Original Article

Influence of Cardiovascular Risk Factors among Patients with Covid 19 Infection and its Association with In-Hospital Outcome - A Multicentre Prospective Observational Study

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Abstract:

Introduction: **The global spread of COVID-19, first identified in Wuhan, China, in December 2019, has ignited an unprecedented ongoing global pandemic. Risk stratification of these patients is crucial to optimize the use of hospital resources. Several associations with adverse outcomes in COVID-19 patients have been identified, including factors that also predispose to cardiovascular disease (CVD), such as older age, male sex, hypertension, overweight and diabetes. In this context we designed this study to observe Association of Cardiovascular risk factors with patients infected with Covid 19 and it's in-hospital outcome.**

Materials and Methods: **In this prospective observational study total 408 adult patients who were reverse transcription polymerase chain reaction (Rt-PCR) positive for COVID-19 were included. They were admitted in Sarkari Karmachari Hospital, Kuwait Bangladesh Friendship Government Hospital and Dr. Sirajul Islam Medical College between June 2020 to June 2022. Patients with severe comorbidities like Acute myocardial infarction, Stroke, Acute kidney injury, malignancy and pregnant women were excluded from the study. Appropriate informed written consent was obtained. Demographic and clinical data were correlated with outcome. The statistical analysis was carried out using the Statistical Package for Social Sciences version 22.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Qualitative variables were expressed as frequency and percentage. Quantitative variables were expressed as mean ± standard deviation and median. Test of significance was performed by unpaired t-test for quantitative variable and Chi square test for qualitative variables. In addition, multivariate logistic regression analysis of possible risk factors was done to determine the association with outcome by calculating odds ratio with 95% confidence intervals. A p value <0.05 was be considered as significant.**

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Results: **The mean age of participants was 45.2±13.4 years among them 263 (64.5%) were male and 145 (35.5%)were female. According to BMI maximum male 126 (47.9%) were normal weight group whereas maximum female 63(43.4%) were obese. Considering cardiovascular risk factors among male and female Smoking were 160 (60.8%) vs. 38 (26.2%), Hypertension were 105 (39.9%) vs. 65 (44.8%), Diabetes Mellitus were 71 (27.0%) vs 55 (37.9%), Dyslipidemia were 69 (26.2%) vs. 36 (24.8%), Family history of CVD were 55 (20.9%) vs.20 (13.8%) and Clustering of risk factors (≥2 factors) were 117 (44.5%) vs. 74 (51.0%). Among the study population 81 (19.9%) needed oxygen therapy , 50 (12.3%) needed Non-invasive ventilation, 34 (8.3%) patients needed Mechanical Ventilation, Among the study subjects total 27 (6.61%) expired and maximum number of patients 15 (55.6%) were in 61-80 years age group. Regression analysis for the predictors of adverse in hospital outcome among the Cardiovascular risk factors showed Age (>60yrs) (p= 0.034), BMI (>25) (p= 0.026), Smoking (p= 0.041), Hypertension (p= 0.037) Diabetes Mellitus (p= 0.013), Dyslipidemia (p= 0.021) and Clustering of risk factors (≥2) (p= 0.012) were statistically significant contributors.**

Conclusion: **In conclusion, this study shows that Age (>60yrs), BMI (>25), Smoking, Hypertension, Diabetes Mellitus, Dyslipidemia, clustering of risk factors (≥2) have greater risk of adverse outcomes including death from COVID-19. It is recommended that individuals with cardiovascular risk factors, especially older men and women, should be focus of public health measures and must be informed regarding increased risk of death in COVID-19. It is likely that with proper preventive and therapeutic interventions the higher risk of adverse outcomes in COVIDF-19 patients with cardiovascular risk factors can be mitigated. We need to be more vigilant in controlling CVD risk factors since it not only increases the morbidity of non-communicable diseases, but also poses to and worsens the outcome of communicable diseases.**

Introduction

The global spread of COVID-19, first identified in Wuhan, China, in December 2019, has ignited an unprecedented ongoing global pandemic.[1] Although most infected individuals experience only mild symptoms that do not require hospitalization, the absolute number of patients requiring hospital admission is staggering. Risk stratification of these patients is crucial to optimize the use of hospital resources.[2] Several associations with adverse outcomes in COVID-19 patients have been identified, including factors that also predispose to cardiovascular disease (CVD), such as older age, male sex, hypertension, overweight and diabetes.[3,4] Furthermore, individuals with overt CVD appear to be affected more seriously by COVID-19 infection.[5]

By the end of 2020, the COVID-19 pandemic had led to an estimated 3 million deaths worldwide.[6] Large, population-based studies show that existing cardiovascular disease (CVD) and some individual cardiovascular risk factors (such as diabetes and hypertension) are associated with COVID-19-related deaths.[7,8,9] Other studies support associations between CVD or individual risk factors and severe COVID-19 outcomes among hospitalized patients.[10]

With a population of over 160 million, Bangladesh is one of the most densely populated (1265 per square km) countries in the world.[11] About 60% of its population is between 15 to 64 years and only 4.7% is above 65 years of age .[12] The care-home facility is virtually non-existent and the extended family structure combines the aged with the young in the same household, Because of economic prosperity, the country has been experiencing an increasing trend of unplanned urbanization, and currently, more than 32% of people live in urban areas. Bangladesh is also undergoing nutrition and epidemiologic transition with a higher burden of non-communicable diseases (NCDs). A recent meta-analysis has shown that overall prevalence for metabolic syndrome (a cluster of health problems including high blood pressure, abdominal fat, high triglycerides, high blood sugar, and low HDL cholesterol) is higher in Bangladesh compared to the estimated world prevalence (30% versus 20 25%).[13] Besides, approximately 34% of adults are overweight and NCDs account for 67% of deaths in Bangladesh.[14] In this context we designed this study to observe Association of Cardiovascular risk factors with patients infected with Covid 19 and it's in-hospital outcome.

Materials and Methods:

In this prospective observational study total 408 adult patients who were reverse transcription polymerase chain reaction (Rt-PCR) positive for COVID-19 were included. They were admitted in Sarkari Karmachari Hospital, Kuwait Bangladesh Friendship Government Hospital and Dr. Sirajul Islam Medical College between June 2020 to

June 2022. Patients with severe comorbidities like Acute myocardial infarction, Stroke, Acute kidney injury, malignancy and pregnant women were excluded from the study. Appropriate consent was obtained from every patient or from legal guardian by reading out the written informed consent according the revised Declaration of Helsinki. We collected demographic data (age, sex, occupation, education), clinical data (symptoms on admission, comorbidities) and correlated them with outcome. The statistical analysis was carried out using the Statistical Package for Social Sciences version 22.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Qualitative variables such as fever, cough etc. were expressed as frequency and percentage. Quantitative variables like age, durations, etc. were expressed as mean ± standard deviation and median. Test of significance was performed by unpaired t-test for quantitative variable and Chi square test for qualitative variables compared separately in different clinical presentation. In addition, multivariate logistic regression analysis of possible risk factors was done to determine the association with outcome by calculating odds ratio with 95% confidence intervals. A p value <0.05 was be considered as significant.

Results:

The mean age of participants was 45.2±13.4 years among them 263 (64.5%)were male and 145 (35.5%)were female. Maximum number of male 82 (31.2%) were in 61-80 years group and maximum female 44 (33.3%) were in 41-60 years group. Among both group 165 (62.7%) male and 62 (42.8%) female were service holder. Considering education status among study population maximum number male 91 (34.6%) were graduated and maximum number of female 38 (26.2%) were XII class passed. According to BMI maximum male 126 (47.9%) were normal weight group whereas maximum female 63(43.4%) were obese **(**Table I**).**

It has been observed among the study population presenting complaints were 355 (87%) Fever, 352 (86.3) Dry cough, 163 (40%) tiredness, 176 (43.1%) Bodyache, 32 (7.8%) Diarrhea, 116(28.4%) Headache, 49 (12%) Loss of taste, 66 (16.2%) Loss of smell, 214 (52.5%) Shortness of breath, 60 (14.7%) Chest pain. Elderly patients presented with most of the complaints (Table II).

Table-I

Distribution of the study population according to age, sex, occupation, literacy and BMI

	Male 263 (64.5%)	Female 145 (35.5%)
Age group		
<21	22 (8.4%)	10 (6.9%)
21-40	52 (19.8%)	40 (43.5%)
41-60	73 (27.8%)	44 (33.3%)
61-80	82 (31.2%)	29 (20%)
>80	34 (12.9%)	22 (15.2%)
Occupation		
Service	165 (62.7%)	62 (42.8%)
Business	57 (21.7%)	16 (11.0%)
Farmer	11 (4.2%)	1 (0.7%)
Housewife	0 (0.0%)	49 (33.8%)
Doctor	4(1.5%)	16 (11.0%)
Others	26 (9.9%)	1 (0.7%)
Education level		
Nil	4 (1.5%)	8 (5.5%)
V	4 (1.5%)	16 (11%)
X	33 (12.5%)	24 (16.6%)
XII	76 (28.9%)	38 (26.2%)
Graduate	91 (34.6%)	27 (%)
Masters	55 (20.9%)	32 (22.1%)
BMI		
<18.5	20 (7.6%)	4 (2.8%)
18.5-24.9	126(47.9%)	49(33.8 %)
25-29.9	92 (35 %)	63(43.4%)
>30	25 (9.5 %)	29 (20 %)

Table-II

Distribution of study population according to presenting sign, symptoms.

	Age group					Total
	<21	21-40	41-60	61-80	>80	
Fever	28	78	93	107	49	355 (87%)
	7.9%	22.0%	26.2%	30.1%	13.8%	
Dry cough	25	79	91	110	47	352 (86.3)
	7.1%	22.4%	25.9%	31.2%	13.4%	
tiredness	16	37	33	53	24	163 (40%)
	9.8%	22.7%	20.2%	32.5%	14.7%	
Bodyache	16	42	37	57	24	176 (43.1%)
	9.1%	23.9%	21.0%	32.4%	13.6%	
Diarrhoea	3	5	5	16	3	32 (7.8%)
	9.4%	15.6%	15.6%	50.0%	9.4%	
Headache	10	29	21	35	21	116 (28.4%)
	8.6%	25.0%	18.1%	30.2%	18.1%	
Loss of taste	1	10	11	20	7	49 (12%)
	2.0%	20.4%	22.4%	40.8%	14.3%	
Loss of smell	3	15	15	22	11	66 (16.2%)
	4.5%	22.7%	22.7%	33.3%	16.7%	
Shortness of breath	14	49	57	65	29	214 (52.5%)
	6.5%	22.9%	26.6%	30.4%	13.6%	
Chest pain	4	11	17	15	13	60 (14.7%)
	6.7%	18.3%	28.3%	25.0%	21.7%	
	7.8%	22.5%	25.0%	30.9%	13.7%	

Table-III

Distribution of study population according to Cardiovascular risk factors.

	Risk factors	
Smoking	160 (60.8%)	38 (26.2%)
Hypertension	105 (39.9%)	65 (44.8%)
Diabetes Mellitus	71 (27.0%)	55 (37.9%)
Dyslipidemia	69 (26.2%)	36 (24.8%)
Family history of CVD	55 (20.9%)	20 (13.8%)
Clustering of risk factors	117 (44.5%)	74 (51.0%)

Considering cardiovascular risk factors among male and female Smoking were 160 (60.8%) vs. 38 (26.2%), Hypertension were 105 (39.9%) vs. 65 (44.8%), Diabetes Mellitus were 71 (27.0%) vs 55 (37.9%), Dyslipidemia were 69 (26.2%) vs. 36 (24.8%), Family history of CVD were 55 (20.9%) vs.20 (13.8%) and Clustering of risk factors (≥2 factors) were 117 (44.5%) vs. 74 (51.0%) (Table III).

Among the study population 81 (19.9%) needed oxygen therapy and maximum number of patients 34 (42.0%) were in 61-80 years age group, 50 (12.3%) needed Non-invasive ventilation and maximum number of patients 19 (38.0%) were in 61-80 years age group, 34 (8.3%) patients needed Mechanical Ventilation and maximum number of patients 18 (52.9%)were in 61-80 years age

Table-IV

Distribution of study subjects according to Oxygen delivery system and death.

		Age group					Total
	<21	21-40	41-60	61-80	>80		
Oxygen therapy	Count	7	19	12	34	9	81 (19.9%)
	% within Oxygen therapy	8.6%	23.5%	14.8%	42.0%	11.1%	
Non-invasive ventilation	Count	3	3	13	19	12	50 (12.3%)
	% within Non-invasive ventilation	6.0%	6.0%	26.0%	38.0%	24.0%	
Mechanical Ventilation	Count	0	3	3	18	10	34 (8.3%)
	% within Mechanical Ventilator	0.0%	8.8%	8.8%	52.9%	29.4%	
Expired	Count	0	2	2	15	8	27 (6.61%)
	% within Expired	0.0%	7.4%	7.4%	55.6%	29.6%	

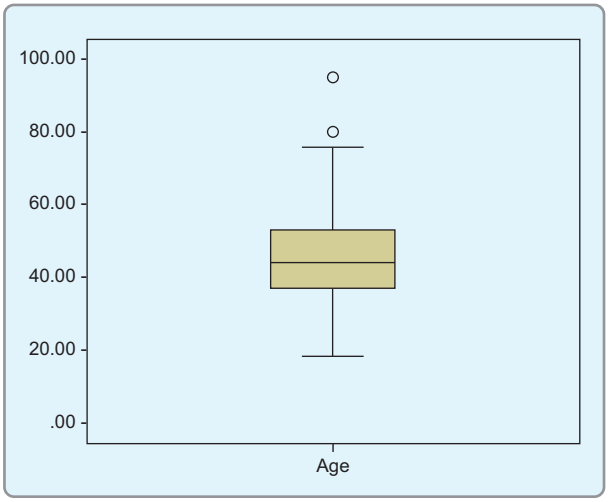

Figure 1: *Box whisker plot showing age distribution of Expired patients*

Table-V

Regression analysis showing influences of Cardiovascular risk factors on outcome.

Expired	B	Std.Error	Wald	Sig.	Exp(B)	95% CI for Exp(B)	
						Lower Bound	Upper Bound
Age (>60yrs)	.101	1.229	.007	0.034	1.106	.199	2.310
BMI (>25)	.081	1.189	.005	0.026	1.085	.105	3.155
Male gender	.231	.779	.076	0.129	1.001	.217	4.610
Smoking	.037	.758	.002	0.041	1.064	.218	4.255
Hypertension	.103	2.243	.122	0.037	1.157	.126	7.047
Diabetes Mellitus	.210	.797	.038	0.013	1.279	.163	3.714
Dyslipidemia	.134	.945	.020	0.021	1.025	.137	5.579
Clustering of risk factors(≥2)	.043	2.216	.069	0.012	1.792	.123	3.916
Comorbidities (2)	.071	.755	.009	0.225	.932	.212	4.091

group (Table IV). Among the study subjects total 27 (6.61%) expired and maximum number of patients 15 (55.6%) were in 61-80 years age group (Figure 1).

Regression analysis for the predictors of adverse in hospital outcome among the Cardiovascular risk factors showed Age (>60yrs) (p= 0.034), BMI (>25) (p= 0.026), Smoking (p= 0.041), Hypertension (p= 0.037) Diabetes Mellitus (p= 0.013), Dyslipidemia (p= 0.021) and Clustering of risk factors (≥2) (p= 0.012) were statistically significant contributors.

Discussion:

The mean age of participants was 45.2±13.4 years among them 263 (64.5%)were male and 145 (35.5%)were female. Maximum number of male 82 (31.2%) were in 61-80 years group and maximum female 44 (33.3%) were in 41-60 years group. According to other studies mean age of participants was 41.7±16.3 years where 63% were male and 37% female.[15]

The mean age of the cohort was 46±18 years, 54% were less than 50 years and about half lived in large family households (>5 persons). Prevalence of low educational status was higher in women while tobacco use was more in men. Comorbidities were present in 28.6% with hypertension (17.8%) and diabetes (16.6%) being the most common. Other comorbidities were chronic pulmonary disease, tuberculosis, coronary heart disease and neurological disease.[16]

Among both group 165 (62.7%) male and 62 (42.8%) female were service holder. Considering education status among study population maximum number male 91 (34.6%) were graduated and maximum number of female 38 (26.2%) were XII class passed. According to

BMI maximum male 126 (47.9%) were normal weight group whereas maximum female 63(43.4%) were obese.

It has been observed among the study population presenting complaints were 355 (87%) Fever, 352 (86.3) Dry cough, 163 (40%) tiredness, 176 (43.1%) Bodyache, 32 (7.8%) Diarrhea, 116(28.4%) Headache, 49 (12%) Loss of taste, 66 (16.2%) Loss of smell, 214 (52.5%) Shortness of breath, 60 (14.7%) Chest pain. Elderly patients presented with most of the complaints. Some study showed Patients got admitted predominantly with fever (69%), cough (54%), breathlessness (41%), fatigue (40%), anorexia (26%) and diarrhea (19%). Less frequent symptoms included chest pain, sore throat, headache and bodyache, nasal congestion, anosmia, nausea, vomiting.[15]

Considering cardiovascular risk factors among male and female Smoking were 160 (60.8%) vs. 38 (26.2%), Hypertension were 105 (39.9%) vs. 65 (44.8%), Diabetes Mellitus were 71 (27.0%) vs 55 (37.9%), Dyslipidemia were 69 (26.2%) vs. 36 (24.8%), Family history of CVD were 55 (20.9%) vs.20 (13.8%) and Clustering of risk factors (≥2 factors) were 117 (44.5%) vs. 74 (51.0%). Other study showed Total 51 patients (51.0%) had comorbidities. Hypertension (21%), diabetes mellitus (16%), heart diseases (8%) and renal diseases (8%) were frequent Thirteen out of hundred patients had history of smoking.[15]

Risk factors, clinical findings and outcomes in patients with hypertension, diabetes and smoking/tobacco use, Hematological and biochemical parameters did not show significant inter-group differences. Patients with known hypertension were older and had higher prevalence of diabetes, cardiovascular disease, hypothyroidism and smoking/tobacco.[17]

Among the study population 81 (19.9%) needed oxygen therapy and maximum number of patients 34 (42.0%) were in 61-80 years age group, 50 (12.3%) needed Non-invasive ventilation and maximum number of patients 19 (38.0%) were in 61-80 years age group, 34 (8.3%) patients needed Mechanical Ventilation and maximum number of patients 18 (52.9%)were in 61-80 years age group. Among the study subjects total 27 (6.61%) expired and maximum number of patients 15 (55.6%) were in 61-80 years age group.

Regression analysis for the predictors of adverse in hospital outcome among the Cardiovascular risk factors showed Age (>60yrs) (p= 0.034), BMI (>25) (p= 0.026), Smoking (p= 0.041), Hypertension (p= 0.037) Diabetes Mellitus (p= 0.013), Dyslipidemia (p= 0.021) and Clustering of risk factors (≥2) (p= 0.012) were statistically significant contributors.

Other study showed regarding the comorbidity status, hypertension, heart disease and renal disease were significantly (p<0.001) associated with death. Other comorbidities were not significantly (p>0.05) associated with death. Multivariate logistic regression analysis revealed that only smoking and renal disease were independently and significantly (p<0.05) associated, having OR = 9.95 (95% CI 1.73- 57.12) and OR = 9.43 (95% CI 1.12 -79.23) respectively.[15]

Previous meta-analyses including studies from India have identified diabetes as equally important as hypertension for adverse COVID-19 related outcomes.[11,12] In the present study the unadjusted OR for diabetes and deaths were 1.88 (CI 1.46–2.43), however, the risk significantly attenuated after age and sex adjustment to OR 1.16 (CI 0.89–1.52) which is different from the previous studies.[17]

Another study showed in patients admitted to the ICU, we found a trend towards increased mortality, with an ICU mortality of 27.2%, 29.1%, 40.1% for patients with 0, 1 and ≥2 CVD-risk factors (p=0.055). In Cox regression analysis, a 5-year age increase was associated with an HR 1.37, 95% CI 1.31 to 1.45) for mortality, while there was no significant association with sex (HR 1.02, 95% CI 0.81 to 1.28). The presence of two or more cardiovascular risk factors was significantly associated with overall mortality (HR 1.52, 95% CI 1.15 to 2.02), but not with ICU admission or ICU mortality. After additional adjustment for smoking, obesity and the combined use of beta-blockers and platelet aggregation inhibitors the presence of two or more risk factors remained associated with mortality (HR 1.38, 95% CI 1.02 to 1.86), while there was no increased risk in the group with 1 CVD risk factor (HR 1.01, 95% CI 0.73 to 1.39).[16]

Oxygen requirement, non-invasive as well as invasive ventilation were more in older age-groups (40–59 and 60 years) with graded escalation. Deaths were significantly higher in age-group 40–59 (7.1%) and 60 (15.0%) when compared to <40 years (2.1%). Women were less literate and had lower prevalence of hypertension, diabetes and tobacco use. Oxygen requirement was significantly more in women while requirement of non-invasive or invasive ventilation were not different. Hematological and biochemical parameters were not significantly different and are not shown. Number of in hospital deaths were significantly more in men (n = 282, 8.3%) as compared to women (n = 58, 4.6%) (Fig 2) with univariate OR 1.88, (95% CI 1.41–3.51).[17]

We also performed age-sex adjusted and multivariate analyses to determine association of various cardiovascular risk factors with COVID-19 related in-hospital mortality and other outcomes. Age 60 years vs <40 years emerged as the most important risk factor with significantly greater deaths on univariate, sex-adjusted and multivariate analyses. In age-group 40–59 years also deaths were significantly higher than <40 y on univariate and multivariate analyses. On univariate analyses, male sex, hypertension diabetes and tobacco were associated with significantly more deaths. There was moderate attenuation of significance with age and sex adjusted analyses, but hypertension and tobacco use continued to be significant. Following multivariate analyses significance of all the risk factors completely attenuated (Fig 3). Analyses of secondary outcomes show that in patients age 60 years as well in age-group 40–59 years, compared with <40 years, the need for invasive ventilation as well as non-invasive ventilation were higher.[17]

Conclusion:

In conclusion, this study shows that Age (>60yrs), BMI (>25), Smoking, Hypertension, Diabetes Mellitus, Dyslipidemia, Clustering of risk factors (≥2) have greater risk of adverse outcomes including death from COVID-19. It is recommended that individuals with cardiovascular risk factors, especially older men and women, should be focus of public health measures and must be informed regarding increased risk of death in COVID-19. Moreover, these high risk individuals must aggressively follow all non-pharmacological physical measures for prevention. Clinicians are advised to seek early evidence of deterioration of pulmonary function and signs of cardiovascular and extra pulmonary manifestation of acute COVID-19 in these patients and provide optimum management. It is likely that with proper preventive and therapeutic interventions the higher risk of adverse outcomes in COVID-19 patients with cardiovascular risk factors can be mitigated. Mechanistic studies investigating how CVD risk factors disproportionately affect COVID-19 patients compared with other infectious diseases are warranted. We need to be more vigilant in controlling CVD risk factors since it not only increases the morbidity of non-communicable diseases, but also poses to and worsens the outcome of communicable diseases.

Conflict of interests

The authors declare that there is no conflict of interests.

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