

## ORIGINAL ARTICLE

## DETECTION OF ATRIAL HIGH-RATE EPISODES IN PATIENTS WITH CARDIAC IMPLANTABLE ELECTRONIC DEVICES - A MULTICENTER EXPERIENCE FROM PAKISTAN: A CROSS- SECTIONAL STUDY

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**Objectives:** Atrial high-rate episodes (AHRE) are associated with an increased risk of subclinical atrial fibrillation (SCAF) and can be identified in patients with cardiac implantable electronic devices (CIEDs). This first study from Pakistan aims to determine the incidence of AHREs and the characteristics of a Pakistani cohort with AHREs.

**Methodology:** In this bicentric Cross-sectional study, there were 162 patients of more than 18 years with CIEDs presenting to the device clinics were enrolled. The AHREs cutoff was predefined and AHREs were documented if they last for >30 seconds. Patients with known atrial fibrillation were excluded.

**Results:** Mean age of the patients was 64.69±11.64 years and men were of 62.3%. AHREs were found in 22 (13.6%) patients out of which 13(8%) lasted more than 5 minutes. Mean AHREs cutoff 182.27±20.93. Mean CHA<sub>2</sub>DS<sub>2</sub>-VASc score; 3.10±1.47. 54.9% on beta-blockers, and 37% on angiotensin receptor blockers (ARB). Dual-chamber pacemaker (75.3%) and AV block (60.5%) mostly complete AV block, were the most common CIED and indication for an implant respectively. 43.8% had mildly dilated LA, only 1.2 % had severe mitral stenosis, and 3.1% had severe mitral regurgitation. Multivariable binary logistic regression analysis showed that patients on ARB had fewer episodes of AHREs (OR=0.2, 95% CI= 0.05 -0.8, P-value =0.023) while positive family history for coronary artery disease (CAD) was associated with more episodes (OR=5.62, 95% CI=1.58 -20, P-value =0.008).

**Conclusion:** The incidence of AHREs was considerably lower in our population on CIEDs interrogation as compared to prior studies, although the CHA<sub>2</sub>DS<sub>2</sub>-VASc score is higher. ARB use and positive family history of CAD had a statistically significant association with AHRE occurrence.

**Keywords:** Atrial high-rate episodes, atrial fibrillation, cardiac implantable electronic devices, Angiotensin receptor blockers

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### INTRODUCTION

The commonest heart rhythm disorder faced by clinicians in practice is atrial fibrillation (AF) with global prevalence of 37,574 million cases (estimating around 0.51% of global population), which have increased by 33% in the last two decades.<sup>1</sup> Broadly defined by the American Heart Association as a 'quivering or irregular heartbeat', AF can precipitate severe morbidity and mortality in the form of stroke, heart failure, and other life-threatening complications.<sup>2-3</sup>

Previous studies show that the risk of AF with dual-chamber devices is still significant, although less than that for single-chamber ventricular devices.<sup>4,5</sup> Prior literatures also reports a higher risk of AF with certain comorbid conditions namely hypertension, diabetes mellitus, and hyperlipidemia.<sup>6,7</sup> However, the primary limitation of these earlier studies has been the preexistence of AF in the study population, and we know that prior AF is a dominant harbinger of more AF.<sup>8</sup> It is evident from prior studies that the occurrence of AF may result in cerebrovascular accident (CVA). The incidence of CVA has been reported in 4.5% of untreated patients with AF per year.<sup>9</sup> Moreover, a

recent study established that among patients with an acute ischemic stroke, 17.2% had AF.<sup>10</sup> Largely, 30-day mortality was more in patients with AF. Thus, early identification of AF and treatment of the above comorbid conditions is necessary to prevent stroke and other forms of cardio-embolism.

Long atrial high-rate episodes (AHRE) are linked to an increased risk of clinical AF.<sup>11</sup> AHREs are episodes of atrial tachycardia with atrial rates above 170 -180 beats/minute detected by cardiac implantable electronic devices (CIEDs).<sup>12</sup> In previous studies, the AHRE term has been used interchangeably with silent or subclinical atrial fibrillation (SCAF). Cases of SCAF have been reported in up to 50% of some patient populations.<sup>13-15</sup> Identification of patients with AHREs has been easier, especially in patients with CIEDs. Modern-day dual-chamber devices and biventricular cardiac resynchronization devices are equipped to record and store circumstantial data about AHREs which includes the frequency, duration, and rates of these episodes.

The detection of AHREs through device interrogation provides an easy and cost-effective way to delineate the burden of AHREs. In this study, we aimed to detect the occurrence of AHREs on device interrogations in post-device-implant patients and to examine the association of various factors including comorbid conditions, medications, transthoracic echocardiographic parameters, and CIEDs parameters with the occurrence of AHRE in our population.

## METHODOLOGY

A cross-sectional study was conducted in two cardiac tertiary care centers in Pakistan over 15 months from 6th September 2019 to 25th November 2020, giving a screenshot of AHRE prevalence.

All patients of more than 18 years attending device clinics for CIED follow-up, with dual-chamber Permanent Pacemakers (PPM), dual-chamber Implantable Cardioverter defibrillators (ICD), Cardiac resynchronization therapy pacemakers (CRT-P), and cardiac resynchronization therapy defibrillator (CRT-D) were included in the study. Patients with prior AF and those with devices that do not store information regarding AHRE were excluded from the study.

The sample size was calculated based on the prior reported frequency of AHRE on device interrogation taken as 29%.<sup>16</sup> A total of 162 consecutive patients who met eligibility criteria were enrolled with a 7% (0.07) bound on the error at a 95% level of confidence.

Data was collected including age, gender, comorbidities, medications used, type of device, and indications for CIEDs implant. The data regarding device parameters was collected as a part of scheduled device interrogation during the device clinic visit and analyzed by electrophysiologist before making necessary entries.

The atrial high rate episodes cutoff was defined as per high rate cut-off programmed for that specific patient and AHRE episodes were documented if they lasted for 30 seconds or more and were further segregated depending upon the duration of the episode (i.e. > 30 seconds, 30 seconds to 1 minute, 1-5 minutes and > 5 minutes) and period at which episode occurred from the date of the current visit to device clinic (i.e. 1 month, 1-6 months & 6-12 months). For the respective subjects, the most recent available echocardiography reports before the device implant were also reviewed and relevant data was collected. Left atrial (LA) dimensions were measured on 2D echocardiography and categorized as per American society of echocardiography guidelines. Left ventricular ejection fraction (LVEF) was estimated by visual estimation and Simpson's biplane method. Patients were informed that the aforementioned data collected will be used anonymously for research purposes and will later be published. As it was a multicenter study and both the institutes had autonomous ethical review committees (ERCs), so ERC approvals of both the committees obtained from (ERC # 2021-1922-16993& ERC# 54-2020).

Descriptive statistics were reported as mean +/- standard deviation for continuous variables while frequency and percentages were reported for categorical variables. The outcome variable i.e. occurrence of AHREs was cross tabulated with age, gender, comorbid, medications, LA diameter, LVEF, and implant duration. The Chi-square test was used for comparing categorical data while the independent samples T-test was used to compare nominal data. Univariable logistic regression was used to determine the association of clinically relevant variables with the occurrence of AHRE and variables with a p-value of less than or equal to 0.20 were taken as candidate explanatory variables for the multivariable binary logistic regression analysis, which was performed with the help of backward selection method to obtain adjusted association of significant variables with the occurrence of AHRE, OR and 95% CI were reported and statistical significance criteria were p-value less than or equal of 0.05. For statistical analysis, SPSS version 20 (IBM corporation, USA) was used.

**RESULTS**

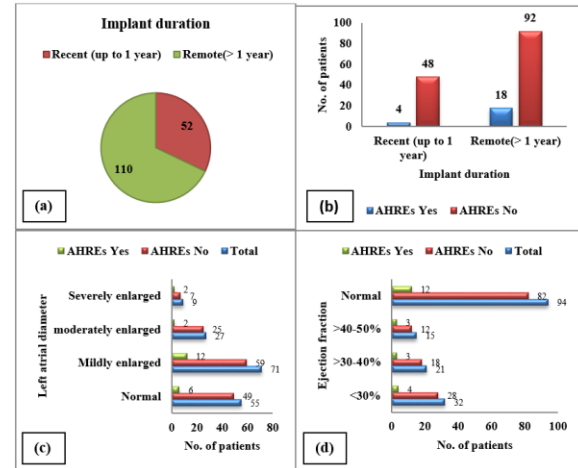
A total of 162 patients were enrolled and out of these 62.3% were men. The mean age was  $64.69 \pm 11.637$  years. 67.3% of the study population was older than 60 years (Table 1 and 2). Mean age of participants with AHRE was less as compared to those without AHRE. Initially on univariate analysis the p-value for age was significant but later on multivariate analysis it was found to have no significant correlation (Table 2 and 3). The mean  $\pm$  standard deviation for CHA<sub>2</sub>DS<sub>2</sub>-VASc score was  $3.10 \pm 1.475$ , score was further reported separately for patients with and without AHRE. Overall, there were no significant differences in lower rate, upper rate, cumulative atrial and ventricular pacing, and AHRE cut-off values between patients with AHRE as compared to patients with no AHRE but mean sensed and paced AV delays were slightly lower in patients with AHREs as compared to patients with no AHRE. Details of descriptive characteristics and device parameters as detailed in Table 1.

In our study population AHRE events occurred in 13.6% (22) participants out of which 8% (13) lasted more than 5 minutes, 3.1% (5) lasted 1-5 min, and 2.5% (4) participants had AHRE events lasting 30 sec to 1 min. Most AHREs occurred between 1-6 months from the last interrogation i.e. 8.6% (14) followed by an interval of 6-12 months and 1 month i.e. 1.9% (3) each, while only 1.2% (2) participants had AHRE episodes occurring at an interval of more than 12 months from the last interrogation.

The most common comorbidities found in the population were hypertension, diabetes mellitus and hyperlipidemia (numbers and percentages are quoted in table 2). Correlation of various comorbid conditions with AHRE events was done and amongst all the comorbid conditions studied concomitant prior hypertension and diabetes were found to have a significant negative association with the occurrence of AHRE events while a positive family history of coronary artery disease was found to have a significant positive association. Here it is noteworthy that negative association of hypertension and diabetes with the occurrence of AHRE was surprisingly seen on univariate analysis thus to further investigate the reliability of this association in our study population multivariable binary logistic regression analysis was performed on which negative association was not verified. The correlation of age groups and gender of study participants with the occurrence of AHRE was

carried out and the results for same are detailed in Table 2.

Majority of the study population had remote implants i.e. CIEDs implanted more than 1 year ago and post-implant duration had no significant correlation with the occurrence of AHRE as shown in Table 2 and figure 1.



**Figure 1: Distribution (a) of recent and remote implants and Correlation of AHRE with (b) implant duration (c) Left atrial dimensions and (d) Left Ventricular Ejection Fraction**

In terms of medications used, more than half of study population was on beta-blockers and statins. Other commonly used medications were angiotensin-converting enzyme (ACE) inhibitors, Angiotensin receptor blockers (ARB), and furosemide. The details of correlation of medications used with occurrence of AHRE events are shown above in Table 2. Amongst all the medications commonly used in cardiac patients in our population, only use of ARB was found to have a significant association with a lesser occurrence of AHRE events.

In our study population, Dual-chamber pacemakers were the most common device 75.3% (122), followed by CRTD 11.1 % (18), while CRTP and dual-chamber ICDs were 6.8% (11) each. The commonest indication for implant was AV Block 60.5 % (98) out of which majority of study participants had complete AV block while others were implanted for 2:1 AV block. AV block was followed by left ventricular systolic dysfunction 25.3% (41), sinus node dysfunction 16% (26), chronic bifascicular and trifascicular block 4.3% (7). Out of the studied population, 58% (n=94) participants were pacemaker dependent and 35.8% (n=58) had the rate response feature turned on.

The most recent transthoracic echocardiogram report before the device implant for each participant was analyzed and shown in Table 2 and Figure 1. LA dimensions were measured on 2D echocardiography and categorized as per contemporary American society of echocardiography guidelines. Left ventricular ejection fraction was estimated by visual estimation and Simpson’s biplane method. The LA dimension was normal to mildly enlarged in the majority while severe LA enlargement was seen only in few study participants. The LVEF was also found to be normal in majority of participants; detailed description regarding LA dimensions and LVEF is given in Table 2. Most of the study population had no severe valvular abnormality as severe MR and MS was seen in only 3.1% (5) and 1.2% (2) of participants. In terms of left ventricular diastolic dysfunction 44.4% (72), 6.2% (10), 24.1% (39), and 1.2% (2) had Grade I, Grade IA, Grade II, and Grade III dysfunction respectively. In 7.4% (12) participants, normal diastolic function was seen while it was not assessed in 16.7% (27).

Multivariable binary logistic regression analysis was performed and odds ratio (OR) / confidence interval (CI) were reported. Use of ARBs had a significant association with a lesser probability of occurrence of AHRE (OR= 0.2, 95 % CI= 0.05 -0.8, P=0.023) while positive family history of coronary artery disease had a significant association with a greater probability of occurrence of AHRE events (OR= 5.62, 95 % CI= 1.58 -20, P=0.008). Other variables included in multivariable analysis namely age more than 60 years , hypertension , diabetes mellitus , use of digoxin were found to have no significant association with the occurrence of AHRE( Table 3). Two other variables i.e. use of aldosterone antagonist and remote implants (more than one year) included in the multivariable analysis had a non-significant association to be included in the final solution. The details of results of the multivariable binary logistic regression analysis have been tabulated in Table 3.

**Table 1: Descriptive Statistics and pacing parameters (n=162)**

Variables	Mean ± Standard Deviation			P-value
	Total	AHRE	No AHRE	
Age (Years)	64.69 ± 11.637	57.50±15.330	65.81±10.578	0.022
CHA <sub>2</sub> DS <sub>2</sub> -VASc score	3.10 ± 1.475	2.55 ± 1.335	3.19 ± 1.482	0.058
Atrial Sensing (millivolt) mv	2.808 ± 1.628	3.127 ± 1.877	2.758±1.586	0.324
Lower rate (beats per minutes) bpm	59.60 ± 4.056	59.55 ± 3.751	59.61± 4.115	0.947
Upper rate (beats per minutes) bpm	129.54±9.322	130.91±2.942	129.32±9.950	0.459
Sensed AV delay (milliseconds) ms	162.93±51.904	145.00±45.774	165.75±52.392	0.081
Paced AV delay (milliseconds) ms	195.90±55.669	175.45±47.079	199.11±56.375	0.064
Cumulative atrial pacing (percent) %	24.443±32.976	25.282±36.066	24.311±32.601	0.898
Cumulative ventricular pacing (percent) %	70.246±38.182	68.127±40.150	70.579±38.003	0.78
Atrial high rate cut off (beats per minutes) bpm	182.27±20.931	179.77±14.758	182.66±21.757	0.549

AHRE= Atrial high rate episode, AV delay = Atrioventricular delay

**Table 2: Comparison of AHRE with baseline variables (n=162)**

Characteristics	Total	AHREs		P-value
		Yes	No	
<b>Gender</b>				
Male	62.3% (101)	59.1% (13)	62.9% (88)	0.735
Female	37.7% (61)	40.9% (9)	37.1% (52)	
<b>Age (years)</b>	64.69 ± 11.64	57.5 ± 15.33	65.81 ± 10.58	0.022*
18 to 40 years	4.3% (7)	18.2% (4)	2.1% (3)	0.002*
41 to 60 years	28.4% (46)	31.8% (7)	27.9% (39)	
61 to 80 years	67.3% (109)	50% (11)	70% (98)	
<b>Co-morbid conditions</b>				
Hypertension	79.6% (129)	59.1% (13)	82.9% (116)	0.010*
Diabetes mellitus	43.8% (71)	22.7% (5)	47.1% (66)	0.032*
Hyperlipidemia	54.3% (88)	45.5% (10)	55.7% (78)	0.369
Previous Stroke	6.8% (11)	9.1% (2)	6.4% (9)	0.644
Heart Failure	17.9% (29)	27.3% (6)	16.4% (23)	0.217
Coronary artery disease (CAD)	40.1% (65)	36.4% (8)	40.7% (57)	0.699
Family history of CAD	11.7% (19)	27.3% (6)	9.3% (13)	0.015*
<b>Medications</b>				
Beta-blockers	54.9% (89)	50% (11)	55.7% (78)	0.617
Statin	60.5% (98)	50% (11)	62.1% (87)	0.279
Amiodarone	2.5% (4)	0% (0)	2.9% (4)	0.422

ACE inhibitor	26.5% (43)	36.4% (8)	25% (35)	0.262
ARB	37% (60)	13.6% (3)	40.7% (57)	0.014*
Digoxin	1.2% (2)	4.5% (1)	0.7% (1)	0.13
Aldosterone antagonist	15.4% (25)	27.3% (6)	13.6% (19)	0.098
Furosemide	29.6% (48)	36.4% (8)	28.6% (40)	0.457
<b>Implant duration</b>				
Recent (up to 1 year)	32.1% (52)	18.2% (4)	34.3% (48)	0.133
Remote(> 1 year)	67.9% (110)	81.8% (18)	65.7% (92)	
<b>Left atrial diameter</b>				
Normal	34% (55)	27.3% (6)	35% (49)	0.484
Mildly enlarged	43.8% (71)	54.5% (12)	42.1% (59)	
Moderately enlarged	16.7% (27)	9.1% (2)	17.9% (25)	
Severely enlarged	5.6% (9)	9.1% (2)	5% (7)	
<b>Left ventricular ejection fraction</b>				
<30%	19.8% (32)	18.2% (4)	20% (28)	0.892
>30-40%	13% (21)	13.6% (3)	12.9% (18)	
>40-50%	9.3% (15)	13.6% (3)	8.6% (12)	
Normal	58% (94)	54.5% (12)	58.6% (82)	

\* = Significant P values, CAD= Coronary artery disease, ARB = angiotensin receptor blocker, ACE inhibitors = Angiotensin-converting enzyme (ACE) inhibitors

**Table 3: Multivariable Logistic Regression Analysis (n=162)**

Parameters	Initial Solution		Final Solution	
	OR [95% CI]	P-value	OR [95% CI]	P-value
Age > 60 years	0.46 [0.16 -1.3]	0.143	0.43 [0.16 -1.17]	0.099
Hypertension	0.52 [0.18 -1.52]	0.232	0.49 [0.17 -1.41]	0.185
Diabetes	0.38 [0.12 -1.22]	0.103	0.37 [0.12 -1.18]	0.094
Family history of CAD	4.64 [1.24 -17.41]	0.023*	5.62 [1.58 -20]	0.008*
Use of ARB	0.21 [0.05 -0.85]	0.029*	0.2 [0.05 -0.8]	0.023*
Use of Digoxin	13.38 [0.38 -475.12]	0.154	11.71 [0.38 -359.49]	0.159
Use of Aldosterone antagonist	1.63 [0.46 -5.8]	0.449	-	-
Remote implants(> 1 year)	1.5 [0.43 -5.18]	0.522	-	-

\*= Significant P values, OR=Odds ratio, CI=Confidence Interval.

## DISCUSSION

This cross-sectional study aimed to observe the prevalence of AHREs on device interrogations in patients with CIEDs and to examine the association of various factors with the occurrence of AHREs. The mean age of our study population was 64.69 years with 67.3% of the study population being older than 60 years of age. In the initial univariate analysis, age has a significant association with the occurrence of AHREs but later on multivariable regression analysis, this correlation was not significant. The mean age in our study population was lower as compared to previous studies this could well be the reason for the decreased occurrence of AHREs in our patient population.<sup>8-9</sup>

A significant negative association was seen in the initial univariate analysis for hypertension and diabetes with occurrence of AHRE but later on multivariable regression analysis, this relationship was not found to be significantly associated.

In our study mean atrial high rate cut-off was 182.27 +/- 20.931. The overall percentage of patients with AHRE was lower 13.6% (22) as compared to prior studies.<sup>13-15</sup> A recent retrospective study also reported

a lower occurrence of AHRE events in the South Asian population to be around 14%.<sup>17</sup> Although this was a retrospective study this still confirms our findings and verifies the lower occurrence of AHREs on device interrogation in the South Asian population. More than half 59.09% (13) of AHRE events were of more than 5 minutes in duration and the majority 63% (14) of events occurred between 1 to 6 months of interrogation. Here it is worth mentioning that all AHREs can't be labeled as AF as for some events EGMs were not stored by the devices for them to be clearly designated as atrial fibrillation so they may represent atrial tachyarrhythmia. As reported in a recent meta-analysis of randomized controlled trials prolonged AHRE events are associated with a greater occurrence of strokes and may be treated with Oral Anticoagulation (OAC).<sup>18</sup> Our study enlightens the fact that the majority of AHREs in our local population are prolonged events and thus treatment with OAC in these patients may be considered.

In our study, we did exclude patients with a prior diagnosis of atrial fibrillation. Although we didn't exclude the patients with concomitant valvular heart disease (VHD) we did exclude the patients with prior AF, which in turn led to a lower number of patients with severe VHD i.e. severe MR and MS were seen in only 3.1% and 1.2% of patients respectively. This

correlates with the fact that the majority of patients in our country have AF associated with VHD.<sup>19</sup> Interestingly none of these patients with severe MS and MR had AHREs.

The LA dimensions were measured on 2D images and reported by imaging cardiologists. A mildly enlarged left atrium was seen in 43% of patients on transthoracic echocardiogram. There was no significant association observed between the LA dimension and AHREs and so was the case for the relation between LVEF and AHRE as well. This could well be due to number of reasons including the lower number of AHREs in study population and the fact that it was not an analytical study or a clinical trial specifically focused on correlation of echo parameters with AHRE occurrence rather it was an observational study. Thus a positive correlation could not be established.

The mean CHA<sub>2</sub>DS<sub>2</sub>-VASc score in our study was 3 (42 out of 162 patients had a score of more than >2 while 106 out of 162 patients had a score of >3). The recent consensus statement by European Heart Rhythm Association (EHRA) advises the institution of OAC in patients with prolonged AHREs and CHA<sub>2</sub>DS<sub>2</sub>-VASc score of >2.<sup>20</sup> Changes in these recent guidelines have been due to some large multicenter clinical trials which showed that sub-clinical Atrial fibrillation (SCAF) is associated with a greater risk of stroke. The studies that highlight this fact recently are TRENDS and ASSERT studies. Data from the TRENDS Study showed that AF detected on device interrogation during pacemaker follow-ups revealed double the risk of stroke amongst patients who had AF episodes lasting longer than 5 and half hours per day in any 30 days as compared to patients having either no AF events or events lasting for a lesser duration.<sup>21</sup> These findings were further confirmed by the ASSERT study which assessed the association between AF occurrence and stroke in a population of aged hypertensive patients without any history of prior anticoagulation on pacemakers or ICD interrogation. This multicenter study established that over a 3-month follow-up after device implantation, any episode of AF lasting longer than 6 minutes accompanies a ≈2.5-fold increment in the risk of stroke subsequently.<sup>22</sup> Two ongoing clinical trials at present are the NOAH-AFNET 6 trial (Trial identification # NCT02618577) which is evaluating the role of non-vitamin K oral anticoagulants in patients with AHREs for reduction of thromboembolic events and the ARTESiA Study (Trial identification # NCT01938248) that aims to assess the role of Apixaban in reducing the occurrence of thromboembolic events amongst patients with device detected SCAF episodes. Although the data from these

trials are still awaited we expect that these large studies will help us in the appropriate management of patients with AHREs or SCAF.

As our study showed our population tends to have a lower prevalence of AHREs but prolonged events and has a higher overall CHA<sub>2</sub>DS<sub>2</sub>-VASc score (table 1) as compared to earlier research work so OAC can be considered in patients with prolonged AHREs to prevent stroke.<sup>18</sup> This finding of a higher CHA<sub>2</sub>DS<sub>2</sub>-VASc score is quite alarming despite a lower age group of patients with CIED implants. It suggests that the assessment of comorbidities in the south Asian population and their identification is extremely important at an earlier age for their appropriate treatment. It could potentially prevent a vast majority of cardiovascular diseases rather than dealing with their complications.

The use of ARB and positive family history of CAD had a significant association with AHRE in the initial analysis and multivariable regression analysis (table 3). The use of ARB in our study population had a protective effect. Primarily ARBs were given for treatment hypertension in our cohort however in patients with heart failure (n=29) they were prescribed as a part of heart failure guideline directed medical therapy. Majority of our study participants were either using valsartan or losartan potassium and this finding of our study confirms prior evidence in this respect as shown by multiple studies.<sup>23,24</sup> The mechanism by which ARBs prevent atrial fibrillation is well-established and is related to the blockade of effects of the renin-angiotensin system through the electrical and structural remodeling of atria.<sup>25</sup> Here it is worth mentioning that although amiodarone is one of the most commonly used antiarrhythmic drug and is known to decrease the occurrence of atrial tachyarrhythmia but in our study it was not associated with reduction of AHRE episodes, this may be due to lesser number of patients using amiodarone as patients with known atrial fibrillation were excluded from the study

Our study included patients with Dual chamber PPM and ICDs as well as patients with CRTD and CRTP whereas in prior studies only a population with pacemakers was studied.<sup>15, 16</sup> Most of participants included in the study were either implanted with Medtronic or Abbot (former St. Jude) devices while a few participants had received Boston scientific devices.

The bulk of the population 75% (122) was implanted with dual-chamber PPM, and AV block 60.5% (98) was the commonest indication for the implant (majority of study participants were implanted for

complete AV block while others were implanted for 2:1 AV block) while 16% (26) were implanted for SND. Despite the number of patients implanted for AV block being much higher in our study as compared to SND as seen in prior studies the occurrence of AHRE events was low.<sup>16</sup> This is an interesting finding as we know that ventricular pacing is associated with more atrial fibrillation and thus AHRE.<sup>4,5</sup>

Our study has provided important data about the Pakistani population with CIEDs presenting in two different tertiary care centers. This is the first study that provided data in this respect as to date no study was done in our local population to determine AHREs burden and related factors. Moreover, it will facilitate the conception of a future framework for the institution of OAC among patients with AHRE episodes later on in our population.

A major limitation of the study was that it was powered to ascertain the occurrence of AHRE events and its relationship with certain covariates so the overall sample size was smaller as compared to prior studies<sup>15</sup> and this might have led to a lower number of patients to significantly prove the associations of some of the study variables with AHRE events, although, in the West and other parts of the world, similar studies have been conducted prospectively due to increased prevalence and larger sample size.

2. The correlation of AHRE with Stroke and heart failure is not fully ascertained as no follow-ups were done because the study was performed on a single encounter basis.

3. As we know LA volume is a better measure of atrial enlargement as compared to LA dimension but in our study for the sake of uniformity of the data LA dimensions were used as a measure.

## CONCLUSION

The occurrence of AHREs was considerably lower in our population on CIED interrogation as compared to prior studies, although the majority of AHRE events are prolonged events and the CHA<sub>2</sub>DS<sub>2</sub>-VASc score is high overall. The use of ARB plays a protective role against the occurrence of AHRE while having a positive family history of CAD significantly predisposes to AHRE events. Although the institution of anticoagulation in patients with AHRE remains an area of debate and ongoing studies will likely bridge this gap by providing these much-needed answers there remains a need of investigating this area of OAC institution amongst AHRE patients in our Southeast Asian population.

## AUTHORS' CONTRIBUTION

MTK and YS: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. SS, AHK, FS, and AS: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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