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Original Research Paper

Spectrum of Cardiac Etiologies and Associated Risk Factors in Cardioembolic Ischemic Stroke: A Prospective Observational Study

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ABSTRACT:

Background: Ischemic stroke is one of the leading causes of morbidity and mortality. There are several cardiac issues associated with the thromboembolic phenomenon resulting in ischemic stroke that are linked with a number of risk factors which can be prevented via early diagnosis and prompt management. **Objective:** The primary objective of this study is to evaluate the spectrum of cardiac etiologies responsible for the incidence of cardioembolic ischemic stroke. The secondary objective is to quantify the risk factors associated with these cardiac etiologies. **Study Design:** A prospective observational study was conducted at a tertiary care hospital from January 2020 to January 2023. A convenience sample of 190 patients who met the inclusion criteria were enrolled in the study. **Results:** Majority of the patients were male n=107, 56%, presented within first 6 hours of onset of stroke symptoms n=63, 33%, p value <0.01, involving posterior circulation n=71, 37%. The most prevalent symptoms were headache 91%, dysarthria 54%, dizziness 51%, and altered sensorium 45%. Atherosclerosis 91%, dyslipidemia 85%, hypertension 77%, and diabetes 53.6% were the most common presenting complaints. Out of 190 patients, 115 patients were diagnosed and 75 were undiagnosed cases of cardiac dysfunction. Dilated cardiomyopathy 43.6%, recent myocardial infarction 15.7%, and regional ventricular akinesis 11.5%. **Conclusion:** Cardiac evaluation after ischemic stroke is crucial to identify the potential cause of stroke as well as to rule out cardiac thromboembolic phenomenon. There are multiple risk factors associated with cardioembolic ischemic stroke which require effective control and management to prevent morbidity and mortality.

Keywords: thromboembolism, ischemic stroke, cardiac manifestations, risk factors, epidemiology

INTRODUCTION:

Stroke is one of the leading causes of mortality and lifelong morbidity, affecting more than 26 million people worldwide with 13.7 million new cases resulting in 5.83% of global deaths annually [1]. The majority of strokes are ischemic in nature, accounting for 62.4% of

all stroke cases and responsible for 2.51% of disability-adjusted life years (DALYs) [2, 3]. Cardioembolic strokes account for 15-30% of all ischemic strokes [4]. Atrial fibrillation is the most common pathology among all cardiac pathologies resulting in the formation of thromboembolism, comprising 20-40% of all cardiogenic ischemic strokes [5]. However, the etiology remains unclear for 30% of ischemic strokes [6]. The incidence of ischemic stroke varies greatly among different countries; nonetheless, stroke remains the leading cause of disability among young adults and elderly people [7]. It is crucial to accurately define the mechanism of stroke for rapid diagnosis and prompt management. Stroke is defined as the loss of blood supply or impaired oxygen supply to a certain part of the brain, resulting in brain tissue damage. Patients present in the emergency department with a constellation of typical symptoms, including dizziness, headache, numbness, facial drooping, weakness on one side of the body, loss of consciousness, and difficulty understanding, writing, or speaking. In case of no neurological impairment, clots produced in the heart can occlude the cerebral arteries, resulting in cardiogenic ischemic stroke [8, 9]. The underlying pathologies and risk factors associated with the occurrence of stroke are diverse, including atrial fibrillation, atherosclerosis of small cerebral blood vessels, uncontrolled hypertension, diabetes, and dyslipidemia [10]. Of all the other causes, cardioembolic stroke is significant for two main reasons: first, it is associated with more severe outcomes and poor prognosis than any other type of stroke; and second, with early diagnosis and effective management of underlying cardiac abnormality, stroke can be prevented. For example, oral anticoagulation therapy in dilated cardiomyopathy can considerably lower the risk of thromboembolism and, hence, ischemic stroke [11, 12]. There are three different widely accepted pathophysiological mechanisms that are potentially responsible for the cardiac thromboembolism that causes ischemic infarcts [10, 12]:

Blood stasis involves structural/functional cardiac alterations that can cause decreased cardiac output, blood pooling, and formation of blood clots. These emboli in the bloodstream clog cerebral arteries leading to cerebral ischemia and infarction, such as in dilated cardiomyopathy, heart failure, and atrial fibrillation.

Hypercoagulability results from the overactivation of coagulation pathways in malignancy and antiphospholipid syndrome, which demands regular anticoagulant treatment to avoid thromboembolic phenomenon. **Endothelial dysfunction** is caused by the multifactorial origin of endothelial damage that leads to infective valvular vegetation formation and calcific degeneration of the valves dislodging septic/aseptic emboli in the bloodstream causing infarctions, such as in hypertension, smoking, and diabetes.

Other causes of cardiogenic ischemic stroke include atherosclerosis, which causes progressive narrowing of the microvasculature (primarily) leading to progressively worsening of cerebral and cardiac perfusion. This is a gradual, progressive, and slow process that gives adequate time for the collateral formation and rehabilitation of cerebral and cardiac perfusion. However, the thrombus produced in the cardiac chambers is often large and, when dislodged, results in sudden occlusion of large arteries causing severe, acute ischemic stroke associated with poor prognosis and death. Cardiogenic ischemic stroke is the most severe type of stroke, leading cause of disability, poorly managed resulting in high early or late recurrences, poor outcomes, and high mortality [13, 14].

There are diverse underlying cardiac anomalies that can easily be missed and can later cause ischemic stroke. Atrial fibrillation, mechanical heart valves, and cardiomyopathy are the leading cardiac causes of ischemic stroke. In patients with uncontrolled diabetes and hypertension, dyslipidemia and cardiomyopathy are often present and overlooked in outpatient follow ups. [15] Due to limited health resources, cardiac screening is often omitted for stroke patients as well, at the time of presentation. It is recommended for stroke patients to undergo cardiac assessment e.g., electrocardiography, echocardiography, and serum cardiac biomarker evaluation. It is also crucial to confirm the pre-existing risk factors in the patients including hypertension, diabetes, hyperlipidemia, alcoholism, and smoking. [16]

Inclusion Criteria:

- Patients who were willing to participate in this research.
- Adult patients of age 18 or more
- Diagnosed cases of acute ischemic stroke
- Confirmed cases of acute cardioembolic stroke based on clinical examination, radiological imaging, and investigations of co-existing cardiac anomaly.

Exclusion Criteria:

- Patients who were reluctant to give consent or were not willing to participate in this study.
- Patients with pre-existing neurological and chronic co-morbidities that might affect the pathophysiological mechanism of stroke.
- Patients who died during the studies or the patient with incomplete follow ups
- Stroke patients with unknown/unusual etiologies
- Patients with the history of recent or previous traumatic brain injury

MATERIAL & METHODS:

Data is collected from the stroke patients at the time of hospital admission, during their hospital stay, and at the time of discharge. The collected data comprised of demographic characteristics (age, sex, race, ethnicity), clinical history (risk factors and comorbidities), investigations (electrocardiography, echocardiography, magnetic resonance imaging MRI brain, magnetic resonance angiography MRA of brain and neck), baseline hematological investigations (Complete blood count CBC, serum electrolyte levels, lipid profile, coagulation profile, and renal function tests) and findings on clinical examinations, stroke severity, and functional outcomes (National Institute of Health Stroke Scale NIHSS at admission and discharge, and modified Rankin Scale mRS at the time of discharge).

Informed, written consent was taken from all the enrolled study subjects. The demographic and clinical information of all patients was kept confidential. This prospective study assessed the patient's status for cardiac anomalies before and after the onset of stroke based on their previous medical record. It has also followed the patients till they got discharged to predict the outcome.

Data Analysis:

To summarize the data, descriptive statistical analysis was performed. Continuous variables were demonstrated as means and standard deviations, whereas categorical variables as frequencies and percentages. The Multivariate logistic regression analysis highlighted the independent risk factors responsible for ischemic stroke in selected patients such as, age, diabetes, hypertension, dyslipidemia, cardiac anomalies, and level of disability at the time of admission. The level of significance was determined at $P < 0.05$ and two-tailed level at 95% Confidence Interval. The data was analyzed by using SPSS v.25.

RESULTS:

The 190 selected patients showed male predominance. The data comprised of males (n=107, 56%, mean±SD 51±3.2 years) and females (n=83, 44%, mean±SD 51±3.2 years) with male to female ratio of 1.3:1. Incidence of stroke was considerably higher in two age groups; 45-50 years (n=52, 27%) and >70 years (n=58, 31%). Most of the patients belonged to district Punjab (n=188, 99%) whereas 2 patients belonged to Khyber Pakhtunkhwa (KPK) district.

Gender	Frequency (n)	Percentage (%)
Male	107	56%
Female	83	44%
Age Group		
<45 years	37	19%
45-50 years	52	27%
51-60 years	24	13%
61-70 years	19	10%
>70 years	58	31%

Table 1. Demographic characteristics of selected patients (n=190).

At the time of admission, patients were clinically assessed to confirm the diagnosis of stroke. The assessment included Glasgow coma scale (GCS), National Institute of Health Stroke Scale (NIHSS), time window from the onset of stroke or development of symptoms to the arrival at hospital, and modified Rankin Scale (mRS). Most of the patients presented with altered sensorium with GCS ranging between 9 to 14 (n=102, 53.6%, CI 0.11 to 0.21) with significant p value of <0.01. According to NIHSS, moderate stroke was diagnosed in 82 patients (43%, CI 0.04 to 2.9, p= 0.01). For the majority of the patients, the period between the onset of the symptoms and arrival at the hospital was unknown (n= 73, 38.4%, CI 0.1-2.8). Most of the cases

were managed effectively within the first hour of admission and before shifting the patient to the stroke ward, the estimated prognosis was good (mRS 0-2) in 112 out of 190 patients, comprising of 58.9% (CI 0.36-2.12).

At the time of Admission					
GCS	**Total (n=190)**	**Male (n=107)**	**Female (n=83)**	**p-value**	**95% Confidence Interval (CI)**
15	67	23	44	0.06	0.12-0.34
9 to 14	102	70	32	<0.01	0.11-0.21
≤8	21	14	7	0.02	0.09-2.42
NIHSS (score)					
TIA (0)	29	11	18	0.02	0.15-2.31
Mild stroke (1-3)	17	6	11	0.003	0.03-1.4
Moderate stroke (4-7)	82	49	33	0.01	0.04-2.9
Moderate to severe stroke (8-15)	47	34	13	0.34	0.14-3.1
Severe stroke (>16)	15	7	8	2.1	0.42-1.7
Time windows					
Admission within 6 hours of stroke onset	63	46	17	<0.01	0.05-1.4
Admission after 6 hours of stroke onset	54	32	22	0.03	0.06-2.53
Time of onset of stroke symptoms is unknown at the time of admission	73	52	21	0.14	0.1-2.8
Prognosis (mRS)					
Good (0-2)	112	75	37	0.01	0.36-2.12
Poor (3-6)	78	32	46	0.26	0.26-3.17

Table 2. Features of clinical assessment at the time of hospital admission, with significant prognostic values

Stroke patients were presented at emergency room with different combinations of symptoms. The most common symptoms (in descending order) were headache (n=172, 91%), dysarthria (n=103, 54%), and dizziness (n=97, 51%). There was a total of 9 symptoms noted in the subjects that are encapsulated in table 3.

Primary presenting symptoms	**Frequency (n)**	**Percentage (%)**
Headache	172	91%
Dizziness	97	51%
Aphasia	46	24%
Hemianopia	62	33%
Dysarthria	103	54%
Facial palsy	71	37%
Altered consciousness	85	45%
Hemi paresthesia	69	36%
Hemiparesis	81	43%

Table 3. Frequency of clinical symptoms in stroke patients at the time of stroke onset.

There are four possible types of ischemic infarcts depending on the area of the brain involved (Table 4). Ischemic lesion to posterior circulation and partial anterior circulation combined were responsible for 129 cases making 68% of total cases. Thirty-two cases of ischemic stroke compromised total anterior cerebral circulation while lacunar infarcts were least common n=29, 15%.

Type of Ischemic Infarct	Frequency (n)	Percentage (%)
Anterior circulation (Total)	32	17%
Anterior circulation (Partial)	58	31%
Lacunar	29	15%
Posterior circulation	71	37%

Table 4. Frequency of different types of ischemic infarct based on area involved.

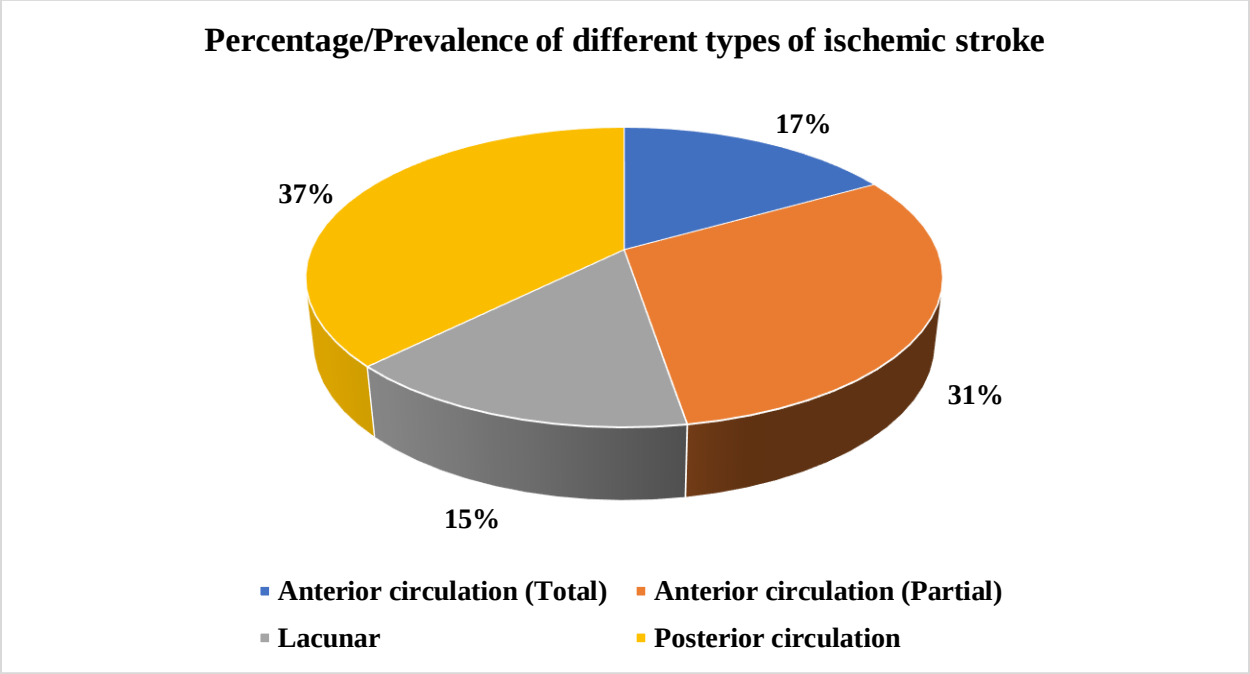

Figure 1. Percentage/Prevalence of different types of ischemic stroke

The results have shown that during the hospital stay, most of the patients recovered with prompt diagnosis and effective management. At the time of discharge, 116 patients, 61% were having GCS 15/15 with mild to moderate impairment in tone and muscle power. The mRS evaluation of 154, 81% patients suggested good prognosis. The rest of the 19% of the patients, n=36 required stroke rehabilitation and prolonged management plan for uncertain period for stroke recovery. Table 5.

At the time of Discharge					
GCS	**Total (n=190)**	**Male (n=107)**	**Female (n=83)**	**p-value**	**95% Confidence Interval (CI)**
15	116	71	45	0.001	0.02-3.1
9 to 14	72	35	37	0.038	0.47-2.5
≤8	2	1	1	0.49	0.67-1.4
Prognosis (mRS)					
Good (0-2)	154	102	52	<0.01	0.1-1.7
Poor (3-6)	36	5	31	0.021	0.04-2.2

Table 5. Clinical assessment of stroke patients at the time of discharge.

There were several predictors or risk factors contributing to the mechanism of stroke. The most common risk factors were modifiable/preventable including Atherosclerosis n=173, 91%, Dyslipidemia n=162, 85.2%, Hypertension n=147, 77.3%, and smoking n=132, 69.4% (in descending order). There was a noticeable difference in the prevalence of these above-mentioned risk factors in males and females with p value of <0.05 for each.

Predictors	Total	Male	Female	p-value
History of CVD	63	39	24	0.01
Smoking	132	115	17	0.02
Hypertension	147	68	79	<0.001
Diabetes	102	67	35	<0.001
Dyslipidemia	162	94	68	<0.001
Atherosclerosis	173	101	72	0.0003
Alcohol consumption	34	26	8	0.06
Atrial fibrillation	57	36	21	<0.001
Heart Failure	38	25	13	0.09
HIV/AIDS	14	12	2	0.12
Chronic Kidney Disease	36	29	7	0.38

Table 6. Risk factors associated with stroke in males and females (significant p-value= <0.05)

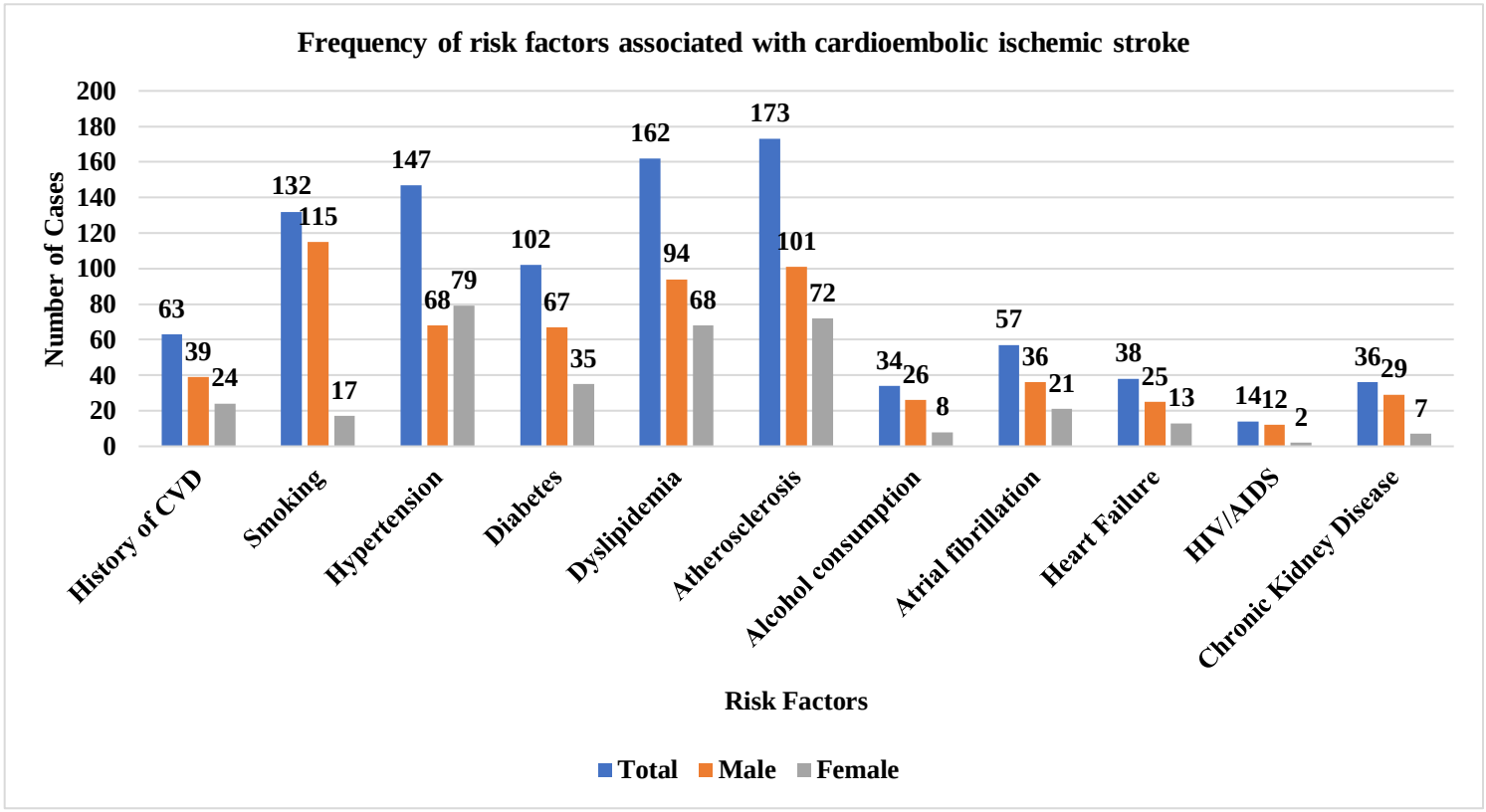

Figure 2. Risk factors associated with stroke in males and females

There are 9 different cardiac anomalies associated with the high risk of ischemic stroke onset (Table 7). On the basis of clinical history and previous medical record, the previous cardiac evaluation was recorded and was matched with the current findings. Most of the cardiac anomalies were occult and incidentally found after the occurrence of stroke, confirmed at echocardiography. In descending order, the diagnosed cardiac anomalies were dilated cardiomyopathy n=83, 43.6%; recent myocardial infarct n=30, 15.7%; regional ventricular akinesis n=22, 11.5%; rhematic heart disease n=15, 7.89%; infective endocarditis n=12, 6.31; ventricular/atrial thrombosis n=10, 5.2%; mechanical prosthetic valve n=7, 3.68%; and atrial myxoma n=5, 2.63%.

Cardiac Anomalies	Frequency n (%)		Total (n=190)
	Diagnosed before stroke onset (n=115)	Diagnosed after stroke onset (n=75)	
Recent Myocardial Infarction (<4W)	12	18	30
Infective endocarditis	7	5	12
Dilated cardiomyopathy	46	37	83
Atrial Myxoma	4	1	5
Rhematic Heart Disease	12	3	15
Regional Ventricular akinesis	16	6	22
Ventricular or Atrial Thrombus	6	4	10
Mitral valves prolapse	5	1	6
Mechanical prosthetic valve	7	0	7

Table 7. Spectrum of cardiac anomalies in stroke patients, diagnosed before and after the stroke onset.

DISCUSSION:

The pathophysiology of ischemic stroke is a complex interplay of multiple factors. Cardiac complications can lead to ischemic stroke and vice versa. In either case, cardiac evaluation of stroke patients is crucial at the time of onset and presentation of stroke. This study underscores the frequency of different cardiac dysfunctions in cardioembolic stroke patients to better understand the relationship between stroke and various risk factors to ensure better stroke management and improved prognosis. [17] According to the results, cardiogenic ischemic stroke was more common among males especially in the adults and elderly. The exact mechanism is unknown. [18] However, the proposed mechanisms include sedentary lifestyle, poor blood pressure and RBS control in hypertensive and diabetic patients and delayed cardiac screening. Most common symptoms at the time of admission were headache of acute onset, dizziness, altered sensorium, blackouts, slurred speech, and sudden motor weakness. [18,19] All the patients were first screened for neurological dysfunction by CT/MRI brain without IV contrast on urgent basis, as per local guidelines. At CT/MRI brain the ischemic patch of brain takes time to fully appear but it is significant enough to make the diagnosis of stroke. Additionally, patients were screened for ongoing cardiac dysfunction. Out of 190 patients, 115 patients were already diagnosed with cardiac issues while in 75 patients, cardiac anomaly was an incidental finding. Our study has also concluded that all the 190 selected study subjects had pre-existing, underlying cardiac complications which later manifested into thromboembolism leading to ischemic stroke. About three-fifths (60%) of the patients were previously diagnosed with cardiac issue while two-fifths (40%) had the cardiac evaluation done for the first time at the time of stroke presentation. It suggests that early diagnosis

and management of cardiac dysfunction can significantly reduce the risk of ischemic stroke. The pathophysiology of cardiogenic ischemic stroke is multifactorial. Nine modifiable factors were recorded in this study with hypertension, diabetes, dyslipidemia, smoking, and atherosclerosis being on the top of the list. In 71 (37%) stroke patients, posterior circulation was compromised which was mainly associated with hypertension and atherosclerosis. All the above-mentioned factors are the preventable causes of cardiac dysfunction and ischemic stroke. Nutritional and medical guidance can considerably reduce the risk of resultant ischemic stroke. [19] Dilated cardiomyopathy was found to be the most common cardiac pathology in stroke patients. Patients with poorly controlled hypertension, diabetes, and hyperlipidemia develop increased peripheral vascular resistance and endothelial damage. The increased peripheral resistance causes the heart to pump blood against high pressures resulting in ventricular hypertrophy followed by dilatation. Routine medical checkups can detect the pathology in early stages before it becomes symptomatic. [20] Once the stroke has occurred, the period between the onset of symptoms and commencement of medical treatment is very crucial. The patients who were presented to the medical emergency within 6 hours showed better prognosis with significant p value. Most of our study subjects were admitted to the hospital and their treatment was started before 6 hours that is the reason why the prognosis for the majority of the subjects was good. [21,22] Most of these studies have been retrospective or cross-sectional in design, limiting their ability to establish causality or make predictions about future events. A prospective observational study design can overcome some of these limitations by identifying risk factors before the onset of the disease and following up with participants over time. This study covers all the possible cardiac complications associated with ischemic stroke including more common/well-studied (atrial fibrillation, valvular heart diseases, and metabolic syndromes) and less common/less studied (infective endocarditis, cardiac myxoma, and dilated cardiomyopathy). With the advancement in acute medical treatment of stroke, mortality has been significantly decreased, however, the incidence of stroke is continuously increasing. Limited research on the spectrum of cardiac etiologies and associated risk factors in patients with cardioembolic stroke. demands extensive knowledge and emphasis on the prevention and effective management of associated risk factors.

Limitations:

This study has several limitations. Firstly, the small sample size and convenience sampling method increases the possibility of selection bias. Secondly, the study was conducted at a single tertiary care center that mostly catered for referrals from primary and secondary healthcare centers. So, the results do not necessarily resonate with the generalized outcomes of cardioembolic stroke patients. Lastly, most of the patients (>90%) of the study subjects belonged to district Punjab. So, an extensive, multicenter, and more diverse study is required to validate the outcomes of this study.

CONCLUSION:

In conclusion, this study provides valuable insights into the spectrum of cardiac etiologies and associated risk factors in patients with cardioembolic ischemic stroke. Limited research has been done to explore the etiological spectrum and risk factors associated with cardioembolic stroke. The findings of this study can inform targeted prevention and treatment strategies for this condition, emphasizing the importance of prevention, early identification, and treatment of risk factors to prevent cardioembolic stroke. Our study results are in accord with the latest studies suggesting that cardiogenic embolism is responsible for most of the ischemic stroke necessitating cardiac screening of all the diagnosed or undiagnosed patients of cardiac anomaly. The findings underscore the importance of a comprehensive cardiac evaluation and early identification and management of risk factors to prevent cardioembolic stroke. However, further research is needed to validate these findings in larger and more diverse populations and to explore potential interventions for less common cardiac etiologies of cardioembolic stroke.

Conflict of Interest: None

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