypertension among Indian adults: Results from the great India blood pressure survey. Indian Heart J. 2019;71(4):309-13.
[7] Clinical guidance for management of adult COVID-19 patients. AIIMS/ICMR-COVID-19 National Task Force/Joint Monitoring Group (Dte.GHS) Ministry of Health & Family Welfare, Government of India. Revised on 14/01/2022. Available from: https://www.mohfw.gov.in/pdf/Clinical Guidancefor ManagementofAdult Covid19Patientsupdatedason17thJanuary2022.pdf.
[8] Diagnosis | American Diabetes Association guidelines [Internet]. [cited 2020 Oct 1]. Available from: https://www.diabetes.org/a1c/diagnosis.
[9] Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International society of hypertension global hypertension practice guidelines. Hypertension. 2020;75(6):1334-57.
[10] Monaco CG, Zaottini F, Schiaffino S, Villa A, Della Pepa G, Carbonaro LA, et al. Chest x-ray severity score in COVID-19 patients on emergency department admission: A two-centre study. European Radiology Experimental. 2020;4(1):01-07.
[11] DC COVID-19 Response Team. Severe outcomes among patients with coronavirus disease 2019 (COVID-19)-United States, February 12-March 16, 2020. Morbidity and Mortality Weekly Report. 2020;69(12):343.
[12] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. The Lancet. 2020;395(10229):1054-62.
[13] Abdi A, Jalilian M, Sarbarzeh PA, Vlaisavljevic Z. Diabetes and COVID-19: A systematic review on the current evidences. Diabetes Res Clin Pract. 2020;166:108347.
[14] Li G, Deng Q, Feng J, Li F, Xiong N, He Q, et al. Clinical characteristics of diabetic patients with COVID-19. J Diabetes Res. 2020;1652403.
[15] Yamada T, Wakabayashi M, Yamaji T, Chopra N, Mikami T, Miyashita H, et al. Value of leukocytosis and elevated C-reactive protein in predicting severe coronavirus 2019(COVID-19): A systematic review and meta-analysis. Clinica Chimica Acta. 2020 ;509:235-43.
[16] Zhao K, Li R, Wu X, Zhao Y, Wang T, Zheng Z, et al. Clinical features in 52 patients with COVID-19 who have increased leukocyte count: A retrospective analysis. Eur J Clin Microbiol Infect Dis. 2020;39(12):2279-87.
[17] Ojo AS, Balogun SA, Williams OT, Ojo OS. Pulmonary fibrosis in COVID-19 survivors: Predictive factors and risk reduction strategies. Pulm Med. 2020;2020:6175964.

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