The Egyptian Journal of Hospital Medicine (October 2020) Vol. 81 (5), Page 2057-2062

Incidence of Atrial Fibrillation in Hemodialysis Patients

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ABSTRACT

Background: Chronic kidney disease patients usually experience several comorbid conditions including cardiovascular disorders and at final end-stage renal disease (ESRD) stage, cardiovascular mortality accounts for about 50% of total mortality. End-stage renal disease (ESRD) patients commonly have a higher risk of developing cardiovascular diseases than general population.

Objective: The aim of the work was to detect the incidence of atrial fibrillation (AF) in hemodialysis patients for six months.

Patients and Methods: The study was a prospective cohort study for six months included 250 adult patients with end stage renal diseases on regular hemodialysis sessions in National Institute of Urology and Nephrology in Cairo, Egypt for at least six months with no past history suggestive of any arrhythmias and normal holter ECG at the start of the study.

Results: The study included 250 patients, of them 37 patients refuse follow up after 6 months and 18 patients were died before our follow up holter ECG so mortality rate 14.4%. For the current study population, there were 102 male patients (52.3%) and 93 female patients (47.7%) with mean age 54.39 ± 9.98 (19:73) and BMI 29.01±1.28 (24.5:34). In study population 96 patients were diabetic (49.2%), 84 patients were hypertensive (43.1%), 100 patients were with ischemic heart diseases (51.3%) with median renal replacement duration 4 (3 – 6) with range (1 – 13). The main etiological causes of dialysis were diabetes mellitus, hypertension and analgesic nephropathy and other different causes of dialysis 35 patients (45%).The study showed association between incidence of AF in hemodialysis patients and different factors as increased BMI (0.006), prolonged duration of renal replacement therapy (0.017), diabetes mellitus (0.005), hypertension (0.000), ischemic heart diseases (0.02) and left atrium dilation (0.000).

Conclusion: It could be concluded that the incidence of AF in patients with ESRD is 16.4% .The risk factors for increased incidence of AF in hemodialysis are; increased BMI, increased duration of renal replacement therapy, hypertension, diabetes mellitus, ischemic heart diseases and left atrium dilation by echocardiography.

Keywords: Chronic kidney disease, End-stage renal disease, Arrhythmias, Atrial fibrillation.

INTRODUCTION

Chronic kidney disease patients usually experienced several comorbid conditions including cardiovascular disorders and at final end-stage renal disease (ESRD) stage, cardiovascular mortality accounts for about 50% of total mortality. End-stage renal disease (ESRD) patients commonly have a higher risk of developing cardiovascular diseases than general population. Chronic kidney disease is an independent risk factor for atrial fibrillation (AF); however, little is known about the AF risk among ESRD patients with various modalities of renal replacement therapy **(1).**

Atrial fibrillation (AF), the most common sustained arrhythmia in clinical practice **(2).** Atrial fibrillation is a serious problem, especially in patients on dialysis. The prevalence of AF in this group of patients is higher than in general population and associated with increased mortality **(3).**

Hemodialysis (HD) is associated with cardiovascular structural modifications; moreover, during HD, rapid electrolytic changes occur. Both factors may favor the onset of atrial fibrillation **(4).**

Factors contributing to the occurrence of AF in patients undergoing dialysis include: age, presence of coronary heart disease, echocardiographic abnormalities (low ejection fraction, atrial enlargement, valvular calcification, left ventricular hypertrophy), heart failure, chronic obstructive pulmonary disease, hypertension, stroke, malnutrition (low levels of albumin, total cholesterol and high-density lipoprotein (HDL), secondary hyperparathyroidism, low pre dialysis systolic blood pressure, duration of renal replacement therapy as well as the method of renal replacement therapy (more frequent in Hemodialysis patients) **(5).**

Patients who have both atrial fibrillation (AF) and renal failure have an increased risk of thrombo-embolism. Renal failure is also a risk factor for bleeding, which makes decisions regarding thromboprophylaxis complicated **(6).**

Clinical trial data support the use of anticoagulant agents to prevent stroke in AF patients. Although several guidelines recommend anticoagulant use for stroke prevention as the

Received:18 /7 /2020
Accepted:17 /9 /2020

primary management for patients with AF, it is controversial in Hemodialysis patients with AF [7].

In routine practice, warfarin is widely used in dialysis patients with atrial fibrillation (AF) for stroke prevention though the ratio of risks to benefits remains unclear. Recent cohort studies investigating the association between warfarin use and the risks of stroke and bleeding in dialysis patients with AF present conflicting results [8].

Aim of the present work was to detect the incidence of AF in hemodialysis patients for six months.

PATIENTS AND METHODS

This Prospective cohort study included a total of 250 adult patients with end stage renal diseases on regular hemodialysis sessions, attending at dialysis units, National Institute of Urology and Nephrology. Selection of patients was based on past history and holter ECG at start of study.

Inclusion Criteria:

- Adult end stage renal disease on regular Hemodialysis for more than six months.
- Hemodialysis patients with ECG showing no AF.
- No history suggestive paroxysmal AF.

Exclusion Criteria:

- Patients known to have AF.

Sampling Method: Nonprobability convenience sample.

Sample Size: Depending on **Zimmerman *et al.*** [9] who found the incidence of atrial fibrillation among Hemodialysis patients is 0.027%, and assuming the confidence interval width=0.025 (on each side) and α=0.05, and by using PASS 11th release the minimal sample size is 203 [10]. 250 cases were included.

Ethical Considerations:

Approval of the ethical committee of Ain Shams University was obtained. Informed written consent after explaining the study purpose, method and benefits was obtained from each patient.

Study Tools:

- **Medical history:** of the patients.
- **Dialysis prescriptions:** for H.D sessions (e.g.: duration of session, number of years of H.D, amount of ultra-filtration every session, pump, filter used**).**
- **Serum electrolytes:** as sodium, potassium, calcium (total and free) and phosphorus.
- **Echocardiography**: for patients.
- **Holter ECG:** for patients at the start of study and after six months.

Statistical analyses

Results were scheduled and analyzed statistically using a PC and programs of MICROSOFT EXCEL 2016 and SPSS v. 21 (SPSS Inc., Chicago, IL, USA**.** Statistical analysis was done using Descriptive: e.g. percentage (%), mean, and standard deviation. Analytical: that involves Paired t-test. A value of P less than 0.05 was considered statistically significant.

RESULTS

Table (1): Shows number and incidence of AF in hemodialysis and other arrhythmias during 6 months

Arrhythmias	Total no. = 195
AF	16 (8.2%)
Bradyarrhythmia	12 (6.2%)
Extra systole	15 (7.7%)
No arrhythmia	152 (77.9%)

AF was occurred in 16 patients during study (6 months) with incidence rate 8.2 % so during one-year, incidence is 16.4%. Brady arrhythmia occurred in 12 patients with incidence rate 6.2% during 6 months, so, during one year is 12.4%. Extra systole occurred in 15 patients with incidence rate 7.7% so incidence rate during one year is 15.4%.

Table (2): Demographic data and AF

		AF group	Non AF group	Test value	P-value	Sig.
		No. = 16	No. = 179			
Age (years)	Mean ± SD Range	59.00 ± 8.28 38 – 70	53.98 ± 10.04 19 – 73	1.942•	0.100	NS
Sex	Male Female	12 (75.0%) 4 (25.0%)	90 (50.3%) 89 (49.7%)	3.598*	0.125	NS
BMI (kg/m²)	Mean ± SD Range	29.85 ± 1.91 27.4 – 34	28.94 ± 1.18 24.5 – 31.7	2.793•	0.006	S

P-value > 0.05: Nonsignificant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
***: Chi-square test; •: Independent t-test. BMI means body mass index**

Age is non-significant with AF group. Sex is non-significant with AF group. BMI is highly significant for AF development.

Table (3): Past medical history

		AF group	Non AF group	Test value	P-value	Sig.
		No. = 16	No. = 179			
D.M	DM	15 (93.8%)	81 (45.3%)	13.822*	0.005	S
	Not DM	1 (6.2%)	98 (54.7%)			
HTN	HTN	11 (68.8%)	73 (40.8%)	4.685*	0.000	S
	Not HTN	5 (31.2%)	106 (59.2%)			
Ischemic heart diseases	IHD	14 (87.5%)	86 (48.0%)	9.152*	0.02	S
	Not	2 (12.5%)	93 (52.0%)			
Other causes of dialysis	Unknown	0 (0.0%)	14 (22.2%)	7.517*	0.276	NS
	ADPKD	0 (0.0%)	10 (15.9%)			
	Analgesics	0 (0.0%)	14 (22.2%)			
	CIN	0 (0.0%)	4 (6.3%)			
	RCC	0 (0.0%)	3 (4.8%)			
	GN	2 (100.0%)	12 (19.0%)			
	Lupus nephritis	0 (0.0%)	6 (9.5%)			

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
***: Chi-square test; ≠: Kruskal-Wallis test. D.M: means diabetes mellitus, HTN means hypertension , ADPKD means adult dominant polycystic kidney diseases, CIN means contrast induced nephropathy, RCC means renal cell carcinoma , GN means glomerulonephritis.**

D.M is significant with AF. HTN is significant with AF. IHD is significant with AF. Other causes of dialysis are non-significant with AF.

Table (4): AF and data correlation:

		AF group	Non AF group	Test value	P-value	Sig.
		No. = 16	No. = 179			
No. of session/week	2	2 (12.5%)	29 (16.2%)	0.150	0.76	NS
	3	14 (87.5%)	150 (83.8%)			
Interdialytic wt. gain/KG	Mean ± SD	2.96 ± 0.85	2.68 ± 0.84	1.297	0.64	NS
	Range	2 – 5	1 – 5			
Session duration/hours	Mean ± SD	3.75 ± 0.45	3.76 ± 0.41	-0.116	0.9	NS
	Range	3 – 4	3 – 4			
Vascular access	AVF	14 (87.5%)	164 (91.6%)	0.313	0.576	NS
	Permcath	2 (12.5%)	15 (8.4%)			
Time occurrence in relation to session	Before session	5 (31.2%)	13 (48.1%)	2.902	0.478	NS
	During session	6 (37.5%)	11 (40.7%)			
	After session	5 (31.2%)	3 (11.1%)			
Duration of RRT/year	Median (IQR)	6 (4 – 10)	4 (3 – 6)	-2.382≠	0.017	S
	Range	2 – 11	1 – 13			

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
***: Chi-square test; •: Independent t-test,**
RRC means renal replacement therapy. Wt. means weight, NO means number,

Number of session per week is non-significant with AF. Intradialytic wt. gain is non-significant with AF. Session duration is non-significant for AF. Vascular access is non-significant for AF. Time occurrence in relation with dialysis session showing non-significant with AF with occurrence is slightly increased during session (37% of total AF). Duration of renal replacement therapy is significant with AF.

Table (5): Showing correlation between LT atrium dilation and AF

		AF group	Non AF group	Test value*	P-value	Sig.
		No. = 16	No. = 179			
LT atrium in ECHO	**LT atrium dilation**	13 (81.2%)	0 (0.0%)	155.826	0.000	HS
	Normal LT atrium	3 (18.8%)	179 (100.0%)			

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant. *: Chi-square test

Left atrium dilation is strongly associated with AF occurrence.

Table (6): Different types of anti-hypertensive drugs

Antihypertensive drugs	Number of patients (195)	Percent %
CCBS	20	23.3%
ACEIs	4	4.7%
BBs	20	23.3%
ARBs	9	10.5%
CCBS and ACEIS	9	10.5%
CCBs and BBS	3	3.5%
CCBs and ARBs	5	5.8%
BBs and ARBS	13	15.1%
ACEIs and BBs	3	3.5%

Different types of anti-hypertensive drugs did not affect or prevent the occurrence of AF with a P.value 0.276. Between our patients (195): 20 patients (23.3%) were on CCBs, 4 patients (4.7%) on ACEIs, 20 patients (23.3%) on BBs, 9 patients (10.5%) on ARBs and other patients were on different combinations without significance between all groups in detection or prevention of AF.

DISCUSSION

Atrial fibrillation (AF) is the most prevalent arrhythmia in clinical practice and leading cause of cardiovascular morbidity. The current estimated prevalence of AF is about between 1% and 4% **[11].** Incidence rate in normal population is 9.4% over 11 years **[12].**

Chronic kidney disease is an independent risk factor for atrial fibrillation (AF); however, little is known about the AF risk among ESRD patients.

Our study was a prospective cohort study for six months included 250 adult patients with end stage renal diseases on regular hemodialysis sessions for at least six months with no past history suggestive of any arrhythmias.

Selection of patients was done using holter ECG at time of selection to exclude the presence of AF and other arrhythmias and repeated after six months in addition to trans-thoracic echocardiography and other labs. Results also were correlated to dialysis session, duration and vascular access.

During the study, 37 patients refused follow up. 18 patients died so mortality rate was 7.2% per six months so supposed to be 14.4% per year in agreement with **Floege *et al.*** **[13]** in which mortality rate was 13.0 %.

In our study new incident cases with AF were 16 patients with incidence rate 16.4% per year in a disagreement with **Zimmerman *et al.*** **[9]** in which incidence rate was 2.7 %which can explained by using more sensitive tools as holter ECG in our study

In our study Gender was not a risk factor for atrial fibrillation in dialysis patients with P. value: 0.125 among AF patients there were 12 males and 4 females, in agreement with **Wizemann *et al.*** **[14]** but in disagreement with **Winkelmayer *et al.*** **[15]** our study was done for short duration done on small number of patients, so new incident cases were few to compare with this study which was done for 14 years on 2.5 million patients.

In Our study age was not risk factors for AF development with P value: 0.1. Patients' age was 38:70 years old in disagreements with **Guo *et al.*** **[16]** which revealed significant correlation between age and AF which can be explained by variable age in our study between 38:70 years old and short duration of our study.

Our study revealed that obesity was a risk factor for development AF with P. value: 0.006. Our patients with BMI ranging from 24.5 to 34 with mean 29.80 ± 1.42 St deviation kg\m2) in agreement with **Badheka *et al.*** **[17].**

In our study hypertension was a significant risk factor for AF development with P value 0.00. All AF patients were hypertensive in agreement with **Liao *et al.*** **[18].**

Different types of anti-hypertensive drugs did not affect or prevent the occurrence of AF with a p.value 0.276. In disagreement to a study **Gorenek *et al.*** **[19]** which revealed that ACE inhibitors and (ARBs) can prevent AF among dialysis patients. Repeated change in patients' anti-hypertensive drugs during study, drugs combinations and lack of enough periods for follow up reveal the dissociation.

In our study diabetes mellitus was a strong significant risk factor for AF development with P value: 0.005 between AF patients 15 patients were diabetic from 16 patients in agreement with **Shen *et al.*** **[20].**

In our study ischemic heart diseases were strongly related to AF development with P value: 0.029. Between our AF patients 14 patients known to have past history of ischemic heart diseases in agreement with **Liao *et al.*** **[18]** **and Shen *et al.*** **[20].**

Left atrium dilation had strong association with AF with P. value 0.00. All AF group were have left atrium dilation in agreement with **Abuhasira *et al.*** **[21].**

Duration of renal replacement therapy was a risk factor for development of AF with P. value 0.017. Which range in AF patients from 2:11 years in agreement with **Mitsuma *et al.*[22]** which was done on 423 patients with end stage renal diseases for 3 years.

Vascular access was not related to development AF with P-value 0.576. Among AF group 14 patients underwent dialysis using AVF and 2 patients with perm-cath with no influence in AF occurrence, in agreement with **Wizemann *et al.*[14].**

Inter diaylatic weight gain was not a risk factor for development of AF with P. value 0.64 which was range from 2 kg to 5 kg (2.5 ± 0.84St. deviation) in AF group in disagreement with study **Korantzopoulos *et al.*[23].** Short duration of study, number of patients, inaccurate weight gain assessment explain the difference.

Numbers of sessions per week and session duration were not significant with AF with P. value 0.76, 0.99 respectively in disagreement to pervious study **[24].** Irregularity in number of session/weeks, inaccurate session duration and inaccurate data registration can limit our results.

Time of hemodialysis session was not related to AF occurrence with P. value 0.478. In relation to dialysis session AF occurrence was observed as: before, during or after dialysis session with no significance between, AF occurred as 5, 6 and 5 respectively in agreement with **Tumlin *et al.* [25].**

Anemia was not as a risk factor for development of atrial fibrillation with P. value 0.38. Hemoglobin was between 8.5: 11.3gm\dl In agreement with **Wetmore *et al.*[26].**

Serum sodium was not affect occurrence of AF in dialysis patients with p-value 0.23. Serum NA ranging from (128 to 139 mmol\l) in agreement with **Vazquez *et al.*[27].**

In our study serum Calcium, Magnesium, phosphorus or parathyroid hormone did not affect the incidence of AF in hemodialysis patients with P. value 0.166, 0.099 and 0.34 respectively in disagreement with **Kim *et al.*[28]** our study included small number of patients and short duration of follow up can explain the disagreement.

Serum potassium is not a risk factor for AF occurrence with P value 0.63 in disagreement with study **Krijthe *et al.*[29]** which was done on 4059 participants. In our study Lack of close follow up, laboratory investigations were done monthly in different labs with inaccurate results can explain the difference.

During the study other arrhythmias rather than AF were detected. Brady arrhythmias were detected in 12 patients with a percentage as 12.4% per year. In disagreement with **Wong *et al.*[30]** 30% done on 50 hemodialysis patients. Patients in our study had variable age, short duration of study and single follow up limit the comparison.

Our study showed time occurrence of Brady arrhythmias was more during hemodialysis session as a ratio 35.3%, 27.8%, 11.1% during, before and after session respectively in disagreement with **Koplan *et al.*[31]**. Small incident cases of bradycardia in our study explain the difference.

Bradyarrhythmia's was no associated with risk factors except hyperkalemia (5.5±0.5) in agreement with study**[32].**

During our study extra systole was detected as incidence rate 15.5% per year in disagreement with **Galeel *et al.*[33]** with corresponding incidence 24.5% respectively. Our study had Small number of patients and short duration which can explain the difference.

CONCLUSION

It could be concluded that atrial fibrillation present in patients with end stage renal diseases on regular hemodialysis with incidence rate as 16.4 %per year, in addition there are other arrhythmias present as bradycardia and extra systole with incidence as 14.4%, 25.5% per year respectively.

The risk factors for increased AF incidence are hypertension, diabetes mellitus and ischemic heart diseases, increased body mass index (BMI), increased duration of renal replacement therapy and left atrial dilation.

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