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Evaluation of the risk factors of hemodialysis procedure-associated cardiac arrhythmias in end stage renal disease Egyptian patients

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***Abstract*---**Background: Hemodialysis patients carry a large burden of cardiovascular disease, accounting for up to 41% of deaths, of which half are ascribed to sudden cardiac death (SCD). The pathophysiology of SCD is thought to result from the combination of a vulnerable myocardium and an acute pro-arrhythmic trigger that leads to a terminal arrhythmia. Approximately two thirds of the cardiac deaths are consistently attributed to arrhythmias. Aim: The study aimed to improve the clinical status of hemodialysis (HD) patients through detection of HD procedure associated cardiac arrhythmias, prevention of its risk factors and related complications. Subjects and Methods: Observational study that included 60 maintenance HD patients to assess the prevalence of electrocardiographic changes before, during, and after HD in patients who are on maintenance HD in the out/inpatient departments of Suez Canal University. Results: The study showed a high prevalence of electrocardiographic changes among the studied sample, representing 78.3%. Receiving HD for more than 5 years, glomerulonephritis (GN) being the primary cause

of end stage renal disease (ESRD), intradialytic hypotension (IDH), and high pre-dialysis Na, K, and Po4 were all factors that were statistically significant associated with electrocardiographic changes. Conclusion: Cardiac arrhythmias are common findings in patients on regular hemodialysis. Different variables are associated with development of cardiac arrhythmias in HD patients.

***Keywords*---**hemodialysis, arrhythmia, sudden cardiac death**,** HD, ESRD.

Introduction

ESRD represents an emerging healthcare challenge due to the exponential increase in its incidence rates over the past few decades. [(1)] Also, cardiovascular disease remains one of the leading causes of mortality worldwide, and causes more than one millions deaths annually in the United States (US) alone. [(2)] Hemodialysis patients carry a large burden of cardiovascular disease, accounting for up to 41% of deaths, of which half are ascribed to SCD. [(3)] Within this complex disease category, it is likely that a large proportion of these events are related to development of fatal cardiac arrhythmia. [(4)]

In Egypt, 27 deaths have been noted during the 1st year of dialysis & the leading causes of death were cardio-vascular events. [(1)] The pathophysiological processes resulting in arrhythmia and SCD in patients with ESRD are unique. The dialysis procedure itself triggers multiple mechanisms that can increase the propensity to cardiac arrhythmias. [(5)] Some of the risk factors of cardiac arrhythmias include dialysate composition, timing &frequency. They are modifiable and hence provide an option for interventions to potentially reduce SCD. [(6)]

In the United States Renal Data System (USRDS) database, 62% of cardiac deaths (27% of all-cause mortality) are attributable to arrhythmic mechanisms. [(3)] Arrhythmic triggers differ in ESRD patients as compared to the general population, with some becoming apparent uniquely from the hemodialysis procedure. Combined, these factors may alter the types of terminal arrhythmias that lead to SCD among hemodialysis patients. [(7)]

Subjects and Methods

The study is a cross-sectional observational descriptive study, conducted on 60 ESRD patients who were scheduled to undergo maintenance HD, at the Hemodialysis Units in Suez Canal University Hospitals, Ismailia Governorate, Egypt. Patients included were of both genders (males and females), aged 18 or more, whose blood pressure (BP) were well controlled through antihypertensive medications. We excluded patients who have been previously diagnosed as having atrial fibrillation (AF), patients who were commenced on beta blockers, and patients who have ICD or pacemaker.

Patients who had a newly inserted hemodialysis catheter (less than one day duration), those on antihypertensive medications that lengthen QT and their ejection fraction (EF) were less than 40%, were excluded as well.

Data collected from each patient included:

- Age (years), gender (male/female), job and residence, smoking (current, near and past), any recent cardiac problem, medications (beta blockers and antihypertensive drugs that lengthen QT).
- Past history of previous hospital admission due to arrhythmias or any other cardiac problems, blood transfusion, operations (coronary artery bypass graft) and chronic illness (hypertension, diabetes mellitus , coronary artery disease, heart failure, cerebrovascular disease and hypercholesterolemia).
- Family history of cardiac problems and chronic illness.
- Primary cause of ESRD (glomerulonephritis, hypertension, diabetes, genetic, obstructive or unknown cause).
- Duration on maintenance hemodialysis.
- Access of dialysis (AVF, graft, temporary catheter and permi-catheter).
- Hepatitis C viral infection (HCV).
- Examination including: body mass index, intradialytic weight gain, vital signs (with blood pressure measured before, during and after HD), chest, cardiac and abdominal examination.
- Dialysis data including: HD session length, ultrafiltration rate in ml/hour, blood flow rate, dialyzer surface area, bicarbonate dialyzing concentrate with same properties for all patients.
- Lab investigations (before and after HD) including: complete blood count, serum sodium, potassium, creatinine, calcium (total and ionized), phosphorus, uric acid, magnesium, bicarbonate levels. Additionally, cardiac enzymes, liver enzymes, lipid profile and albumin.
- Standard 12 leads ECG before HD and before using holter ECG.
- Transthoracic Echocardiography.
- Holter ECG monitoring: Patients underwent 48 hours holter ECG monitoring (one day before HD and the day of HD session) which was removed the day after dialysis, to detect QTc, QT interval, PVCs burden and heart rate variability. Risk of hemodialysis induced arrhythmia was defined in our study by the electrocardiographic changes of QTc interval prolongation and high burden of PVCs.

The obtained data were entered and analyzed using Statistical Package of Social Science (SPSS) version 24. Data were compared by using Chi-square test for qualitative variables while independent t-test was used for quantitative variables. Multiple logistic regression analyses were used to examine the extent to which a set of variables independently predicts a dependent variable. P-value was used to indicate the level of significance; P less than 0.05 was considered significant.

This study was approved by the local Ethics Committee of Faculty of Medicine, Suez Canal University (approval number: 4359, approval date 02/11/2020) and performed in accordance with the Helsinki Declaration of 1975, as revised in 2000. Informed oral consent was obtained from all patients included in the study.

Results

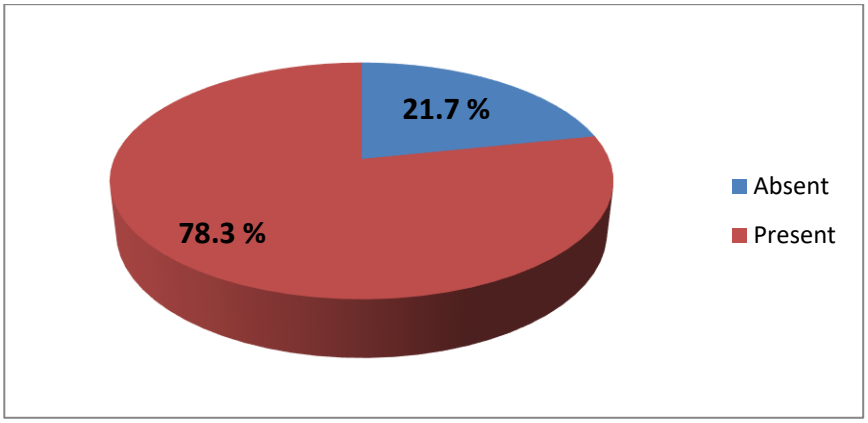

Figure 1: shows that the prevalence of HD related electrocardiographic changes among the studied sample was 78.3%.

Table 1. Demographic and clinical characteristics of hemodialysis patients

Variables	Total patients (n=60)	Hemodialysis induced *electrocardiographic changes		p-value
		Absent (n= 13)	Present (n=47)	
Gender, n (%)				
Male	45 (75)	10 (76.9)	35 (74.5)	0.856[c]
Female	15 (25)	3 (23.1)	12 (25.5)	
Age, n (%)				
18 – 27 years	12 (20)	3 (23.1)	9 (19.1)	
28 – 37 years	23 (38.3)	7 (53.8)	16 (34)	0.328 [c]
38 – 47 years	9 (15)	0 (0)	9 (19.1)	
> 48 years	16 (26.7)	3 (23.1)	13 (27.7)	
Smoking, n (%)				
Yes	26 (43.3)	0 (0)	26 (43.3)	<0.001*
No	34 (56.7)	13 (100)	34 (56.7)	
Hypertension, n (%)	37 (61.7)	10 (76.9)	27 (57.4)	0.334
Diabetes Mellitus, n (%)	12 (20)	2 (15.4)	10 (21.3)	0.722
Heart Failure, n (%)	18 (30)	3 (23.1)	15 (31.9)	0.736
Cerebrovascular disease, n (%)	8 (13.3)	3 (23.1)	5 (10.6)	0.353
Hyperlipidemia, n (%)	17 (28.3)	6 (46.2)	11 (23.4)	0.163
HCV, n (%)	10 (16.7)	3 (23.1)	7 (14.9)	0.675
Family history, n (%)				
Absent	38 (63.3)	6 (46.2)	32 (68.1)	0.197
Present	22 (36.7)	7 (53.8)	15 (31.9)	
BMI, n (%)				
Underweight (<18.5)	17 (28.3)	7 (53.8)	10 (21.3)	
Normal (18.5-24.9)	31 (51.7)	3 (23.1)	28 (59.6)	0.056
Overweight (25-29.9)	9 (15)	3 (23.1)	6 (12.8)	
Obese >/= 30	3 (5)	0 (0)	3 (6.4)	

[c] P values are based on Fisher Exact test. Statistical significance at P < 0.05.
*electrocardiographic changes mean prolongation of QTc (more than 440 in males & 460 in females) and the presence of PVCs more than 1%.

Table 1: summarizes the baseline and clinical characteristics of studied groups of patients. Regarding patients with HD induced electrocardiographic changes. Males formed 74.5% of the patients. About 34% of the patients were between 28 to 37 years and about 27.7 % of them above 48 years old. Regarding co-morbidities, 57.4% of the patients had hypertension, while 21.3% had Diabetes Mellitus and only 23.4 % had Hyperlipidemia. It was found that HD induced arrhythmia was significantly associated with smoking (p<0.001).

Table 2. Clinical characteristics related to dialysis

Variables	Total patients (n= 60)	Hemodialysis induced electrocardiographic changes		p-value
		Absent (n= 13)	Present (n=47)	
Primary disease, n (%)				0.007*
Glomerulo-nephritis	19 (31.7)	0 (0)	19 (40.4)	
Hypertension	0 (0)	0 (0)	0 (0)	
Diabetes	12 (20)	3 (23.1)	9 (19.1)	
Genetic	9 (15)	3 (23.1)	6 (12.8)	
Obstruction	4 (15)	0 (0)	4 (19.1)	
Unknown	16 (26.7)	7 (53.8)	9 (19.1)	
Duration of hemodialysis, n (%)				
< 1 years	9 (15)	6 (46.2)	3 (6.4)	
1 – 5 years	18 (30)	3 (23.1)	15 (31.9)	
> 5 years	33 (55)	4 (30.8)	29 (61.7)	0.004*
Access of hemodialysis, n (%)				
Artrio-venous fistula	54 (90)	13 (100)	41 (87.2)	
Graft	3 (5)	0 (0)	3 (6.4)	0.435
Permi- catheter	3 (5)	0 (0)	3 (6.4)	
Hemodialysis length, n (%)				
< 4hours	19 (31.7)	7 (53.8)	12 (25.5)	0.089
≥ 4hours	41 (68.3)	6 (46.2)	35 (74.5)	
Hemodialysis frequency, n (%)				
< 3 times/ week	0 (0)	0 (0)	0 (0)	1.000
≥ 3 times/week	60 (100)	13 (100)	47 (100)	

[a] P values are based on Chi-Square test. Statistical significance at P < 0.05
[c] P values are based on Fisher Exact test. Statistical significance at P < 0.05

Table 2: summarizes Clinical characteristics related to dialysis. Regarding patients with HD induced electrocardiographic changes. The most common primary disease was glomerulonephritis (40.4%) (p=0.007). Moreover, it was found that HD induced electrocardiographic changes were significantly associated with disease duration more than 5 years (p=0.004).

Table 3. Clinical characteristics related to dialysis (continued)

IDWG, n (%) < average Average > average	 11 (18.3) 25 (41.7) 24 (40)	 4 (30.8) 6 (46.2) 3 (23.1)	 7 (14.9) 19 (40.4) 21 (44.7)	0.296
ID hypotension, n (%) Yes No	 47 (78.3) 13 (21.7)	 6 (46.2) 7 (53.8)	 41 (87.2) 6 (12.8)	0.004*
UFR, n (%) Accepted More than accepted	 54 (90) 6 (10)	 13 (100) 0 (0)	 41 (87.2) 6 (12.8)	0.324
BLF, n (%) <300 ml/min ≥ 300 ml/min	 6 (10) 54 (90)	 3 (23.1) 10 (76.9)	 3 (6.4) 44 (93.6)	0.109
Dialyser type high flow not high flow	 3 (5) 57 (95)	 0 (0) 13 (100)	 3 (6.4) 44 (93.6)	0.589
Heparin on HD yes no	 54 (90) 6 (10)	 13 (100) 0 (0)	 41 (87.2) 6 (12.8)	0.324

[a] P values are based on Chi-Square test. Statistical significance at P < 0.05
[c] P values are based on Fisher Exact test. Statistical significance at P < 0.05

Table 3: Summarizes remain of clinical characteristics related to dialysis. Regarding patients with HD induced electrocardiographic changes. It was found that HD induced electrocardiographic changes was significantly associated with intradialytic hypotension (p=0.004).

Table 4. Comparison between HD patients with and without electrocardiographic changes regarding pre-dialysis laboratory characteristics

Variables	Total patients (n= 60)	Hemodialysis induced electrocardiographic changes		p-value
		Absent (n= 13) mean ±SD	Present (n=47) mean ±SD	
Hemoglobin (11-12 mg/dl)	9.74 ± 1.67	10.26 ±2.18	9.59 ±1.49	0.083[b]
TLC (4-11000)	7.85 ± 1.83	7.55±1.72	7.93 ±1.87	0.535 [b]
PLT(150-450.000)	166.6 ± 57.28	163.07 ±40.67	167.57 ±61.42	0.753 [b]
Na^+ (135-145 mg/dl)	139.5 ± 4.07	137.69 ±2.89	140.10 ±4.21	0.018* [b]
K^+ (3.5-5.5 mg/dl)	5.67 ± 0.69	4.68 ±0.44	5.95 ±0.46	<0.001* [b]
Creatinine	10.37 ± 1.93	10.26 ±1.15	10.41 ±2.10	0.753 [b]
Total calcium (8.6-10.3 mg/dl)	8.97 ± 0.91	9.20 ±0.87	8.90 ±0.92	0.281 [b]
Phosphorus (2.8-4.5 mg/dl)	4.50 ± 1.39	3.63 ±1.41	4.73 ±1.30	0.030* [b]
UA (3.5-7.2 mg/dl)	5.74 ± 0.98	5.78 ±0.78	5.72 ±1.03	0.876 [b]

Mg (1.3-2.1 mg/dl)	1.81 ± 0.23	1.81 ±0.21	1.81 ±0.24	0.842 [b]
HCO_3 (22-29 mEq/l)	14.3 ± 2.33	13.38 ±2.46	14.55 ±2.26	0.107 [b]
Cardiac enzymes Normal High	 60 (100) 0 (0)	 13 (100) 0 (0)	 47 (100) 0 (0)	1.000[c]

[b] P values are based on Mann Whiney U test. Statistical significance at P < 0.05
[c] P values are based on Fisher Exact test. Statistical significance at P < 0.05

Table 4: compares between HD patients with and without electrocardiographic changes regarding pre-dialysis laboratory characteristics. It was found that patients with electrocardiographic changes had statistically significant higher pre-dialysis Na+ and K+ levels compared to patients without electrocardiographic changes (p=0.018) and (p<0.001), respectively. Moreover, patients with electrocardiographic changes had statistically significant higher pre-dialysis phosphorus levels compared to patients without electrocardiographic changes (p=0.030).

Table 5. Comparison between HD patients with and without electrocardiographic changes regarding post-dialysis laboratory characteristics

Variables	Total patients (n=60)	Hemodialysis induced electrocardiographic changes		p-value
		Absent (n= 13) mean ±SD	Present (n=47) mean ±SD	
Hemoglobin, n (%)	9.47 ±1.60	10.00 ±2.05	9.33 ±1.45	0.072[b]
TLC, n (%)	7.96 ± 1.74	7.90 ±1.69	7.98 ±1.77	0.879 [b]
PLT, n (%)	167.8 ± 57.4	165.07 ±38.60	168.55 ±61.98	0.634 [b]
Na^+, n (%)	131.5 ± 4.9	130.53 ±5.37	131.87 ±4.89	0.534 [b]
K^+, n (%)	4.09 ± 0.61	4.21 ±0.46	4.06 ±0.64	0.280 [b]
Creatinine, n (%)	7.14 ± 1.69	6.96 ±1.38	7.19 ±1.77	0.733 [b]
Total calcium, n (%)	8.86 ± 0.96	9.03 ±0.778	8.82 ±1.01	0.377 [b]
Phosphorus, n (%)	4.01 ± 1.17	3.43 ±1.19	4.17 ±1.12	0.060 [b]
UA	5.21 ±0.79	5.30 ±0.81	5.19 ±0.79	0.815 [b]
Mg	1.53 ± 0.26	1.50 ±0.23	1.53 ±0.27	0.737 [b]
HCO_3	17.10 ± 2.01	15.84 ±2.03	16.44 ±1.88	0.085 [b]
Cardiac enzymes Normal High	 60 (100) 0 (0)	 13 (100) 0 (0)	 47 (100) 0 (0)	1.000[c]

[b] P values are based on Mann Whiney U test. Statistical significance at P < 0.05
[c] P values are based on Fisher Exact test. Statistical significance at P < 0.05

Table 5: compares between HD patients with and without electrocardiographic changes regarding post dialysis laboratory characteristics. It was found that there was no statistically significant difference between patients with and without electrocardiographic changes regarding laboratory measures post-dialysis.

Table 6. Comparison between HD patients with and without electrocardiographic changes regarding 48 hours halter assessment

Variables	Total patients (n=60)	Hemodialysis induced electrocardiographic changes		p-value
		Absent (n= 13)	Present (n=47)	
QTc interval				
Normal (male 440/female 460)	16 (26.7)	13 (100)	3 (6.4)	<0.001*
Prolonged	44 (93.6)	0 (0)	44 (93.6)	
QT				
Normal (400-440)	57 (93.6)	13 (100)	44 (93.6)	0.350
Prolonged	3 (5)	0 (0)	3 (6.4)	
RR/SDNN				
low risk (>100)	16 (26.7)	4 (30.8)	12 (25.5)	<0.001*
moderate risk (50-100)	32 (53.3)	3 (23.1)	29 (61.7)	
High risk (<50)	12 (20)	6 (46.2)	6 (12.8)	
LF/HF ratio (Sympathetic over activity)				
Normal (>/= 1.5)	37 (61.7)	9 (69.2)	28 (59.6)	0.749
Over activity (<1.5)	23 (38.3)	4 (30.8)	19 (40.4)	
PVCs				
Normal (<1%)	42 (70)	13 (100)	29 (61.7)	0.006*
Abnormal (>1%)	18 (30)	0 (0)	18 (38.3)	

[c] P values are based on Fisher Exact test. Statistical significance at P < 0.05

Table 6: compares between HD patients with and without electrocardiographic changes regarding 48 hours halter assessment. More than 90% of the patients with HD induced electrocardiographic changes had prolonged QTc and about 38.3% of the patients had abnormal PVCs. Moreover, 40.4% of the patients had LF/HF ratio over activity. About 61.7% of the patients had moderate risk RR/SDNN ratio.

Table 7. Multivariate logistic regression analysis of the risk factors of HD induced electrocardiographic changes

Variables	B	S.E.	OR	95% C.I.		p-value
				Lower	Upper	
Constant	-3.495	1.532	0.030	-		0.023*
Smoking (present)	0.731	0.485	2.076	0.802	5.377	0.132
Duration of hemodialysis (< 1 year)	Reference					
Duration of hemodialysis (1 - 5 year)	1.386	1.000	4.000	0.563	28.396	0.166
Duration of hemodialysis (> 5 year)	1.792	0.913	6.000	1.003	35.908	0.045*
ID hypotension (present)	2.133	1.274	8.437	0.695	102.424	0.094
Pre-dialysis Na^+	0.385	0.298	1.469	0.820	2.633	0.196
Pre-dialysis K^+	2.218	0.756	9.185	2.087	40.428	0.003*
Pre-dialysis Phosphorus	1.398	0.796	4.046	0.850	19.254	0.079

* Statistical significance < 0.05.

Table 7: shows that patients who had HD duration of more than 5 years have 6 times more likely to have HD induced electrocardiographic changes compared to patients who had HD duration less than one year (p=0.045). Moreover, for every one mmol/L increase in pre-dialysis K^+, the odds of having HD induced electrocardiographic changes increases by 9.18 times (p=0.003).

Discussion

The current study showed that 78.3% of the sample experienced electrocardiographic changes (fig: 1) so prolonged QTc and abnormal PVCs are predisposing factors for arrhythmias.

The increase in QT dispersion on the ECG reflects increased tendency for ventricular repolarization that predisposes to arrhythmias. Non-homogeneity of ventricular repolarization in chronic uremic patients may be due to myocyte hypertrophy, increased collagen interstitial matrix, and autonomic neuropathy. Hypoperfusion of myocardial segments could happen during hemofiltration and also influence the homogeneity of repolarization. [8]

The high prevalence of electrocardiographic changes reported in the current work is consistent with the previous literature which studied patients on maintenance HD. In Adam *et al.* cross sectional study of intradialytic arrhythmias among patients with ESRD on maintenance HD, the prevalence of arrhythmia was 92% .[9] Similarly, in Al-Ameen *et al.* study, the prevalence of arrhythmia was 84% among the HD patients. [10] The relatively close numbers in the previous two studies and our study may be due to the close number of the sample size and the usage of the same method (halter) in recording the occurrence of arrhythmia.

However, Tumlin *et al.* observed 97% as the prevalence of reviewer confirmed arrhythmia in HD patients during following-up. This relatively higher prevalence could be explained as reviewer confirmed arrhythmia was defined as an implantable loop recorder identified or patient marked event in which a manual review of the stored ECG tracing confirmed the presence of abnormal rhythm .[11]

In contrast to our study, Rogovoy *et al.* reported relatively lower prevalence in his prospective ancillary study which aimed at detection of sudden cardiac death associated arrhythmias; Almost half of the participants (n=13, 46%) had arrhythmias detected during monitoring.[5]

This difference may be due to that, all arrhythmic events in his study were captured by a different method which was an ECG patch applied over the left pectoral region and the participant was instructed to activate a trigger button in the event of cardiac symptoms (presumed arrhythmia). Additionally, patients in his study underwent continuous ECG monitoring for at least 7 days while in our study it was only for 2 days.

In the current work, we found no statistically significant difference between HD patients who experienced HD induced electrocardiographic changes and those who did not regarding gender (P = 0.856), Age (P = 0.328), family history (P = 0.197) or BMI (P = 0.056) (table: 5). That was supported by the findings of Al-Ameen *et al.* who described that there was no significant difference between those developed arrhythmia and those did not regarding demographics and body weight changes. [10] This insignificance could be contributed to the small number of patients in each category.

In contrast, Adam *et al.* reported that ESRD patients, 60 years or older, were 34 times more likely to present with intradialytic clinically significant arrhythmia compared to those aged 20 - 39 years (OR 34; 95% CI: 5.15-236; P< 0.001). [9] This could be explained by that hemodialysis is associated with hemodynamic changes and autonomic imbalance which predispose the myocardium to arrhythmias. It was found that youths and young adults are likely to tolerate these physiological changes, on other hand, older adults are less likely to tolerate these changes and are prone to suffer from arrhythmias.[5]

In our study, the relatively younger population could be an explanation of this discrepancy as only 26.7% of our patients were > 48 years. While, in Adam *et al.*'s work, 52% of patients were 40-59 years and 29% were over 60 years. The older the age, the more common is the heart structural abnormalities (More than half of the sample of Adam et al.'s study, 54%, had Left ventricular hypertrophy) and the more is the susceptibility of arrythmias. [12]

Our current study showed that HTN, HF, DM, hyperlipidemia and CVD were present in 61.7%, 30%, 20%, 28.3%, and 13% respectively (table: 5). Alawwa *et al.* reported nearly similar percentages as three-quarters of the participants were hypertensive, almost 40% and 30% had diabetes mellitus or dyslipidemia.[12] Also, the majority of the participant in Adam *et al.* and Mahmood et al. *study* (78.8% and 59.16% respectively) had hypertension. [9, 13] Which is consistent with our study results, this could be due to the closer sample size in these studies and our study.

The primary causes of ESRD in our study were, mainly, the GN representing 31.7% (P= 0.007), DM representing 20%, and 26.7% of the participants showed unknown primary disease (table: 6). Similarly, the RAKUEN (Registry of atrial fibrillation in chronic kidney disease under hemodialysis from Niigata) study studied 423 Japanese patients undergoing maintenance HD (age 65.2 ± 12.4 years) and reported that GN was the leading cause of ESRD (44%) followed by DM (25%), HTN, polycystic kidney disease and unknown causes.[14]

Different encounters were found in the Monitoring in Dialysis (MiD) study which enrolled 81 patients, and 66 were implanted with an ILR: 43 from the United States and 23 from India. Mean age in the MiD Study was 56.3±12.2 which was lower than it in the RAKUEN study which was 65.2 ± 12.4. This could be an explanation of that inconsistency. Additionally the difference in the ethnicity between our group and the MiD study group could be a cause of that difference.

Hemodialysis induced electrocardiographic changes were, statistically significantly, present more in HD patients with GN as the primary cause of ESRD (p= 0.007) (table: 5). No studies - to our knowledge - have examined the association between the primary disease in HD patients and the prevalence of hemodialysis induced electrocardiographic changes. This could be because GN represented about one third of our population as the primary disease of ESRD.

In our study, hemodialysis induced electrocardiographic changes were statistically significantly associated with duration of HD more than five years (p= 0.004) (table: 5). Additionally, by multivariate logistic regression, patients who had HD duration of more than 5 years have 6 times more likely to have HD induced electrocardiographic changes compared to patients who had HD duration less than one year (p=0.045) (table: 10).

These findings are supported by the previous studies. The RAKUEN study showed that the patients with AF had a significantly longer duration of hemodialysis (p < 0.01). Additionally, the multiple logistic regression analysis showed that AF was independently associated with longer duration of hemodialysis (P= <0.001). [14]

However, the MiD trial showed no statistically significant association between the prevalence of arrhythmia and ESRD vintage in years (p=0.41). [15] The mean ESRD vintage in years of patients included in the MiD trial is 2.4 years while in our study 55% of our sample were more than five years on dialysis. This could be an explanation of the association and discrepancy of findings.

Prevalence of hemodialysis induced electrocardiographic changes was not significantly associated with access of hemodialysis, IDWG, dialyzer type, heparin on HD, UFR, or BLF (table: 5). Similarly, Roy-Chaudhury showed that number of clinically significant arrhythmias during follow-up was not statistically associated with the vascular access, IDWG and UFR.[15]

The same was observed in Sacher *et al.* study to assess the determinants of significant conduction disorders and ventricular arrhythmias in HD patients and found that there was no relationship with several other parameters linked to HD such as ultrafiltration rate and percentage of body weight loss during HD. [16] These similarities between our study and the two studies of Roy-Chaudhury and Sacher could be due to the close number of the studied population in each one (60, 61 & 71 respectively).

There was no statistical significance between the occurrence of electrocardiographic changes and the frequency of hemodialysis per week (P= 0.089) because all the patients in our study received ≥3 sessions per week. Also, while comparing between HD patients with and without electrocardiographic changes regarding 48 hours halter assessment. About 53.3% of the patients had a moderate risk RR/SDNN ratio, out of which 61.7% of the patients had electrocardiographic changes (P= <0.001) (table: 9). This could be contributed to the lesser the variability, the limited is the autonomic regulation.

Coincident with our study results, Adam *et al.* reported that doing three dialysis sessions per week was associated with 86% reduced odds for intradialytic

clinically significant arrhythmia (OR 0.14; 95% CI: 0.03-0.67; P=0.013). Also, patients doing less than three sessions per week had relatively higher water retention compared to those doing three sessions, which is a risk factor for developing arrhythmia.[9]

Rogovoy *et al.* added to the growing evidence of the harmful consequences of a prolonged interdialytic interval. He stated that while every-other-day hemodialysis preserved relatively normal cardiovascular autonomic tone, a second day without hemodialysis was characterized by parasympathetic withdrawal and a steady increase in sympathetic predominance, which may explain the previously observed increased rate of SCD after the long interdialytic interval.[5]

There was a statistically significant association between hemodialysis induced electrocardiographic changes and IDH (p=0.004) (table: 5), this may be because 78.3% of our whole population developed IDH. These findings are largely supported by the previous studies. For example, Adam *et al.* reported that intradialytic blood pressure decline of ≥10 mmHg (OR 3.85; 95% CI: 1.27-11.7; P = 0.017) was significantly associated with increased odds of clinically significant arrhythmia. [9]

Another study, McCausland *et al.* which analyzed the intradialytic hypotension and cardiac arrhythmias in patients undergoing maintenance hemodialysis from the results of MiD study. IDH was associated with a 7.3 fold higher rate of clinically significant arrhythmia (IRR, 7.3; 95% CI, 2.3 to 23.7; P=0.004), compared with sessions without IDH. Also, with logistic regression, similar patterns of association were noted (odds ratio, 4.1; 95% CI, 0.9 to 19.3; P=0.08 for IDH0–20). Events are likely to be directly caused by hypo perfusion-related myocardial ischemia or changes in autonomic tone, longer-term adverse consequences with micro infarction leading to scar and long-term disruption of conduction pathways and increase in the chronic risk of arrhythmia.[4]

In our study, it was found that patients with electrocardiographic changes had statistically significant higher pre-dialysis Na+, K+, and Ph levels compared to patients without electrocardiographic changes (p= 0.018, <0.001 & 0.030 respectively) (table: 6). There is no consensus in the literature on the relation between different serum electrolytes and the prevalence of arrhythmia. Tumlin *et al.* showed that there were no significant differences in pre-dialysis electrolyte concentrations or intra-dialytic change in electrolytes in sessions with or without reviewer confirmed arrhythmia. [11]

Sacher *et al.* reported that high serum K was associated with conduction disorder. In the multivariate analysis of the determinants of significant VA, serum K <4 mmol/l (HR: 17.9; p = 0.004) was associated with a higher risk for VA. Also, results of the univariate and multivariate analysis of the determinants of AF showed that serum K <4mmol/l (HR: 2.5; p = 0.01), and serum phosphate >1.45 mmol/l (HR: 1.9; p = 0.006) were associated with an increased risk for AF. [16]

Al-Ameen *et al.* found that there was no significant difference between patients who developed arrhythmia and those who did not regarding electrolytes before

and after HD except for significantly lower level of magnesium and higher level of calcium in patients with arrhythmia. [10]

All the previous differences between our study and the other studies could be explained by the presence of a lot of cofounders in this association as it is affected by various factors: Dialysate temperature, potassium, sodium, calcium, magnesium, bicarbonate. Tumlin *et al.* hypothesized the effects of pre-dialysis electrolytes, the dialysis prescription, and the dialysis procedure would be most apparent during dialysis or the 8 hours immediately after HD (the period with maximal arrhythmia incidence rate) so this could be a cause as well, as we measured the electrolytes before and after dialysis. [11]

Limitation

The sample size limited construction of models incorporating all potential confounding factors and correction for multiple comparisons in dialysis parameter and serum electrolyte analyses. Longer monitoring for up to 48 hours could improve our findings on prevalence and factors associated with arrhythmia; however, it was challenging to know the exact time of (prolongation of QTc interval & the occurrence of PVCs) because the computer system of the 48 hour halter does not define its exact time so it has to be done manually.

Conclusion

Cardiac arrhythmias are common findings in patients with ESRD on regular hemodialysis. Additionally, different variables are associated with development of cardiac arrhythmias in HD patients; receiving HD for >5 years, GN being the primary cause of ESRD, intra-dialytic hypotension, and high pre-dialysis sodium, potassium, and phosphorus.

Recommendations

It is recommended to check all patients on hemodialysis for cardiac arrhythmias and blood pressure variability before, during and after their hemodialysis sessions, and provide appropriate management in due time for each patient according to his/her clinical situation. Longer cardiac monitoring at a mean duration of 6 months is recommended as longer cardiac monitoring overcomes the problem of spontaneous and circadian variability of arrhythmic events.

Mounting evidence of the harmful effect of the 2-day interval without hemodialysis, we suggest that more frequent dialysis should be considered the preferred prescribed treatment schedule. Whether more frequent hemodialysis attenuates arrhythmic propensity remains to be determined. More studies to be conducted on the relation between the primary kidney disease and the occurrence of hemodialysis associated cardiac arrhythmia.

References

1. Ali, O. M., Sayed, A. A., Mohammed, W. S., & Mohammed, R. R. (2020). Cardiovascular System Affection and Its Relation to First-Year Mortality in

Patients Initiating Maintenance Hemodialysis. International Journal of General Medicine, 13, 379.

2. Ajam, F., Patel, S., Alrefaee, A., Calderon, D., Hossain, M. A., & Asif, A. (2019). Cardiac Arrhythmias in Patients with End Stage Renal Disease (ESRD) on Hemodialysis; Recent Update and Brief. American Journal of Internal Medicine, 7(1), 22-26.
3. Saran, R., Robinson, B., Abbott, K. C., Agodoa, L. Y., Albertus, P., Ayanian, J., Chen, J. L. (2017). US renal data system 2016 annual data report: epidemiology of kidney disease in the United States. American Journal of Kidney Diseases, 69(3), A7-A8.
4. McCausland, F.R., Tumlin, J.A., Roy-Chaudhury, P., Koplan, B.A., Costea, A.I., Kher, V., williamson, D., et al. (2020), "Intradialytic hypotension and cardiac arrhythmias in patients undergoing maintenance hemodialysis results from the monitoring in dialysis study", Clinical Journal of the American Society of Nephrology, Vol. 15 No. 6, pp. 805–812.
5. Rogovoy, N.M., Howell, S.J., Lee, T.L., Hamilton, C., Perez-Alday, E.A., Kabir, M.M., Zhang, Y., et al. (2019), "Hemodialysis Procedure–Associated Autonomic Imbalance and Cardiac Arrhythmias: Insights From Continuous 14-Day ECG Monitoring", Journal of the American Heart Association, Vol. 8 No. 19, available at:https://doi.org/10.1161/JAHA.119.013748.
6. Samanta, R., Chan, C., & Chauhan, V. S. (2019). Arrhythmias and Sudden Cardiac Death in End Stage Renal Disease: Epidemiology, Risk Factors, and Management. Canadian Journal of Cardiology, 35(9), 1228-1240.
7. Makar, M. S., & Pun, P. H.(2017). Sudden cardiac death among hemodialysis patients. American Journal of Kidney Diseases; 69(5), 684-695.
8. Oktavia, D., Suhardjono, Nasution, S.A. and Setiati, S. (2013), "The clinical factors' prediction of increased intradialytic QT dispersion on the electrocardiograms of chronic hemodialysis patients.", Saudi Journal of Kidney Diseases and Transplantation : An Official Publication of the Saudi Center for Organ Transplantation, Saudi Arabia, Vol. 24 No. 2, pp. 274–280.
9. Adam, W. and Mutagaywa, R. (2021), Intradialytic Arrhythmias Among Patients with End Stage Renal Disease on Maintenance Hemodialysis at Muhimbili National Hospital.
10. Al-Ameen, A.M., Atia, M.A., Bashandy, M.S., Ahmed, O.M. and Nawar, B.E.M. (2019), "Cardiac Arrhythmia and Blood Pressure Variability in Hemodialysis Patients", The Egyptian Journal of Hospital Medicine, Vol. 76 No. 1, pp. 3291–3298.
11. Tumlin, J. A., Roy-Chaudhury, P., Koplan, B. A., Costea, A. I., Kher, V., Williamson, D., . . . Charytan, D. M. (2019). Relationship between dialytic parameters and reviewer confirmed arrhythmias in hemodialysis patients in the monitoring in dialysis study. BMC nephrology, 20(1), 80.
12. Alawwa, I., Al-Hindi, R., Alfraihat, N., Obeid, A., Ibrahim, S., Jallad, S., Al-Awwa, A., et al. (2020), "Prevalence and associated factors of undiagnosed atrial fibrillation among end-stage renal disease patients on maintenance haemodialysis: A cross-sectional study", BMC Cardiovascular Disorders, BMC Cardiovascular Disorders, Vol. 20 No. 1, pp. 1–9.
13. Mahmood, N., Haq, A.M., Giasuddin, A., Jhuma, K.A., Hoque, M.M. and Chowdhury, S.S. (2017), "Patterns of Cardiac Arrhythmia in Haemodialysis Patients", Anwer Khan Modern Medical College Journal, Vol. 7 No. 1, pp. 28–33.

14. Mitsuma, W., Matsubara, T., Hatada, K., Imai, S., Saito, N., Shimada, H. and Miyazaki, S. (2016), “Clinical characteristics of hemodialysis patients with atrial fibrillation: The RAKUEN (Registry of atrial fibrillation in chronic kidney disease under hemodialysis from Niigata) study”, Journal of Cardiology, Japanese College of Cardiology, Vol. 68 No. 2, pp. 148–155.
15. Roy-Chaudhury, P., Tumlin, J. A., Koplan, B. A., Costea, A. I., Kher, V., Williamson, D., Pokhariyal, S., Charytan, D. M., Tumlin, J., & Reddy, V.(2018). Primary outcomes of the Monitoring in Dialysis Study indicate that clinically significant arrhythmias are common in hemodialysis patients and related to dialytic cycle. Kidney international; 93(4), 941-951.
16. Sacher, F., Jesel, L., Borni-Duval, C., De Precigout, V., Lavainne, F., Bourdenx, J.P., Haddj-Elmrabet, A., et al. (2018), “Cardiac Rhythm Disturbances in Hemodialysis Patients: Early Detection Using an Implantable Loop Recorder and Correlation With Biological and Dialysis Parameters”, JACC: Clinical Electrophysiology, Vol. 4 No. 3, pp. 397–408.