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Metabolic syndrome correlates with significantly adverse disease outcomes in COVID-19 patients during the second wave of pandemic

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Abstract---Background: This Retrospective Study was conducted by collecting patient records from the COVID-19 registry of Parul Sevasharm Hospital. The goal of this study was to investigate the risk and mortality of COVID-19 patients with Metabolic Syndrome especially during the second wave of pandemic. Methods: This Retrospective Study was conducted by collecting patient records from the COVID-19 registry of Parul Sevasharm Hospital. The record of

COVID-19 patients admitted during the second wave of pandemic (April – June, 2021) were included and analyzed for Metabolic syndrome, Demographic characteristics and Clinical Outcomes. Comorbidities were classified into the following Groups: DM (having DM with or without comorbidities), only DM (having DM without other comorbidities); HT (having HT with or without other comorbidities), only HT (having HT without other comorbidities); CVD (having CVD with or without comorbidities), only CVD (having CVD without other comorbidities). Correlation analysis was also done for sub-groups of DM+CVD, CVD+HT, HT+DM, (with or without other comorbidities). Results: Among 994 Patients with COVID-19, 748/994 (75.25%) were discharged as cured and 246 (24.74%) succumbed to death. The mean age of the study population was 52.64 ± 14.72 , in which 366 (36.82%) were Females and 628/994 (63.57%) were Males. We compared the clinical characteristics of Survival versus Death in conditions of different comorbidities. The frequency of patients with Diabetes Mellitus was 407/994 (40.94%) and the same patients constituted 79/246 (32.11%) of all non-survivors and 328/748 (43.85%) of all survivors. The frequency of patients with Hypertension was 105/994 (10.56%), out of which 43/246 (17.47%) were non-survivors and 62/748 (8.2%) were survivors. Similarly, the total representation of patients having any CVD was 299/994 (30.08%), from which 66/246 (26.82%) represented the non-survivor group and 230/748 (30.74%) constituted the survivor group. The P-value of all causes of Mortality was found to be significant P- Value <0.005). Conclusion: In this study, Diabetes Mellitus and Hypertension patients were at increased risk of Mortality, following those with cardiovascular disease. Thus, either of these metabolic syndromes can be a significant predictor for the death of COVID-19 patients.

Keywords---COVID-19, metabolic syndrome, diabetes mellitus, hypertension, cardiovascular disease survivors, non-survivors.

Introduction

Corona virus disease produced by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-cov-2) is a worldwide pandemic that began in Wuhan, China, and quickly spread throughout the world, infecting over 180 countries. As the corona virus continues to develop, (1,2) the more severe form of diseases leading to death, have supposed to occur more frequently in older patients and those who have some underlying comorbidities. Among several comorbidities, Diabetes Mellitus (DM) and Hypertension both have been reported to be present in a large number of COVID-19 patients across the world (3–7). Among many other comorbidities, the older patients with Cardiovascular Diseases (CVD) were observed to be highly represented, suggesting that there was a higher risk for worse outcomes of COVID-19 on this population (8)(9). Patients infected with COVID-19 may develop multiple organ failure suggesting that severe acute respiratory syndrome coronavirus-2 (SARS-cov-2) not only causes damage to the lungs, but also to the heart, kidney, gastrointestinal duct, kidneys, etc. (10).

COVID-19 severity varies from mild self-limiting flu-like illness to pneumonia, respiratory failure, and death. Factors associated with severity and worse prognosis of COVID-19 are age, the presence of chronic diseases, such as type 2 diabetes mellitus, cardiovascular disease and hypertension (4,11,12). Retrospective research has shown that COVID-19 is frequently observed in people with obesity, diabetes, and hypertension [which are pivotal components of metabolic syndrome (5,13–15)]. Obesity is a complex chronic metabolic and multifactorial disease that, associated with a chronic inflammatory state, has an essential role in the development of, hypertension, cardiovascular disease (CVD), or cancer (4). COVID-19-related deaths have been reported in India (as of July 23, 2020). Individuals with diabetes are more likely to suffer severe consequences, including death. Recent studies have shown that advanced age or underlying medical comorbidities, such as Cardiovascular Disease, Diabetes Mellitus, Hypertension, and Obesity are risk factors for severe illness and mortality among Patients with COVID-19 (16).

Methods

Study design

A Retrospective observational study was conducted at a tertiary care hospital.

Study setting

Parul Sevasharm Hospital, Taluka-Waghodia, District-Vadodara, Gujarat, India between the duration of April-2021 to June-2021

Inclusion and Exclusion criteria

Medical Record of indoor patients with confirmed COVID-19 infection as per Radiological diagnosis and RT-PCR was collected from April-2021 to June-2021. Records containing any metabolic syndrome above the age of 35 years for both the sexes were included in the study. Records of patients below 35 years of age, without any comorbidities or missing data were excluded out of the study.

Sample size

A total of 811 participants record was included in final analysis and their data was collected based on the master chart template prepared in the spreadsheet.

Main outcome measures

Primary was hospitalization due to COVID-19. Secondary Outcome measures were presence of any underlying comorbidity related to metabolic syndrome. Tertiary outcome measures were unfavourable clinical outcomes measured by survival or death during the treatment period.

Patients and Public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Data collection

From the electronic record system, the extracted data on clinical and demographic characteristics (such as gender, age, having any other comorbidities, O₂ saturation, systolic blood pressure, diastolic blood pressure, respiratory rate, and being ventilated) as well as laboratory findings of each patient on first day of hospital admission, the date of patients' hospitalization, and discharge date (survive or death), Chest Computed Tomography (CT) imaging were collected from Medical Records Division (MRD) of Parul Sevasharm Hospital. The research was conducted according to the protocol of PUIECHR/PIMSER/00/081734/2904 (Institutional Ethics Committee for Human Research) of Parul University.

Radiological diagnosis of COVID-19 disease

The diagnosis was based on the presence of clinical symptoms of COVID-19 infection in combination with metabolic syndrome; which included fever, headache, breathlessness, vomiting, loss of taste, loss of smell as well as a positive pulmonary abnormality on chest CT imaging, however, x-ray was more reliable and rapid method to diagnose.

Laboratory findings

Medical laboratory findings, included the counts of (white blood cells) WBC, (red blood cells) RBC, (mean corpuscle haemoglobin) MCH, (mean corpuscle haemoglobin concentration) MCHC, (mean corpuscle volume) MCV, globulin, albumin, Creatinine, lactate dehydrogenases (LDH), haemoglobin, erythrocyte sedimentation rate (ESR), C- reactive protein (CRP), HBA1C, random blood sugar (RBS), fasting blood sugar (FBS), plasma glucose, postprandial blood sugar (PP2BS).

Statistical analysis

The data was recorded into MS excel spreadsheet and analysed using statistical package for social sciences (SPSS-version -16) for Kaplan Meier curve. Logistic regression was performed to investigate the link between underlying comorbidities and covid-19 patients. 95 percent confidence interval for logistic regression analysis was reported. Multivariate analysis including gender, age, and laboratory test were potential cofounders. Stratified analysis was performed according to gender and age (<35 and >35), retrospective study statistics includes continues variables with or without normal distribution and are reported as mean, standard deviation, median, inter quartile range (IQR), categorical variable were present as number (percentage), the T-test was used to examine variables between survivors and non survivors. Statistical significance for single continuous variables were performed using Z score test and a P-value of less than 0.005 was considered as statistically significant.

Result

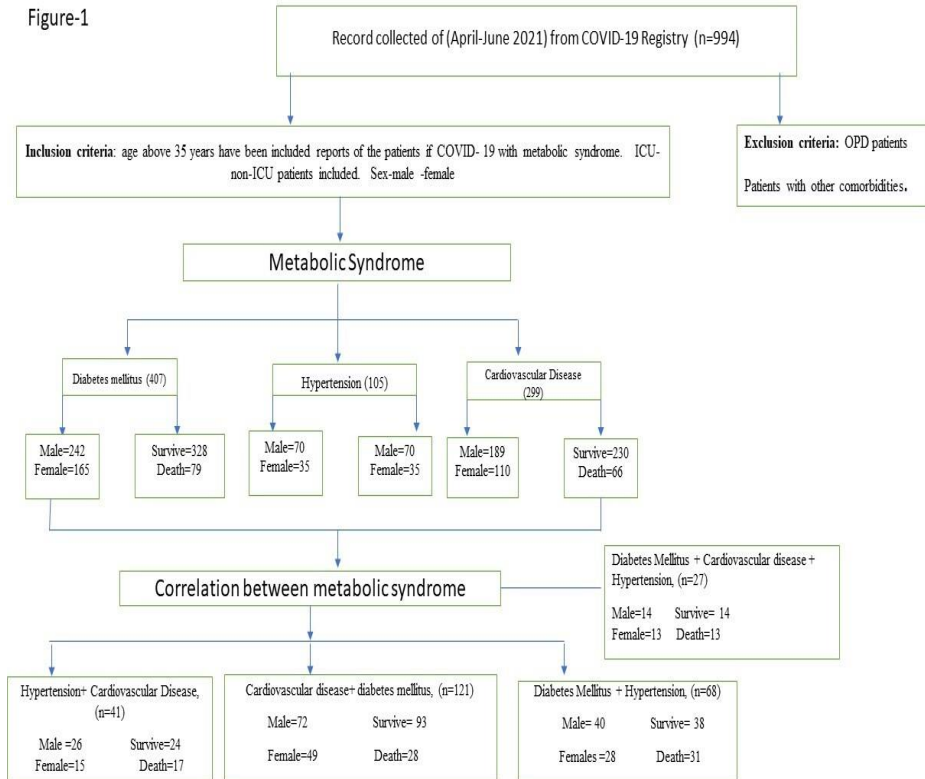


Figure I. Study of Flow Chart

Table-I shows the total patients of 994 radiologically – confirmed COVID-19 cases, whereby 892 (89.70%) patients were confirmed having age above 35 and 102 (10.26%) patients were confirmed with age below 35 years. In terms of severity, 349 (35.11%) were ward patients and 645 (64.88%) were ICU patients. The frequency of genders was 626 (62.97%) male and 364 (36.61%) female. One or more comorbidities were present in COVID -19 patients, diabetes mellitus was present in 407 (40.94%) patients; hypertension was present in 105 (10.56%) patients, and cardiovascular disease was present in 299 (30.08%) patients. Hypertension and diabetes mellitus were present in 69 (6.94%) patients; diabetes mellitus and cardiovascular disease were present in 121 (12.12%) patients and hypertension and cardiovascular disease were present in 41 (4.12%) patients. Patients over the age of 35 were found to have a higher prevalence of the assessed comorbidities.

Table I
Demographic of Overall Patient Population

Variables	Frequency	%	P value
Age	994	-	-
35 Above	892	89.70%	1.62

35 Below	102	10.26%	1.1
Gender			
Male	626	62.97%	0.72
Female	364	36.61%	0.02*
Indoor Admission			
Ward	349	35.11%	0.04*
ICU	645	64.88%	0.78
Comorbidities			
Diabetes Mellitus	407	40.94%	0.0003*
Hypertension	105	10.56%	1.08
Cardiovascular Disease	299	30.08%	0.14
No Comorbidities			
Diabetes Mellitus	587	59.05%	0.59
Hypertension	889	89.43%	1.61
Cardiovascular Disease	695	69.91%	0.95
Combine Comorbidities			
Hypertension + Diabetes Mellitus	69	6.94%	1.35
Diabetes Mellitus +cardiovascular disease	121	12.12%	0.97
Hypertension +scardiovascular disease	41	4.12%	1.58

Demographic and baseline clinical features of our study participants can be observed in Table-II. Diabetes Mellitus was the most frequent comorbidity (32.11%) far ahead of cardiovascular disease (26.82%) and hypertension (17.47%). When we distinguished all population by survivor/non-survivor group, age has distinctly higher influence in non-survivor group. Likewise, all the severe comorbidities had significantly higher prevalence in the survival group.

Table 2
Demographic based on survivor status

Variables	Total Population	Study	Non-Survivors	Survivors	P-value
Characteristics	(N=994) %		(N=246) %	(N=748) %	-
Age, years	52.64±14.72		58.45±13.08	52.59±14.79	3.09
Male%	(628) 63.17%		(163) 66.26%	(465) 62.16%	N/A
Female%	(366) 36.82%		(83) 33.73%	(283) 37.83%	N/A
ICU%	(645) 64.88%		(215) 87.30%	(430) 57.48%	N/A
Ward%	(349) 35.11%		(31) 12.6%	(316) 42.24%	N/A
Diabetes Mellitus%	(407) 40.94%		(79) 32.11%	(328) 43.85%	0.005*
Cardiovascular Disease%	(299) 30.08%		(66) 26.82%	(230) 30.74%	0.24
Hypertension%	(105) 10.56%		(43) 17.47%	(62) 8.2%	0.001*

SpO2%	97.47±3.84	97.35±4.03	97.35±3.059	0.001*
Systolic BP, MM hg	132.34±6.39	112.5±4.82	115.97±6.51	1.27
Diastolic BP, MM hg	77.80±5.96	78.71±5.37	78±6.1	0.005*
Respiratory Rate/ min	20.57±2.76	20.28±1.54	20.65±3.01	0.006
Pulse	82.5±6.44	81.5±4.53	82.8±4.53	0.006

Figure-II shows that diabetes mellitus is more prevalent than any other comorbidities. Diabetes mellitus in male (65.94%) is more than female (44.95%) patients. Prevalence of all comorbidities (diabetes mellitus, hypertension, cardiovascular disease) in patients were (3.54%) in female and (2.23%) in male.

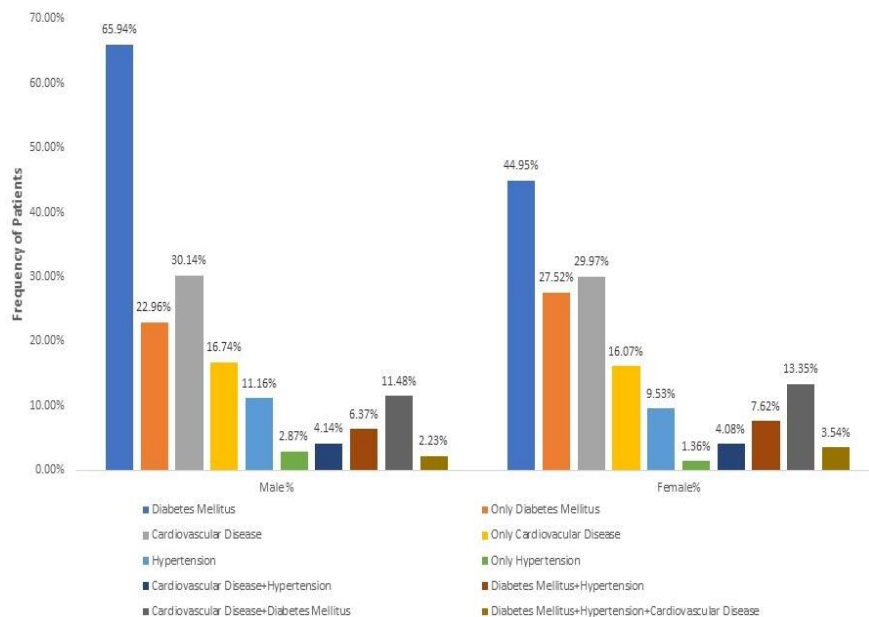


Figure II. Gender based Prevalence for Different Comorbidities in COVID-19 Patients

Figure-III A shows the correlation between the age group (above 35 years vs below 35 years) for different comorbidities such as diabetes mellitus (41.52% vs 33.66%), cardiovascular disease (29.85% vs 36.63%) were observed in patients with comparatively higher than the patients below the age of 35 years, however only diabetes mellitus (24.80% versus 36.63%) or only cardiovascular disease patients (16.27% versus 18.18%) without any other comorbidities was higher in the patients below the age 35 years than those above 35 years. Patients with both diabetes mellitus and cardiovascular disease were more in the age below 35 years (12.87%) than the age above 35 year (12.12%)

Figure-III B shows the correlation between the patients of age group above 35 years versus below 35 years for different comorbidities such as diabetes mellitus (2.35% versus 1.98%), hypertension (11.33% versus 3.96%) observed in the

patients above 35 years were comparatively higher than the patients below 35 years, however only diabetes mellitus (24.80% versus 23.76%) and only hypertension (2.35% versus 1.98%) without any other comorbidities were present in higher frequency in patients above 35 years than below 35 years. Similarly, patients with hypertension and diabetes mellitus were more in the age above 35 years (7.51%) than age below 35 years (1.98%).

Figure-III C shows the correlation between the age group (above 35 years versus below 35 years) for different comorbidities such as hypertension (11.33% vs 3.96%) in patient above 35 years were comparatively higher than the patients below age of 35 years, cardiovascular disease (29.85% versus 32.67%) in the patient below 35 years were comparatively higher than age above 35 years. However only hypertension (2.35% versus 1.98%), only cardiovascular disease (16.27% versus 18.18%) without any other comorbidities was higher in age below 35 years than age above 35 years, patients with hypertension + cardiovascular disease were more in age above 35 years (4.37%) than the age below 35 years (1.98%).

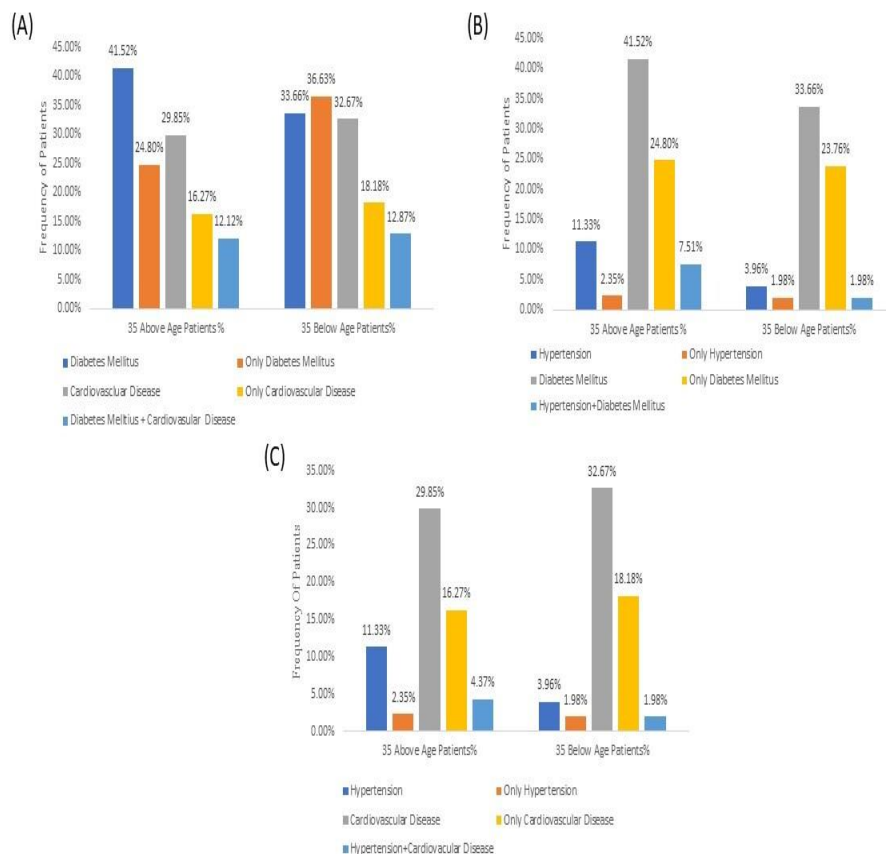


Figure III. Age Based Prevalence for Different Comorbidities in COVID-19 Patients.
 (A) Cardiovascular Disease-Diabetes Mellitus (B) Hypertension-Diabetes Mellitus
 (C) Hypertension-cardiovascular disease

Table-III shows the laboratory results at the time of admission for all patients, organised by survival status. Non-survivors out-number the survivors by a wide margin. RBC count (m/ml) [4.4(4.01-4.9) vs 4.3(3.92-4.77), P-value<0.001], MCV count (Femtoliter) [83.1(76.15-88.3)] vs 84.6(77.9-89.75) p-value<0.001] and LDH count (u/l) [696(48-1005) vs 753(552-1453), P-value< 0.01] all lab comorbidities were included as significantly. RBS (mg/dl) [223(155-332) vs 154(310.7-429.7), P-value <0.001] and Plasma glucose (mmol/mM) [158(118-235) vs 229(182-273.7) P-value <0.001]. All assessed history of comorbidities (months) compared to survivor and non-survivors included were significantly correlated. Diabetes Mellitus [24(12-36) vs 36(12-60), P-value <0.005]; Hypertension [24(12-36) vs 48(24-102) P-value <0.001] and only Hypertension [21(12-36) vs 48(24-102) P-value <0.001].

Table III
Laboratory findings upon admission of COVID-19 patients based on Survivor status and Presence/Absence of Comorbidities

Characteristics	Total Median (IQR)	Non-Survivor (IQR)	Survivor (IQR)	P- value
WBC Count $\times 10^3$ per μ l	8.8 (5.9-12.5)	11.3 (6.4-17.7)	8.2 (5.8-11.6)	8.65
RBC Count $\times 10^5$ per μ l	4.37 (3.98-4.94)	4.3 (3.92-4.77)	4.4 (4.01-4.9)	0.002*
Platelet Count $\times 10^4$ per μ l	24.6 (18.2-34.0)	25.3 (17.1-39.5)	24.3 (18.6-33.1)	1.49
HB Level g/dl	12.5 (11.1-13.75)	12.6 (11.45-13.9)	12.4 (11-13.7)	0.32
MCV fl	83.4 (82.8-88.7)	84.6 (77.9-89.75)	83.1 (76.15-88.3)	0.0007*
MCH pg	27.9 (25.3-29.9)	28.1 (25.4-29.8)	27.9 (25.2-29.9)	0.37
MCHC gm/dl	33.1 (32.4-33.1)	33.1 (32.4-33.9)	33.3 (32.3-33.7)	0.18
CRP Level mg/l	48.35 (20.7-74.4)	64.7 (39.5-97.5)	39.8(16.95-67.15)	2.92461E-11*
LDH Level u/l	700 (486-1043)	753 (552-1453)	696 (48-1005)	0.01*
Comorbidities Laboratory. Findings				
HBA1C %	6.9 (6.1-7.75)	6.8 (6.47-7.52)	6.9 (6.1-7.8)	0.3
RBS mg/dl	230 (162-340)	372.5 (310.7-429.7)	223 (155-332)	0.001*
PP2BS mg/dl	151 (109-218.5)	154.5 (111.5-183.7)	149 (108-224.5)	0.39
Plasma Glucose mmol/mM	165 (119.5-244.5)	229 (182-273.7)	158 (118-235)	0.01*
History Of Comorbidities (months)				
Diabetes Mellitus	24 (12-36)	36 (12-60)	24 (12-36)	0.005*
Only Diabetes Mellitus	24 (12-36)	24 (12-36)	24 (2-36)	0.3
Hypertension	36 (16.5-48)	48 (24-60)	24 (12-36)	0.001*
Only Hypertension	24 (12-48)	48 (24-102)	21 (12-36)	0.02*
Cardiovascular Disease	24 (12-60)	24 (12-48)	24 (12-60)	0.24
Only Cardiovascular Disease	24 (12-24)	24 (12-48)	36 (12-60)	0.13

Figure-IV shows the Kaplan-Meier survival curves according to all co-morbidities (diabetes mellitus, hypertension, cardiovascular disease) indicates an increase in all-causes mortality in all comorbidity's patients from the very beginning of the observation period. Note, hypertension group initially matches the curve of the former two groups, but there was clear separation at around 4-5 days of all hospitalization mortality of all co-morbidities and it is maximum between 12-15 days of hospitalization.

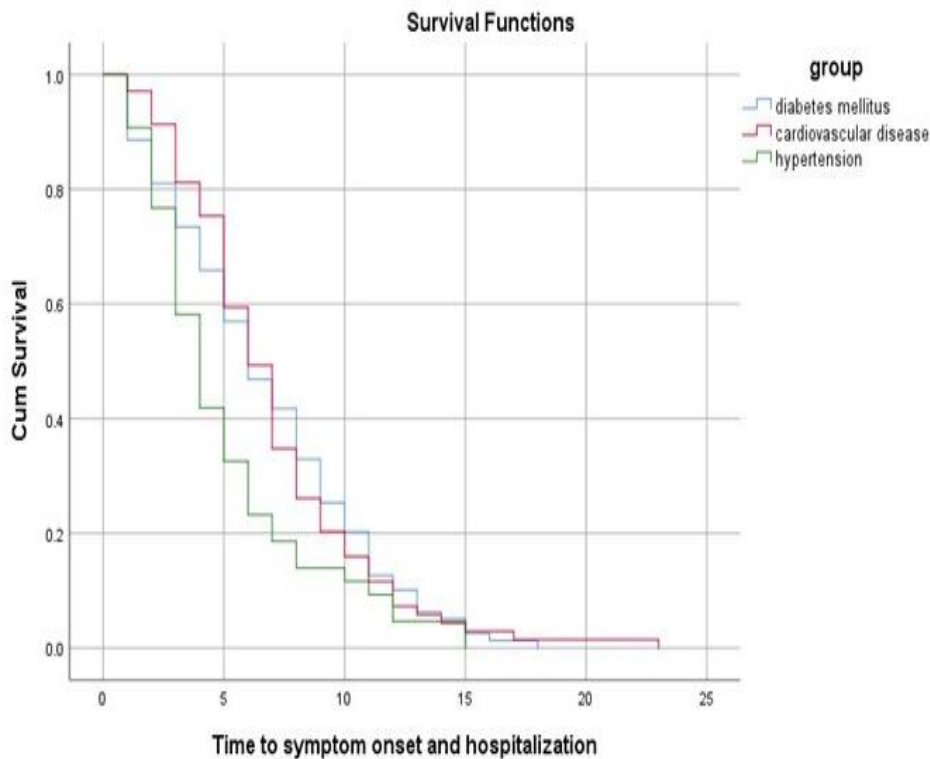


Figure IV. Kaplan Meier survival curve

The findings of logistic regression model are shown in table-4. In comorbidities, diabetes mellitus (95%CI); [24(30.06,37.36), P-value <0.001], only diabetes mellitus [24(26.94,37.02), P-value <0.005], cardiovascular disease [24(37.04,47.22), P-value 0.005], only cardiovascular disease [24(36.41,52.59), P-value <0.001], hypertension [12(23.34,38.4), P-value <0.001], only hypertension [34(25.73,60.73) P-value <0.001] and the presence of assessed comorbidities remained statically significant with the patients above the age of 35 years.

Table IV
Logistic Regression Model

Characteristics	Total 95% Confidence Interval ²	High 95% CI	Low 95% CI	P -Value
Diabetes Mellitus	24(30.06, 37.36)	37.36	30.06	0.003*
Only Diabetes Mellitus	24(26.94, 37.02)	37.02	26.94	0.005*
Cardiovascular Disease	24(37.04, 47.22)	47.22	37.04	0.008
Only Cardiovascular Disease	24(36.41, 52.59)	52.59	36.41	0.02*
Hypertension	12(23.34, 38.4)	38.4	23.34	0.07
Only Hypertension	34(25.73, 60.73)	60.73	25.73	0.003*

Discussion

Severity of COVID-19 was linked with multiple comorbidities. Many of the patients' outcomes for COVID-19 were related to cardiovascular conditions, diabetes mellitus and hypertension. Patients with type 2 diabetes suffered from increased severity of COVID-19. In our study of 994 patients with COVID-19, 407 patients were having a history of diabetes mellitus, 299 were having cardiovascular disease and 105 were having hypertension. The correlation between diabetes and COVID-19 outcomes was previously detected in meta-analyses. Patients with diabetes mellitus also have a more unfavourable outcome in other common infections such as COVID-19. Multiple pathophysiological mechanisms can support the association between DM and COVID-19 severity and also, hypertension and COVID-19 (17,18). In measuring the risk of mortality due to comorbidity in patients with COVID-19, we showed that DM increased death significantly in all patients(3). Many groups analysed the comorbidities of COVID-19 patients in other countries. They found that HT was the most frequent pre-existing condition. After adjusting for all other clinical conditions, only age, diabetes mellitus, chronic obstructive, and chronic kidney disease—not HT—showed predictive value for death from COVID-19 (9).

Developing information suggests that individuals with diabetes are at increased risk for complications including death among COVID-19 patients. According to other countries involving confirmed COVID-19 patients, hypertension was the second most common comorbidity among severe 173 cases (16). Hypertension was identified as the comorbidity associated with the prognosis of COVID-19 in another retrospective study, admission to ICU, the need for mechanical ventilation and death after adjusting for baseline characteristics, other comorbidities and the results of laboratory tests (19). We analysed the impact of cardiovascular disease, hypertension, and diabetes mellitus on COVID-19 pneumonia development in this retrospective study. The main findings regarding METS (Metabolic Syndrome) were that our patients with METS presented moderate COVID-19 symptoms. To achieve the main objective of study, influence of METS on the COVID-19 clinical course were discovered. Patients with METS were older and more frequently had previous comorbidities, such as CVD or respiratory illnesses. Moreover, they presented with a higher frequency of severe pneumonia or respiratory failure than patients without METS. Interestingly, the

mortality rate was increased in METS patients, higher mortality among patients with cardiovascular disease, diabetes mellitus and hypertension (4).

Conclusion

Over 180 countries were affected by COVID-19 resulting in mass death worldwide. Among those, patients above the age of 35 were severely affected. However, the patients with comorbidities have more severe outcomes compared with patient without comorbidities. Patients with hypertension, diabetes mellitus and cardiovascular disease had important risk factor for severity and mortality. Therefore, patients with comorbidities should take necessary precautions to avoid getting infected with COVID-19 or there should be a separate line of treatment and protocol for patients with comorbidities.

Abbreviations

CRP- C-Reactive Protein, CVD-Cardiovascular Disease, HT-Hypertension, DM-Diabetes Mellitus, MCV-Mean corpuscle volume, MCH-Mean corpuscles haemoglobin, MCHC-Mean corpuscle haemoglobin concentration, LDH-Lactate Dehydrogenase, SBP- Systolic blood pressure, DBP-Diastolic blood pressure, METS-Metabolic Syndrome.

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Conflict of interest: Author declare no conflicts of interest

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