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Electrocardiogram and echocardiogram patterns among ischemic stroke patients during COVID-19 pandemic

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ABSTRACT

Objectives. Diabetic Ischemic strokes are mostly thromboembolic mainly originating from cardiac diseases. We aimed to assess electrocardiogram and echocardiogram abnormalities in patients with ischemic stroke during the COVID-19 pandemic.

Material and methods. This retrospective cross-sectional, hospital-based study was conducted among 299 ischemic stroke patients who were hospitalized in the stroke center, in the north of Iran in 2021. All the data were gathered by checklist from electronic health records.

Outcomes. The mean age of participants was 70.37 ± 11.89 (Range: 39, 79) and 134 (44.82%) of them were men. Out of 299 patients, 44 (14.72%) were diagnosed with COVID-19 infection and 75 (25.1%) died in hospital. The most common abnormalities of electrocardiogram and echocardiogram were AF rhythm (22.41%) and mitral valve dysfunction (89.63%), respectively. In univariate analysis, associations were detected between COVID-19 with diastolic and aortic valve dysfunction (P=0.024, P=0.053, respectively) but not with electrocardiogram abnormalities. EF<40 (P=0.005), left ventricular enlargement (P=0.027), right ventricular enlargement (P=0.021), diastolic dysfunction (P=0.003), left atrial enlargement (P<0.001), mitral valve dysfunction (P=0.037) and aortic valve dysfunction (P=0.005) were significantly associated with mortality. In multivariate analysis, no significant association was detected between COVID-19 with echocardiogram and electrocardiogram abnormalities.

Conclusions. Aging, comorbidities and atrial fibrillation play an important role in ischemic stroke incidence. COVID-19 may not have any significant associations with echocardiogram and electrocardiogram abnormalities in ischemic stroke patients.

Keywords: ischemic stroke, electrocardiogram, echocardiogram, COVID-19, SARS-CoV-2

OBJECTIVES

Stroke is a leading cause of mortality and disability globally, affecting 13.7 million people each year. With 5.5 million deaths per year, stroke is considered as the second leading cause of death. In Iran, the mortality rates for in-hospital, 1-month, and 1-year were reported as 18.71%, 23.43%, and 34.44%, respectively [1]. Stroke can result in significant disability, which imposes a rehabilitation burden on society [2]. Stroke is classified into hemorrhagic stroke and ischemic stroke. Ischemic stroke accounting for approximately 71% of all strokes worldwide, is defined as loss of blood supply and subsequent tissue damage in the brain, spinal cord or retina [3].

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Age, sex and genetic factors are considered as non-modifiable risk factors for ischemic stroke. Age is considered as the strongest risk factor for ischemic stroke, so that a higher incidence and prevalence are observed in developed countries compared with developing countries after the age of 49 and 39, respectively [4]. Modifiable risk factors, identified in INTERSTROKE study, include hypertension, low levels of physical activity, a high ApoB-to-ApoA1 ratio, diet, a high waist-to-hip ratio, stress and depression, smoking and alcohol, cardiac causes and diabetes mellitus [5].

Identifying the primary cause of ischemic stroke is crucial as it can define approaches for therapy and also avoidance of recurrent stroke [6]. Ischemic strokes are mostly thromboembolic in origin and the embolism is mostly originated from cardiac diseases, especially atrial fibrillation as well as the atherosclerosis of large arteries. Small vessel diseases, associated with hypertension and diabetes mellitus is also another source of ischemic stroke [6]. Considering the vascular origin of ischemic stroke, currently the best management options are intravenous thrombolysis or endovascular thrombectomy [7].

Cardiac abnormalities can be found in patients with ischemic stroke due to common vascular risk factors. In a large meta-analysis pooled results showed that one-third of patients with ischemic stroke and no cardiac history had greater than 50% coronary artery stenosis and a 3% risk of developing MI within one year [8]. Cardiovascular diseases are among the risk factors for ischemic stroke. Atrial fibrillation (AF) is associated with a five to six-fold increase in stroke risk and a two-fold increase in mortality risk. Furthermore, left ventricular hypertrophy in patients with ischemic heart disease is considered as a strong risk factor for stroke [8,9].

COVID-19 caused by SARS-CoV-2 is demonstrated to be linked with numerous systemic complications leading to substantial mortality and morbidity [10]. Various studies have reported cardiovascular complications (including arrhythmia, pericarditis, acute myocarditis, cardiomyopathy, microvascular clot formation and shock) that may lead to an elevated incidence of ischemic stroke in patients with COVID-19 [11-13]. Most ischemic strokes associated with COVID-19 were classified as either cardioembolic (14.3–40%), undetermined source (35.0–42.8%), small vessel occlusion (6– 21.4%), strokes of other etiology (7.2-20%) and strokes due to atherosclerosis of large arteries (6-14.3%) [14,15].

Considering the relationship between cardiovascular complications and incidence of ischemic stroke, here we aimed to determine and compare different electrocardiogram and echocardiogram abnormalities among patients with ischemic stroke, with or without COVID-19.

MATERIAL AND METHODS

Study design

We performed this cross-sectional, hospital-based study with retrospective data collection of 299 confirmed ischemic stroke patients who were hospitalized in our stroke center, Poursina hospital in Guilan, Iran between March 2020 and March 2021. All the hospitalized ischemic stroke patients during this timeframe were included in the study whether COVID-19 positive or negative. Patients who were discharged or expired within the first 24 hours of admission were excluded from the study.

Data collection

A checklist that consisted of demographic variables (age, sex), comorbidities (hypertension, diabetes mellitus, hyperlipidemia, cardiovascular diseases, left ventricle hypertrophy), smoking cigarette and COVID-19 diagnosis as well as electrocardiogram and echocardiogram abnormalities was filled out for all included patients by means of their electronic health records.

Patients were categorized according to the presence or absence of COVID-19 pneumonia, diagnosed by Polymerase Chain Reaction (PCR) test and high-resolution computed tomography (HRCT) findings which was confirmed by an expert radiologist. Additionally, interpretation of ECGs and echocardiograms was done by an expert cardiologist.

The ECG data included abnormalities in ST segment, T wave, AF rhythm, bradycardia, tachycardia, Atrioventricular (AV) block, Right bundle branch block (RBBB) or left bundle branch block (LBBB), axis deviation and any other observed abnormality. Furthermore, the echocardiogram data included ejection fraction (EF), Left ventricular hypertrophy (LVH), enlargement of left and right ventricles and atrium, diastolic dysfunction and abnormalities of cardiac valves.

Mortality was the outcome in this study. All patients were followed up carefully in the hospital. Patients were discharged from the hospital if their neurologic condition was stabilized after stroke attack and if they were COVID-19 positive simultaneously, they were discharged as soon as their pneumonia ameliorated.

Statistical analysis

Analysis was performed using SPSS version 23. Descriptive statistics were used for analysis. For quantitative variables, central and dispersion indices including mean, standard deviation, median and interquartile range were used and for qualitative variables, counts and percentage were used. Chi-Square test, Fischer's exact test and multivariate linear re-

gression model were used to determine the association between ECG and echocardiogram abnormalities as well as outcome of ischemic stroke patients with COVID-19 by adjusting the effects of individual factors, comorbidities and intervening variables. A significance level of 0.05 was set.

Informed consent was obtained from all participants. This research was approved by the Medical Ethics Committee of Guilan University of Medical Sciences, Rasht, Iran (Registration Number: IR.GUMS.REC.1401.478) and was conducted according to the principles stated in the Declaration of Helsinki (2013).

OUTCOMES

A total of 299 patients with ischemic stroke who were hospitalized met the inclusion criteria and entered our study. The mean age was 70.37 ± 11.89 (Range: 39, 79) and 134 (44.82%) of participants were men. Out of 299 patients, 44 (14.72%) were diagnosed with COVID-19 infection and also 75 (25.1%) of patients died in hospital. Table 1 represents the demographic and clinical characteristics of participants. The most common comorbidities were hypertension (76.25%) and diabetes mellitus (47.16%). Echocardiogram and electrocardiogram abnormalities were detected in 265 (88.63%) and 149 (49.83%) of the participants, respectively. Furthermore, the most common abnormalities found in electrocardiogram and echocardiogram of the patients were AF rhythm (22.41%) and mitral valve dysfunction (89.63%), respectively.

TABLE 1. Demographic and clinical characteristics of participants. Values are reported as Number (Percentage)

Variable	Value (Total=299)
Age (Years)	
Mean ± SD	70.37±11.89
Min, Max	39, 79
≤65	110 (36.79)
>65	189 (63.21)
Gender	
Male	134 (44.82)
Female	165 (55.18)
Smoking	
Yes	39 (13.04)
No	260 (86.96)
Comorbidities	
Renal failure	12 (4.01)
Diabetes mellitus	141 (47.16)
Hyperlipidemia	96 (32.11)
Hypertension	228 (76.25)
Hypertension drug usage	197 (86.4)
Coronary artery disease	107 (35.79)
Heart valve disease	10 (3.34)
Other heart disorders	21 (7.02)
COVID-19 Positive	44 (14.72)
Death outcome	75 (25.08)
Echocardiogram abnormalities	265 (88.63)
Ejection fraction	
40 < EF < 55	188 (62.88)
30 < EF < 39	73 (24.41)
EF < 30	38 (12.71)
Left ventricular hypertrophy	108 (36.12)
Ventricular enlargement	
right	18 (6.02)
left	15 (5.02)
Diastolic dysfunction	171 (57.19)
grade I	127 (74.27)
grade II	33 (19.3)
grade III	11 (6.43)
Atrial enlargement	
right	9 (3.01)
left	63 (21.07)
Mitral valve dysfunction	268 (89.63)
mild	177 (66.04)
moderate	87 (32.46)
severe	4 (1.49)
Aortic valve dysfunction	178 (59.53)
mild	150 (83.8)
moderate	28 (15.64)
severe	1 (0.56)
Tricuspid valve dysfunction	265 (88.63)
mild	208 (78.49)
moderate	57 (21.51)
Pulmonary valve dysfunction	13 (4.35)
mild	13 (100)
Other echocardiogram abnormalities	63 (21.07)
ECG abnormalities	149 (49.83)
ST segment	29 (9.7)
T wave	19 (6.35)
AF rhythm	67 (22.41)
Bradycardia	6 (2.01)
Tachycardia	7 (2.34)
AV block	2 (0.67)
type I	1 (50)
type II	1 (50)
Bundle branch block	21 (7.02)
RBBB	6 (28.57)
LBBB	15 (71.43)
Axis deviation	9 (3.01)
right axis	0 (0)
left axis	9 (3.01)
Other ECG abnormalities	37 (12.37)

Abbreviations: LBBB: left bundle branch block; RBBB: right bundle branch block; AV: Atrioventricular; AF: Atrial fibrillation; ECG: electrocardiogram; EF: ejection fraction; SD: standard deviation

Association between demographic factors, comorbidities and COVID-19 with echocardiogram

Results of our study were indicative of a significant association between COVID-19 infection and echocardiogram abnormalities in the univariate analysis (P=0.04). There was a significant association between diastolic dysfunction and COVID-19 (P=0.024). Furthermore, an association was detected between aortic valve dysfunction and COVID-19 (P=0.053). Some other echocardiogram abnormalities are found to be associated with the outcome of patients. Ejection fraction less than 40 (P=0.005), left ventricular enlargement (P=0.027), right ventricular enlargement (P=0.021), diastolic dysfunction (P= 0.003), left atrial enlargement (P<0.001), mitral valve dysfunction (P=0.037) and aortic valve dysfunction (P=0.005) are among the echo-

cardiogram factors associated with the outcome of patients. Table 2 represents the association between COVID-19 and outcome of participants with echocardiogram findings. In the regression model, a significant association was seen between age and echocardiogram abnormalities, so that these abnormalities were mostly detected in patients older than 65 years of age (P= 0.037). In the multivariate analysis after eradication of other factor effects, no significant association was seen between COVID-19 and echocardiogram abnormalities (P=0.067). Table 3 shows the association between comorbidities and demographic factors, comorbidities and COVID-19 with echocardiogram in the regression model.

TABLE 1. Demographic and clinical characteristics of participants. Values are reported as Number (Percentage)

Variable	COVID-19	P Value	Outcome		P Value
	Positive (N=44)		Discharged (N=224)	Died (N=75)	
Echocardiogram abnormalities					
+	43 (97.73)	0.040 *	194 (86.61)	71 (94.67)	0.057 *
-	1 (2.27)		30 (13.39)	4 (5.33)	
Ejection fraction					
40 < EF < 55	24 (54.55)	0.216 *	151 (67.41)	37 (49.33)	0.005 *
30 < EF < 39	14 (31.82)	0.216 *	52 (23.21)	21 (28)	0.404 *
EF < 30	6 (13.64)	0.216 *	21 (9.38)	17 (22.67)	0.003 *
Left ventricular hypertrophy					
+	21 (47.73)	0.083 *	79 (35.27)	29 (38.67)	0.596 *
-	23 (52.27)		145 (64.73)	46 (61.33)	
Left ventricular enlargement					
+	3 (6.82)	0.470 **	7 (3.13)	8 (10.67)	0.027 **
-	41 (93.18)		217 (96.88)	67 (89.33)	
Right ventricular enlargement					
+	3 (6.82)	0.736 **	9 (4.02)	9 (12)	0.021 **
-	41 (93.18)		215 (95.98)	66 (88)	
Diastolic dysfunction					
+	32 (72.73)	0.024 *	139 (62.05)	32 (42.67)	0.003 *
-	12 (27.27)		85 (37.95)	43 (57.33)	
Diastolic dysfunction					
Grade I	24 (75)	0.202 *	109 (78.42)	18 (56.25)	0.032 *
Grade II	8 (25)		22 (15.83)	11 (34.38)	
Grade III	0 (0)		8 (5.76)	3 (9.38)	
Left atrial enlargement					
+	9 (20.45)	0.914 *	35 (15.63)	28 (37.33)	<0.001 *
-	35 (79.55)		189 (84.38)	47 (62.67)	
Right atrial enlargement					
+	1 (2.27)	0.999 **	6 (2.68)	3 (4)	0.696 **
-	43 (97.73)		218 (97.32)	72 (96)	
Mitral valve dysfunction					
+	43 (97.73)	0.061 **	196 (87.5)	72 (96)	0.037 *
-	1 (2.27)		28 (12.5)	3 (4)	
Mitral valve dysfunction					
mild	22 (51.16)	0.039 **	143 (72.96)	34 (47.22)	<0.001 **
moderate	21 (48.84)		52 (26.53)	35 (48.61)	
severe	0 (0)		1 (0.51)	3 (4.17)	
Aortic valve dysfunction					
+	32 (72.73)	0.053 *	123 (54.91)	55 (73.33)	0.005 *
-	12 (27.27)		101 (45.09)	20 (26.67)	
Aortic valve dysfunction					
mild	29 (87.88)	0.830 **	105 (85.37)	45 (80.36)	0.332 **
moderate	4 (12.12)		18 (14.63)	10 (17.86)	
severe	0 (0)		0 (0)	1 (1.79)	
Tricuspid valve dysfunction					
+	41 (93.18)	0.303 *	194 (86.61)	71 (94.67)	0.057 *
-	3 (6.82)		30 (13.39)	4 (5.33)	
Tricuspid valve dysfunction					
mild	33 (80.49)	0.735 *	158 (81.44)	50 (70.42)	0.064 **
moderate	8 (19.51)		36 (18.56)	21 (29.58)	
Pulmonary valve dysfunction					
+	1 (2.27)	0.700 **	8 (3.57)	5 (6.67)	0.324 **
-	43 (97.73)		216 (96.43)	70 (93.33)	
Other echocardiogram abnormalities					
+	9 (20.45)	0.914 *	45 (20.09)	18 (24)	0.472 *
-	35 (79.55)		179 (79.91)	57 (76)	

** Chi-square test **Fischer's exact test*

TABLE 3. Multivariate analysis of association between demographic factors, comorbidities and COVID-19 with echocardiogram (Regression model)

		B	S. E	P Value	Exp (B)	95% C.I for EXP (B)	
						Lower	Upper
First Model	Gender (Female/Male)	- 0.321	0.421	0.445	0.725	0.318	1.654
	Age (>=65/<65)	0.733	0.392	0.062	2.081	0.965	4.487
	Smoker (Yes/No)	-0.362	0.530	0.494	0.696	0.247	1.966
	Renal Failure (Yes/No)	0.082	1.113	0.941	1.086	0.123	9.613
	DM (Yes/No)	0.036	0.415	0.931	1.037	0.460	2.337
	HLP (Yes/No)	0.436	0.470	0.354	1.546	0.615	3.885
	HTN (Yes/No)	0.162	0.459	0.724	1.176	0.478	2.891
	CAD (Yes/No)	0.576	0.449	0.199	1.780	0.738	4.292
	Heart Valve Disease (Yes/No)	-0.520	0.869	0.550	0.595	0.108	3.264
	COVID-19 (Yes/No)	1.907	1.038	0.066	6.735	0.881	51.476
	Constant	1.310	0.474	0.006	3.705		
Final Model	Age (>=65/<65)	0.774	0.370	0.037	2.168	1.050	4.479
	COVID-19 (Yes/No)	1.889	1.031	0.067	6.614	0.877	49.887
	Constant	1.467	0.264	<0.001	4.336		

Association between comorbidities and demographic factors with clinical features

Among the comorbidities and demographic factors, a significant association was seen between age and echocardiogram abnormalities, so that these abnormalities were mostly detected in patients older than 65 years of age (P=0.038). Furthermore, there was a significant association between age and coronary artery disease (CAD) with electrocardiogram abnormalities, so that the abnormalities were mostly seen in patients with CAD and those higher than 65 years of age (P=0.001, P=0.002, respectively). No significant association was detected between comorbidities and demographic factors with COVID-19 infection. Additionally, Patients older than 65 years of age had a significantly higher risk of dying during their hospitalization (P<0.001). In our regression analysis, no significant association was detected between COVID-19 and outcome of the patients (P=0.43). Association between comorbidities and demographic factors with electrocardiogram, echocardiogram, COVID-19 and outcome of the participants and the regression model are shown in table 4 and table 5, respectively.

TABLE 4. Univariate analysis of association between comorbidities and demographic factors with electrocardiogram, echocardiogram, COVID-19 and outcome of the participants; Data are presented as numbers (percentage)

Variable	Echocardiogram	P Value	Electrocardiogram	P Value	COVID-19	P Value	Outcome		P Value
	Abnormal (N=265)		Abnormal (N=149)		Positive (N=44)		Discharged (N=224)	Died (N=75)	
Gender									
Female	118 (88.06)	0.780 *	59 (44.03)	0.071 *	19 (43.18)	0.813 *	102 (45.54)	32 (42.67)	0.665 *
Male	147 (89.09)		90 (54.55)		25 (56.82)		122 (54.46)	43 (57.33)	
Age									
≤65	92 (83.64)	0.038 *	41 (37.27)	0.001 *	17 (38.64)	0.783 *	98 (43.75)	12 (16)	<0.001 *
>65	173 (91.53)		108 (57.14)		27 (61.36)		126 (56.25)	63 (84)	
Smoker									
+	32 (82.05)	0.177 **	19 (48.72)	0.881 *	4 (9.09)	0.399 *	30 (13.39)	9 (12)	0.757 *
-	233 (89.62)		130 (50)		40 (90.91)		194 (86.61)	66 (88)	
Renal failure									
+	11 (91.67)	0.999 **	5 (41.67)	0.564 *	2 (4.55)	0.692 **	9 (4.02)	3 (4)	0.999 **
-	254 (88.5)		144 (50.17)		42 (95.45)		215 (95.98)	72 (96)	
DM									
+	127 (90.07)	0.458 *	65 (46.1)	0.223 *	26 (59.09)	0.086 *	106 (47.32)	35 (46.67)	0.922 *
-	138 (87.34)		84 (53.16)		18 (40.91)		118 (52.68)	40 (53.33)	
HLP									
+	88 (91.67)	0.255 *	51 (53.13)	0.433 *	15 (34.09)	0.760 *	72 (32.14)	24 (32)	0.982 *
-	177 (87.19)		98 (48.28)		29 (65.91)		152 (67.86)	51 (68)	

Variable	Echocardiogram	P Value	Electrocardiogram	P Value	COVID-19	P Value	Outcome		P Value
	Abnormal (N=265)		Abnormal (N=149)		Positive (N=44)		Discharged (N=224)	Died (N=75)	
HTN									
+	205 (89.91)	0.210 *	114 (50)	0.917 *	33 (75)	0.832 *	165 (73.66)	63 (84)	0.069 *
-	60 (84.51)		35 (49.3)		11 (25)		59 (26.34)	12 (16)	
HTN drug									
+	178 (90.36)	0.529 **	103 (52.28)	0.082 *	30 (90.91)	0.585 **	141 (85.45)	56 (88.89)	0.499 *
-	27 (87.10)		11 (35.48)		3 (9.09)		24 (14.55)	7 (11.11)	
CAD									
+	99 (92.52)	0.113 *	66 (61.68)	0.002 *	14 (31.82)	0.552 *	80 (35.71)	27 (36)	0.964 *
-	166 (86.46)		83 (43.23)		30 (68.18)		144 (64.29)	48 (64)	
HVD									
+	8 (80)	0.317 **	7 (70)	0.218 **	1 (2.27)	0.999 **	6 (2.68)	4 (5.33)	0.276 **
-	257 (88.93)		142 (49.2)		43 (97.73)		218 (97.32)	71 (94.67)	
Other heart disease									
+	21 (100)	0.147 **	11 (52.38)	0.809 *	5 (11.36)	0.211 **	11 (4.91)	10 (13.33)	0.013 *
-	244 (87.77)		138 (49.7)		39 (88.64)		213 (95.09)	65 (86.67)	

Abbreviations: DM: diabetes mellitus; HLP: hyperlipidemia; HTN: hypertension; CAD: coronary artery disease; HVD: heart valve disease

** Chi-square test **Fischer's exact test*

TABLE 5. Multivariate analysis of association between demographic factors, comorbidities, COVID-19, electrocardiogram and echocardiogram with outcome (Regression model)

		B	S. E	P Value	Exp (B)	95% C.I for EXP (B)	
						Lower	Upper
First Model	Gender (Female/Male)	-0.104	0.305	0.733	0.901	0.496	1.638
	Age (>=65/<65)	1.402	0.359	<0.001	4.063	2.008	8.219
	Smoker (Yes/No)	0.318	0.465	0.494	1.374	0.553	3.417
	Renal Failure (Yes/No)	0.105	0.716	0.884	1.111	0.273	4.519
	DM (Yes/No)	-0.011	0.307	0.971	0.989	0.542	1.805
	HLP (Yes/No)	-0.080	0.321	0.804	0.924	0.492	1.733
	HTN (Yes/No)	0.637	0.392	0.104	1.891	0.878	4.074
	CAD (Yes/No)	-0.154	0.306	0.616	0.858	0.471	1.562
	Heart Valve Disease (Yes/No)	1.160	0.760	0.127	3.190	0.719	14.154
	COVID-19 (Yes/No)	0.304	0.386	0.431	1.355	0.636	2.887
	Echocardiogram (Abnormality/ normality)	0.844	0.578	0.144	2.325	0.749	7.218
	Electrocardiogram (Abnormality/ normality)	0.014	0.294	0.963	1.014	0.570	1.803
	Constant	-3.370	0.713	<0.001	0.034		
Final Model	Age (>=65/<65)	1.407	0.343	<0.001	4.083	2.087	7.991
	Constant	-2.100	0.306	<0.001	0.122		

Association between demographic factors, comorbidities and COVID-19 with electrocardiogram

Results of our study showed no significant association between any of electrocardiogram abnormalities and COVID-19 infection among study group. However, AF rhythm was found to be significantly associated with outcome of the patients (P=0.003). Regression analysis (Table 7) indicated a significant association between age and electrocardiogram abnormalities (P=0.002). Those older than 65 years were more likely to develop electrocardiogram abnormalities. Furthermore, a significant association was seen between CAD and electrocardiogram abnormalities (P=0.004). No significant association was found between COVID-19 and electrocardiogram abnormalities in any subgroups of univariate and multivariate analysis. Table 6 represents the association between demographic factors, comorbidities and COVID-19 with electrocardiogram.

TABLE 6. Univariate analysis of association between COVID-19 and outcome with electrocardiogram findings; Data are presented as numbers (percentage)

Variable	COVID-19	P Value	Outcome		P Value
	Positive (N=44)		Discharged (N=224)	Died (N=75)	
Electrocardiogram abnormality					
+	20 (45.45)	0.529 *	108 (48.21)	41 (54.67)	0.333 *
-	24 (54.55)		116 (51.79)	34 (45.33)	
ST segment abnormality					
+	2 (4.55)	0.277 **	26 (11.61)	3 (4)	0.054 *
-	42 (95.45)		198 (88.39)	72 (96)	
T wave abnormality					
+	2 (4.55)	0.999 **	15 (6.7)	4 (5.33)	0.791 **
-	42 (95.45)		209 (93.3)	71 (94.67)	
AF rhythm					
+	11 (25)	0.655 *	41 (18.3)	26 (34.67)	0.003 *
-	33 (75)		183 (81.7)	49 (65.33)	
Bradycardia					
+	0 (0)	0.597 **	4 (1.79)	2 (2.67)	0.643 **
-	44 (100)		220 (98.21)	73 (97.33)	
Tachycardia					
+	0 (0)	0.599 **	4 (1.79)	3 (4)	0.373 **
-	44 (100)		220 (98.21)	72 (96)	
AV block					
+	0 (0)	0.999 **	2 (0.89)	0 (0)	0.999 **
-	44 (100)		222 (99.11)	75 (100)	
Bundle branch block					
+	5 (11.36)	0.211 **	16 (7.14)	5 (6.67)	0.889 *
-	39 (88.64)		208 (92.86)	70 (93.33)	
Bundle branch block					
RBBB	1 (20)	0.999 **	5 (31.25)	1 (20)	0.999 **
LBBB	4 (80)		11 (68.75)	4 (80)	
Left axis deviation					
+	3 (6.82)	0.132 **	9 (4.02)	0 (0)	0.118 **
-	41 (93.18)		215 (95.98)	75 (100))	
Other ECG abnormalities					
+	3 (6.82)	0.226 *	29 (12.95)	8 (10.67)	0.604 *
-	41 (93.18)		195 (87.05)	67 (89.33)	

** Chi-square test **Fischer's exact test*

TABLE 7. Multivariate analysis of association between demographic factors, comorbidities and COVID-19 with electrocardiogram (Regression model)

		B	S. E	P Value	Exp (B)	95% C.I for EXP (B)	
						Lower	Upper
First Model	Gender (Female/Male)	0.399	0.266	0.135	1.490	0.884	2.512
	Age (>=65/<65)	0.774	0.259	0.003	2.168	1.305	3.602
	Smoker (Yes/No)	0.376	0.390	0.335	1.456	0.678	3.123
	Renal failure (Yes/No)	-0.710	0.651	0.275	0.491	0.137	1.761
	DM (Yes/No)	-0.393	0.269	0.144	0.675	0.398	1.144
	HLP (Yes/No)	0.247	0.282	0.380	1.281	0.737	2.224
	HTN (Yes/No)	-0.153	0.311	0.623	0.858	0.466	1.579
	CAD (Yes/No)	0.819	0.266	0.002	2.269	1.347	3.820
	Heart valve disease (Yes/No)	0.969	0.739	0.190	2.635	0.619	11.219
	COVID-19 (Yes/No)	-0.093	0.349	0.789	0.911	0.459	1.805
	Constant	-0.825	0.349	0.018	0.438		
Final Model	Age (>=65/<65)	0.775	0.249	0.002	2.171	1.332	3.539
	CAD (Yes/No)	0.712	0.251	0.004	2.039	1.247	3.332
	Constant	-0.752	0.217	0.001	0.471		

DISCUSSION

According to the findings of the present study, higher portion of patients hospitalized with ischemic stroke were females and older than 65 years. The mean age of the participants was 70.37 ± 11.89 years. The most common concomitant conditions were hypertension, diabetes mellitus and coronary artery disease which are in accordance with previous studies [16,17]. Various echocardiogram and electrocardiogram abnormalities were detected in 88.63% and 49.83% of the patients, respectively. COVID-19 pneumonia was detected in 14.72 % of the patients and ultimately, one fourth of the patients succumbed to death.

Aging, as the strongest non-modifiable risk factor for incidence of stroke, highly correlated with coronary abnormalities and outcome of the patients. Roughly 75% of all strokes take place in individuals 65 years and above. Age-related structural and functional alterations in cerebral circulatory may lead to stroke in elderly [18]. Ischemic stroke in patients with AF is strongly predicted by older age, especially for patients with low to intermediate risk of stroke [19].

Sharma et al. investigated the clinical utility of transthoracic echocardiogram (TTE) at the time of ischemic stroke. In accordance with our study findings, they found that nearly 81% of echocardiograms showed abnormalities and older patients with coronary artery disease, atrial fibrillation, hypertension and diabetes were more likely to have an abnormal echocardiogram and higher recurrent stroke risk [20]. AF, ventricular thrombus, valvular heart disease, cardiac tumors, and structural heart defects can lead to embolic stroke [21]. A significant portion of our study group had mild mitral and tricuspid valves dysfunction. It is well established that patients with valvular heart disease, especially those with mitral stenosis and underlying atrial fibrillation or flutter, have a higher susceptibility to ischemic stroke [22]. Studies are also indicative of high prevalence of heart failure in ischemic stroke patients [23] which is in accordance with the noticeable portion of our study population with low ejection fraction. Prevalence of LVH in our study was 36% which is slightly higher than 25% and 26% reported by Amin et.al [24] and Sharma et al. [20], respectively. This could be due to low sample size of our study population. Moreover, prevalence of diastolic dysfunction and right ventricular enlargement in our study was 57% and 6% which was concordant with results of Oates et al. [17] by 51% and 12%, respectively.

The most common ECG abnormality in our study was AF rhythm which is shown to be associated with ischemic stroke. Left ventricular systolic dysfunction was demonstrated as a predictor of stroke in patients with atrial fibrillation (RR=2.5, P<0.001) [24]. LVH was the other most common abnormality detected in our study which is associated with a twofold increased risk of ischemic stroke [26,27].

We found a significant association between EF<40, left and right ventricular enlargement, left atrial enlargement, diastolic dysfunction, mitral and aortic valve dysfunction with outcome of the patients. However, Purushothaman et al. reported higher mortality rates in ischemic stroke patients with abnormalities in ST segment and T wave [28]. Brammas et al. investigated ischemic stroke patients who ended up dead and found that 22% had prior heart failure, 34.8% had atrial fibrillation 31% had ST segment abnormalities [29].

We anticipated to discover a notable correlation between COVID-19 infection and cardiac disorders concordant with previous studies. Furthermore, we expected to observe a significant disparity in the occurrence of cardiac disorders between individuals with and without COVID-19 infection. However, in the present study, although in univariate analysis a slight significant association was found between COVID-19 infection and echocardiogram abnormalities, in multivariate analysis this association has disappeared. In this study, we found a significant association between COVID-19 with diastolic and aortic valve dysfunction in univariate analysis. In the study of Szekely et al. [30], 16% of patients with COVID-19 had LV diastolic dysfunction. Huang et al. [31] and Dvir et al. [32] reported the occurrence of aortic regurgitation in 16.7% and 8.1% of patients with COVID-19, respectively. Nevertheless, the exact association between COVID-19 with diastolic and aortic valve dysfunction is not yet clarified and further studies are warranted. Other studies implicate that COVID-19 viral infection can lead to myocardial scarring and thinning as well as myocarditis, cardiomyopathy, arrhythmia, cardiac arrest, LV and RV abnormalities [33, 34]. Additionally, other cardiac abnormalities are reported in COVID-19 patients including, left and right ventricular abnormality (39% and 33%) [33]

Also, no association was found between COVID-19 infection and electrocardiogram abnormalities in our study, but previous studies have reported associations between COVID-19 infection and electrocardiogram abnormalities including, sinus tachycardia, atrial fibrillation, ventricular tachycardia or fibrillation, bradycardia, interval and axis changes (QT prolongation) and alterations in ST segment and T wave [35]. Although we found no association between COVID-19 and outcome of the patients, but previous studies are indicative of this link. A cohort study of patients with COVID-19 indicated significant correlations between in-hospital mortality and cardiac complications including, left axis deviation

(P=0.039), inverted T-wave (P=0.002), ST-depression (P=0.027) and atrioventricular node block (P=0.002) [36]. Jabbari et al. demonstrated that a non-sinus rhythm in the admission ECG was associated with nearly eight times higher odds of mortality [37]. Kaeley et al. found that COVID-19 patients with new-onset atrial fibrillation, intraventricular conduction abnormalities, and sinus tachycardia had higher rates of mortality [38].

Discrepancy between the present study and the other investigations could be due to some reasons. First, the population of our study in both groups consisted of ischemic stroke patients in whom cardiac disorders are more frequently observed even without the presence of COVID-19 infection. So, further well-designed case control studies are required to overcome this issue. Second, this could be due to low sample size of our COVID-19 group. However, COVID-19 infection showed correlations with diastolic and aortic valve dysfunction in our study. Our study suffered from some limitations. Due to low sample size of COVID-19 patients we had to consider it as a dependent variable leading to inappropriate study design and limitations in evaluation of COVID-19 association with other variables. Further prospective well designed case control studies are required to resolve these limitations.

CONCLUSIONS

Findings of our study are indicative of the crucial role of aging, comorbidities and atrial fibrillation in ischemic stroke incidence as well as various consequent cardiac abnormalities like diastolic and aortic valve dysfunction in ischemic stroke patients.

Ischemic stroke patients with EF<40, left and right ventricular enlargement, left atrial enlargement, diastolic dysfunction, mitral and aortic valve dysfunction are more likely to end up dead.

COVID-19 was not significantly associated with echocardiogram and electrocardiogram abnormalities as well as the outcome in patients with ischemic stroke.

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