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Prevalence of atrial fibrillation in acute ischemic stroke patients: A hospital-based study from India

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Abstract:

BACKGROUND: Secondary stroke prevention is as important as the treatment of acute ischemic stroke in regards to halt neurological disability and to lower down mortality due to recurrent episodes. The effective secondary prevention depends on finding the specific risk factors leading to cerebrovascular insult.

AIMS AND OBJECTIVES: We aimed this study to find prevalence of persistent/Paroxysmal AF in stroke patients from single center hospital based study.

METHODS: Hospital based study enrolled all prospective patients of acute ischemic stroke from January 2016 to December 2018. All patients were subjected to test for risk factors analysis after detail clinical history and examination of these patients. Following variables were recorded; age, gender, stroke territory, stroke severity by NIHSS (National Institute of Health Stroke Scale), LDL-C (Low Density Lipoprotein - cholesterol) of more than 100 mg/dl, HBA1C (Glycosylated Hemoglobin) of more than 6.5, Homocystine of more than 15 Mc Mol/L, 2D-Echocardiographic abnormalities, electrocardiography/24 hour Holter Monitoring, cerebral angiography of brain and neck findings and outcome of patients in 90 days follow-up based on Modified Rankin Scale.

Results: Total 246 patients (69.5% men and 30.5% women) of Acute Ischemic stroke were recorded during study period. Mean age was 61.4 years, with 31 (12.4%) patients were below 45 years. Atrial fibrillation (AF) was detected either on conventional ECG or 24 hour Holter monitoring in 62 (25.2%) patients.

CONCLUSION: Stroke with AF is found in 25% patients, more common in elderly, female large atrial size and associated with poor outcome.

Keywords:

Cardioembolic stroke, ischemic stroke, secondary prevention

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Introduction

Stroke is a global health problem with a leading cause of death and disability together, and more than 80% of all stroke-related deaths are reported from low- and middle-income countries.[1] About 20% of survivors have to continue institutional care even after 3 months.[2] Other than severe motor disability in one-third, stroke is also accountable for epilepsy, depression, and dementia in another one-third.[3] Stroke thrombolysis, effective secondary prevention, and stroke rehabilitation based on guidelines are an effective way to prevent death and disability.

Secondary stroke prevention is as important as the treatment of acute ischemic stroke in regard to halt neurological disability and to lower down mortality due to recurrent episodes. The effective secondary prevention depends on finding the specific risk factors leading to cerebrovascular insult.

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For underlying etiology, one Indian hospital-based study from South India has attributed 41% stroke to large artery atherosclerosis, 18% lacunar stroke, 10% to cardioembolic causes, and 4% other rare causes. In about 27% of patients, no cause could be found (cryptogenic) attributing to stroke.[4] Among cardioembolic stroke, rheumatic and ischemic heart diseases were the predominant causes.

The Indian Collaborative Acute Stroke Study was conducted on 2,162 patients from southern, northern, and western Indian cities. Ischemic stroke was found in 77% and hemorrhagic in 22% of patients. Pooled data of all studies revealed that 68%–80% of Indian patients suffer from ischemic stroke and 41% had large vessel stroke, 18% lacunar, 10% cardioembolic, 10% other determined causes, and 20% undetermined causes.[5]

Atrial fibrillation (AF) was studied in few Indian studies as a risk factor of stroke. One study from southern India by Sylaja *et al*. in 2018 reported that in their study, 4% of patients had nonvalvular AF and 5.6% had rheumatic heart disease (RHD) (not mentioned about AF).[6] Another study from Ludhiana in 2017 had specifically looked at the profile of stroke patients with AF in a population-based study.[7] They reported that burden of AF in stroke patients is reported only in few studies in India and maximum up to 8% from Trivandrum, Kerala. The study from Ludhiana evaluated 1,942 patients of stroke and found AF in 203 (10%) patients (3% – RHD and rest – nonvalvular).[7]

We could not find any hospital-based study, which have done 24-h Holter monitoring in all consecutive patients of stroke to find the prevalence of persistent or paroxysmal AF (PAF) in stroke patients. Therefore, we aimed this study to find the prevalence of persistent/PAF in stroke patients from a single-center hospital-based study.

Methods

This is a prospective observational case–control analytic study. In this hospital-based study, we enrolled all prospective patients of acute ischemic stroke (new onset or recurrent) from January 2016 to December 2018. As a part of routine care, all patients were subjected to test for risk factor analysis after detail clinical history and examination of these patients. Following variables were recorded on datasheet; age, gender, stroke territory, stroke severity by NIHSS (National Institute of Health Stroke Scale), LDL-C (Low Density Lipoprotein - cholesterol) of more than 100 mg/dl, HBA1C (Glycosylated Hemoglobin) of more than 6.5, Homocystine of more than 15 Mc Mol/L, 2D-Echocardiographic abnormalities, Electrocardiography/24 hour Holter Monitoring, Cerebral angiography of brain and neck findings and outcome of patients in 90 days follow-up based on Modified Rankin Scale (MRS).

Statistical analysis was done for frequency analysis and Chi-square test for significance of association among categorical variables.

Table 1: General demography and descriptive analysis of all patients

Factor	Finding	Number of patients (%)
Age group (years)	<45	31 (12.6)
	>45	215 (87.4)
Gender	Male	171 (69.5)
	Female	75 (30.5)
Stroke territory	Anterior circulation	147 (59.8)
	Posterior circulation	59 (24)
	Multifocal territories	40 (16.2)
NIHSS at admission	<5	51 (20.7)
	Between 6-15	110 (44.7)
	>15	85 (34.6)
LDL-C levels	Normal <100 mg/dl	143 (58.1)
	Mild high (100-129)	64 (26)
	Moderate high (130-159)	32 (13)
	Severe high (>160)	7 (2.9)
HbA1c of >6.5	Yes	81 (32.9)
	No	165 (67.1)
Homocysteine level (mcmol/L)	Normal (<15)	207 (84.1)
	Mild high (15-30)	20 (8.1)
	Moderate high (30-100)	18 (7.3)
	Severe high (>100)	1 (0.5)
Echocardiography findings	Ejection fraction (%)	
	Normal (>50)	210 (85.4)
	31-50	19 (7.7)
	<30	17 (6.9)
	Valvular heart disease	
	Yes	16 (6.5)
	No	230 (93.5)
	Dilated left or right atria	
	Yes	39 (15.9)
	No	207 (84.1)
CT/MRI angiography of brain and neck	Not done	41 (16.7)
	Normal	132 (53.7)
	Extracranial vascular Stenosis of >50%	48 (19.5)
	Intracranial vascular stenosis of >50%	25 (10.1)
Atrial fibrillation on 24-h Holter recording	Yes	62 (25.2)
	No	184 (74.8)
Outcome of MRS	Good (<2 MRS)	92 (37.4)
	Fair (3-4 MRS)	147 (59.8)
	Poor (5-6 MRS) (2 death)	7 (2.8)

MRS: Modified Rankin Score, MRI: Magnetic resonance imaging, CT: Computerized tomography, HbA1c: Glycosylated hemoglobin, LDL-C: Low-density lipoprotein-cholesterol

Results

General demography and descriptive analysis

A total of 246 patients (69.5% men and 30.5% women) of acute ischemic stroke were recorded during the study period. The mean age was 61.4 years, with 31 (12.4%) patients being below 45 years. Totally 147 (59.8%) patients suffered from anterior circulation stroke and 40 (16.2%) patients had multiple territory stroke. According to the stroke severity scale (NIHSS), 34.6% patients had a severe form of stroke and one-fifth had a milder form of stroke [Table 1].

When risk factor assessment done, 81 (32.9%) had abnormal HbA1c, nearly 42% had a high level of bad cholesterol (LDL) values of >100 mg/dl, and nearly 15% of patients had high homocysteine level.

2D echocardiography was done in all the patients and was normal in 172 (70%) patients. Less than 30% ejection fraction was found in 17 (6.9%), valvular heart disease in 16 (6.5%), and dilated atrium in 39 (15.9%) patients on 2D echo.

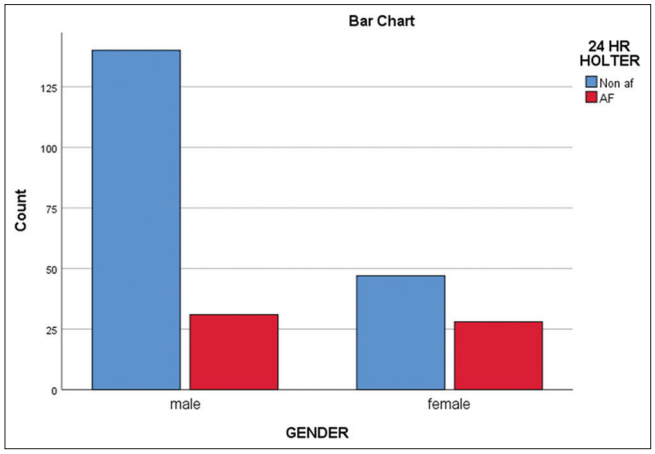

Figure 1: Gender versus atrial fibrillation

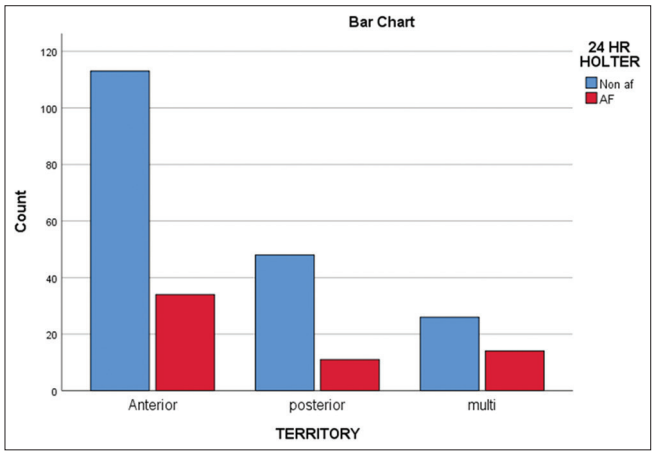

Figure 3: Vascular territory versus atrial fibrillation

Cerebral and neck angiography with either CT or MRI was done in 205 (83.3%) patients, and more than 50% stenosis in extracranial or intracranial vessels was found in 29.6% of patients.

AF was detected either on conventional ECG or 24-h Holter monitoring in 62 (25.2%) patients. Among the 62 patients

Table 2: Cross tabulation: Gender versus atrial fibrillation on 24-h Holter monitoring

Variable	Distribution	Non-AF	AF	Total	*P*	OR (95% CI)
Gender	Male	137	34	171	0.0032	2.54
	Female	46	29	75	(Significant)	(1.39-4.61)
Total		183	63	246		

OR: Odds ratio, CI: Confidence interval, AF: Atrial fibrillation

Table 3: Cross tabulation: Age versus atrial fibrillation on 24 h Holter monitoring

Variable	Distribution	Non-AF	AF	Total	*P*	OR (95% CI)
Age	60 year or more	97	50	147	0.0002	3.4
					(significant)	(1.7-6.7)
	<60 year	86	13	99		
Total		183	63	246		

OR: Odds ratio, CI: Confidence interval, AF: Atrial fibrillation

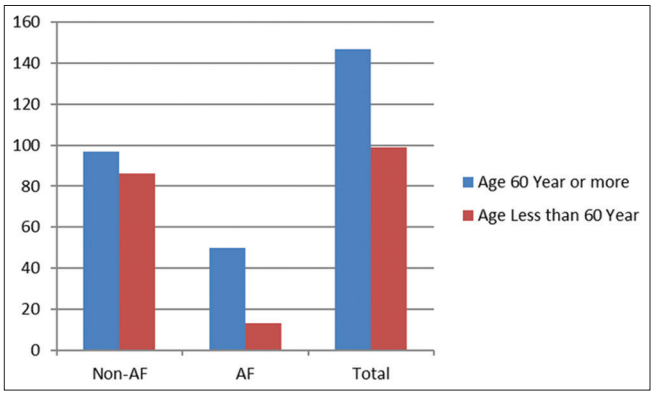

Figure 2: Age versus atrial fibrillation

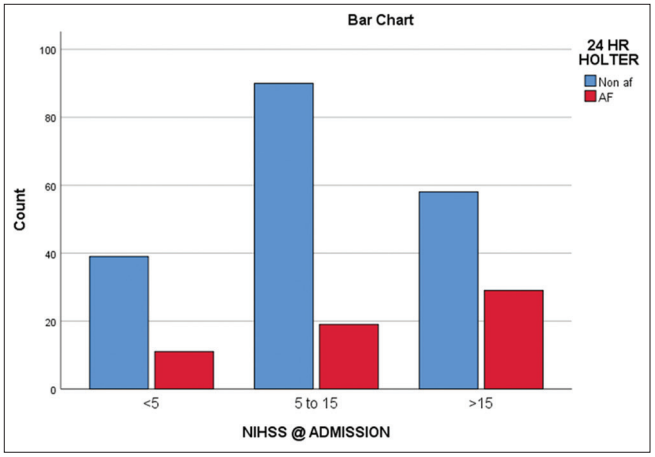

Figure 4: National institute of health stroke scale versus atrial fibrillation

Table 4: Cross tabulation: Vascular territory versus atrial fibrillation on 24-h Holter monitoring

Variable	Distribution	Non-AF	AF	Total	*P*	OR (95% CI)
Territory	Anterior	110	37	147	0.1 (not-significant)	0.94 (0.52-1.6)
	Posterior	48	11	59		
	Multiple	25	15	40		
Total		183	63	246		

OR: Odds ratio, CI: Confidence interval, AF: Atrial fibrillation

Table 5: Cross tabulation: National Institute of Health Stroke Scale versus atrial fibrilation on 24 hour holter

Variable	Distribution	Non-AF	AF	Total	*P*	OR (95% CI)
NIHSS	<5	40	11	51	0.01	2.3
	6-15	89	21	110	(significant)	(1.28-4.16)
	>15	54	31	85		
Total		183	63	246		

OR: Odds ratio, CI: Confidence interval, AF: Atrial fibrillation, NIHSS: National Institutes of Health Stroke Scale

with AF, 18 (29%) had a paroxysmal event. Total 40 (16.2%) patients had recurrent stroke on regular antiplatelates and 15 (37.5%) patients were found to have atrial fibrillation.

Among 246 patients, two patients died in hospital stay and 5 more died within a 3-month follow-up, and thus, stroke-related mortality within 3 months was 2.8%.

After 90-day follow-up, 90 (37.4%) patients had a favorable outcome with the Modified Rankin Scale of <2.

Cross tabulation for correlation analysis

Stroke variables were cross analyzed in patients with or without AF. Patients with stroke with atrial fibrillation were significantly more common in female gander ($P = 0.0032$, OR and 95% CI = 2.54 (CI = 1.39–4.61), Table 2 and Figure 1), more in elderly ($P = 0.0002$, OR and 95% CI = 3.4 (1.7–6.7), Table 3 and Figure 2). Vascular territory was not significantly different in two groups ($P = 0.1$, OR and 95% CI = 0.94 (0.52–1.6), Table 4 and Figure 3). Patients with atrial fibrillation had more severe stroke as compared to Non-AF group (OR 2.3 (95% CI = 1.28-4.16) and risk ratio (RR) was 1.8 (95% CI =1.2–2.78, $P = 0.0045$), Table 5 and Figure 4). Left ventricular ejection fraction ($P = 0.2$, OR and 95% CI = 0.55 (0.26–1.17), Table 6 and Figure 5) and valvular lesion ($P = 0.08$, OR and 95% CI = 0.41 (0.14–1.16), Table 7 and Figure 6) were not found significantly associated with atrial fibrillation. Prevalence of atrial fibrillation was significantly associated with larger atrial size ($P = 0.045$, OR and 95% CI = 2.07 (1–4.25), Table 8 and Figure 7). Patients with AF had worse outcome as compared to stroke without AF ($P = 0.036$, OR and 95% CI = 2.6 (1.3–5), Table 9 and Figure 8).

Discussion

Our key findings suggested that more than a quarter of ischemic stroke patients can have underlying AF

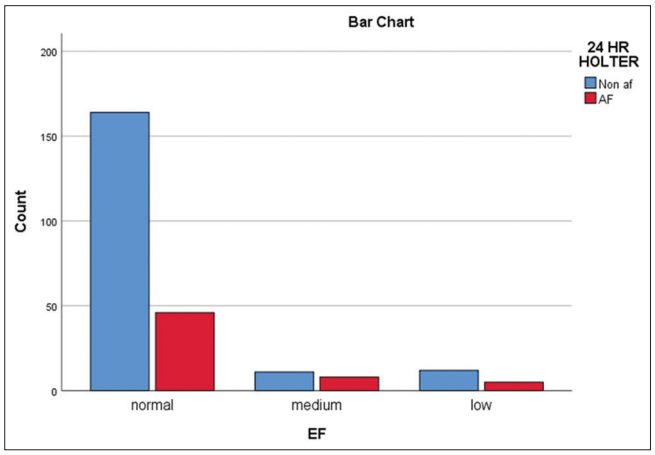

Figure 5: Left ventricular ejection fraction versus atrial fibrillation

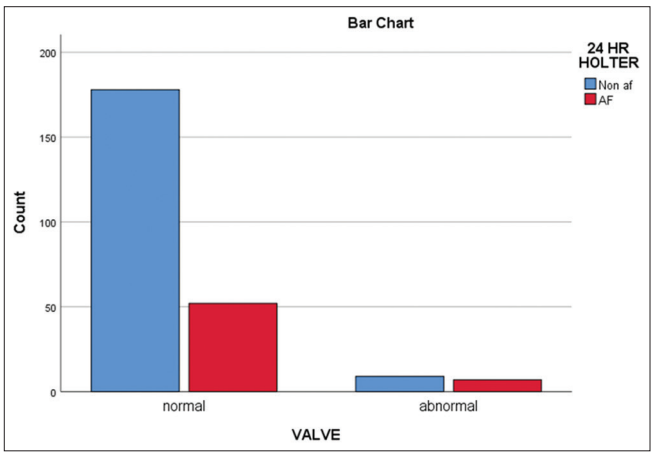

Figure 6: Cardiac valvular status versus atrial fibrillation

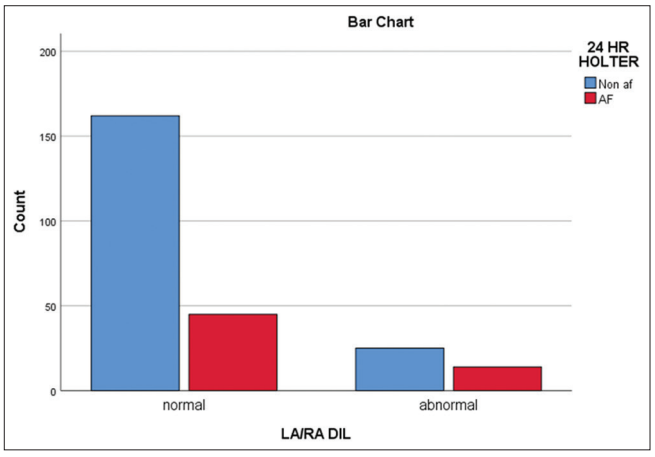

Figure 7: Size of atrial chamber versus atrial fibrillation

Table 6: Cross tabulation: Left ventricular ejection fraction versus atrial fibrillation on 24-h Holter monitoring

Variable	Distribution	Non-AF	AF	Total	*P*	OR (95% CI)
Ejection fraction on Echo	Normal	160	50	210	0.2 (not-significant)	0.55 (0.26-1.17)
	Medium	11	8	19		
	low	12	5	17		
Total		183	63	246		

OR: Odds ratio, CI: Confidence interval, AF: Atrial fibrillation

Table 7: Cross tabulation: Cardiac valvular status versus atrial fibrillation on 24-h Holter monitoring

Variable	Distribution	Non-AF	AF	Total	*P*	OR (95% CI)
Heart valve status	Normal	174	56	230	0.08 (not-significant)	0.41 (0.14-1.16)
	Abnormal	9	7	16		
Total		183	63	246		

OR: Odds ratio, CI: Confidence interval, AF: Atrial fibrillation

Table 8: Cross tabulation: Size of atrial chamber versus atrial fibrillation on 24-h Holter monitoring

Variable	Distribution	Non-AF	AF	Total	*P*	OR (95% CI)
Atrial dilatation	No dilatation	159	48	207	0.045 (significant	2.07 (1-4.25)
	Dilated	24	15	39		
Total		183	63	246		

OR: Odds ratio, CI: Confidence interval, AF: Atrial fibrillation

Table 9: Cross tabulation: Outcome versus atrial fibrillation on 24-h Holter monitoring

Variable	Distribution	Non-AF	AF	Total	*P*	OR (95% CI)
Outcome	Partial recovery	105	49	154	0.036 (significant)	2.6 (1.3-5)
	Full recovery	78	14	92		
Total		183	63	246		

OR: Odds ratio, CI: Confidence interval, AF: Atrial fibrillation

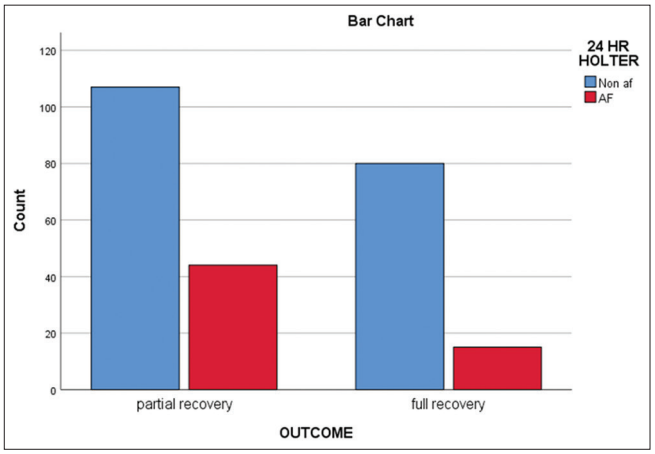

Figure 8: Outcome of patients versus atrial fibrillation

as a risk factor for stroke and will not be prevented adequately with antiplatelet medications. Correlation analysis showed that AF was significantly more common in females ($P = 0.003$, OR = 2.54) with ischemic stroke and was more common in the age group of >60 years ($P = 0.0002$, OR = 3.4). Left/right atrial dilatation of >40 mm was found to have a significant association of AF in stroke patients ($P = 0.045$, OR = 2.07). Patients with ischemic stroke with AF were significantly associated with more severe stroke on NIHSS ($P = 0.01$, OR = 2.3) and poor outcome ($P = 0.036$, OR = 2.6).

Stroke is associated with a case fatality rate of about 41% in the Indian population.[8] About 70.45% of death was primarily due to index stroke and 19.27% due to recurrent stroke. The Indo-US Collaborative Stroke Project showed that three-fourth of strokes are of mild-to-moderate severity on NIHSS.[6] The best practices in stroke suggest that thrombolysis (medical or endovascular), supportive medical therapy, effective rehabilitation, and effective secondary prevention can minimize death and disability. The secondary prevention of stroke is very important to prevent recurrent stroke that causes progressive disability and death of high-risk patients. The best way of preventing recurrent stroke depends on specific risk factors for the first stroke. Antiplatelet medications are a mainstay of the primary and secondary prevention in atherosclerotic stroke and oral anticoagulation (older or newer) in stroke with AF or with cardioembolic background. It is important to find the best way of secondary prevention after the first event of transient ischemic attack/stroke. Patients, caregivers, and health-care providers become very much disappointed when a person develops recurrence of stroke on regular preventive medications.

In one study on 2,584 patients of stroke on dual antiplatelet drugs, 212 (8.2%) had a recurrent stroke.[9] Another study by Hier *et al*. showed a 14.1% risk of recurrence in 2 years poststroke.[10] Study published in JAMA Neurology (2018), 25,268 adults monitored with an extended continuous ambulatory electrocardiographic monitoring for 14 days and 1,965 persons had paroxysmal AF, with median burden of 4.4% and longest duration of AF was 171 minutes.[11] Totally 1,965 had PAF, with a median burden of 4.4%, and the longest duration of AF was 171 min.[11] Finally, the authors concluded that a greater burden of AF is associated with a higher risk of recurrent

ischemic stroke. Our study showed that the higher rate of AF might be due to selection bias at a tertiary hospital of ischemic stroke with a higher proportion of patients aged >60 years (about 60%). AF is one of the most common risk factors of stroke among the elderly, as with advancing age, the prevalence of AF increases to 8% above 80 years.[12] In our cohort, 42 (67.7%) of 62 patients with AF were above the age of 65 years.

According to one estimate, 25%–60% of patients have PAF, therefore, difficult to diagnose on baseline electrocardiogram or on clinical examination.[13] Our study showed that 18/62 (29%) had PAF that can be missed without Holter monitoring.

The American Heart Association guidelines suggested that cardiac monitoring should be conducted routinely after an acute cerebrovascular event to screen for serious cardiac arrhythmias."[13] If we miss the underling AF in the index case of stroke, then one can face a recurrence of stroke even on regular antiplatelet drugs. Our study has shown that one-fourth of patients who had AF can be wrongly put on antiplatelet in the absence of Holter monitoring.

The appropriate duration of cardiac monitoring is not well defined in the guidelines. We have done 24-h Holter monitoring that can miss few cases and underestimate the prevalence of AF in stroke. One nonsystemic review suggested that 72-h continuous recording is a better option, especially in patients of cryptogenic stroke.[12] About 30% of patients of stroke remain as cryptogenic after extensive investigations and according to current recommendation suggest the usage of antiplatelet drugs in such a situation. Although, this policy can lead to higher risk of recurrence in patients having PAF and not put on anticoagulation.

One important observation in our study was that the larger size of the atrium (>40 mm) can be an effective biomarker of associated AF. Therefore, patients with large-sized atria should have prolonged cardiac monitoring. We do not know that atrial enlargement is a cause or consequence of AF as on longitudinal study showed that atrial enlargement can occur as a consequence of AF.[14]

The study from Ludhiana (Punjab) showed that 10% of patients of stroke had AF and these patients had higher age group and poor outcome.[7] Our data also suggested that stroke patients with AF had a significantly high NIHSS score and poor outcome.

Therefore, we conclude that all patients with stroke should be investigated with cardiac monitoring for at least 24 h to find AF. Patients with undetermined cause and elderly age group (>60 years) with stroke or TIA should be subjected to longer duration of cardiac monitoring (up to 72 h), to select appropriate drugs for the secondary prevention. A large-sized atrium can be good biomarker for AF in stroke patients. Lastly, patients with AF were associated with severe stroke and poor outcome on the Modified Rankin Scale. Finally, the novel finding in the study suggested that elderly age, female sex, and large atrial size on echocardiogram should be intensively investigated for AF in stroke patients.

The limitation of our study is that it is a single-center study with large elderly population; therefore, we need a multicenter study with more heterogeneous population to confirm the findings.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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