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Deep venous thromboses complicating central vascular access for renal replacement therapy in a tertiary health centre of a developing country

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Abstract

Background/objectives: Central venous cannulation remains an important process in haemodialysis practises world-wide. The study is designed to determine the prevalence of central access deep venous thrombosis (DVT) and its associated risk factors in the studied population.

Methods: A prospective observational study of kidney disease patients who underwent haemodialysis between January 2021 and December 31st2021 was carried out. Socio-demographic and clinical data were extracted using structured pro-forma. Data was analyzed using SPSS version 20.

Results: Of the 98 patients that underwent haemodialysis, 36 (36.8%) were male and 62 (63.2%) were female. Mean age was 48.3±16.7 years. Fifteen (15.3%) had acute kidney injury while 83 (85.0%) had chronic kidney disease. All the patients had emergency dialysis totaling508 sessions. Femoral vein was the most frequently used vascular access (95%) while other vascular access accounted for the remaining (5%). Femoral DVT was seen in 8 (8.2%) patients with majority having CKD (8.4%) .

Conclusion: Iliofemoral DVT was most common (P=0.537). Statistically significant association was observed between occurrence of femoral DVT and AKI (P<0.02).

Keywords: Deep Venous Thromboses, Central vascular access, Haemodialysis, Chronic kidney disease.

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Thrombose veineuse profonde compliquant l'accès vasculaire central pour la thérapie de remplacement rénal dans un centre de santé tertiaire d'un pays en développement

***Bamikefa T A[1,2], Olayemi O A[2,3], Oyedepo D S[4], Yusuf A O[2,3],Hassan M O[1,5], Alebiosu C O[1,2]**

Resume

Contexte/objectifs: La canulation veineuse centrale demeure un processus important dans les pratiques d'hémodialyse dans le monde entier. L'étude est conçue pour déterminer la prévalence de la thrombose veineuse profonde (TVP) d'accès central et ses facteurs de risque associés dans la population étudiée.

Méthodes: Une étude observationnelle prospective de patients atteints d'insuffisance rénale ayant subi une hémodialyse entre janvier 2021 et le 31 décembre 2021 a été réalisée. Les données socio-démographiques et cliniques ont été extraites à l'aide de formulaires structurés. Les données ont été analysées à l'aide de SPSS version 20.

Résultats: Sur les 98 patients qui ont subi une hémodialyse, 36 (36,8 %) étaient des hommes et 62 (63,2 %) étaient des femmes. L'âge moyen était de 48,3 ± 16,7 ans. Quinze (15,3 %) souffraient d'insuffisance rénale aiguë tandis que 83 (85,0 %) souffraient d'insuffisance rénale chronique. Tous les patients ont eu une dialyse en urgence totalisant 508 séances. La veine fémorale était l'accès vasculaire le plus fréquemment utilisé (95 %) tandis que les autres accès vasculaires représentaient le reste (5 %). Une TVP fémorale a été observée chez 8 (8,2 %) patients dont la majorité avait une IRC (8,4 %).

Conclusion: La TVP ilio-fémorale était la plus fréquente (P=0,537). Une association statistiquement significative a été observée entre la survenue d'une TVP fémorale et l'IRA (P<0,02).

Mots clés: Thrombose veineuse profonde, Accès vasculaire central, Hémodialyse, Insuffisance rénale chronique.

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INTRODUCTION

There are various forms of kidney diseases ranging from acute kidney injury (AKI), chronic kidney injury (CKD) and ultimately end stage renal disease (ESRD) requiring renal replacement therapy with diverse indications. Although there are various forms of renal replacement therapy, haemodialysis (HD) still remains a frontline treatment modality world-wide with its attendant peculiarities (1). Since the inception of haemodialysisas a viable option of renal replacement therapy many decades ago, Sub-Saharan Africaand Nigeria haswitnessed establishment of many centers to meet the ever-increasing population of kidney disease patients requiring dialysis (2,3).

Vascular route is needed for haemodialysis to be carried out and may affect outcome in patients with renal disease. This is because some known causes of kidney diseases also have vessel affectation as part of their clinical syndromes. Temporary access into the femoral and or jugular vessels which is commonly practiced in Sub-Saharan Africa including Nigeria where health resources and personnel are scarce has been reported as one of the causes of in-effective dialysis which may culminate in death when complication/s arises (3,4,5,6). Permanent vascular access use is increasing gradually in Nigeria with more Nephrologist been trained to carry out tunneled jugular catheterization although patients undergoing dialysis_via arterio-venous fistula are still not many (7).

Central venous cannulation is the process which involves insertion of catheters into central veins which could be femoral, subclavian or internal jugular vein under aseptic condition for in and or out-patient use (6). There are other advantageous uses of central vascular lines offer which ranges from administration of drugs, blood products, parenteral feeding, fluid administration to mention a few (6). Despite the numerous advantages of central line, it has some associated complications which range from arterial puncture, blood stream colonization by infectious micro-organisms, pneumothorax and rarely death making observing strict asepsis as well as utilization of experienced and competent nephrologist during and after the procedure extremely important (8).

Arterial puncture affecting the carotid artery was the most frequently reported complication while thrombosis affecting the internal jugular veins was reported as theleast observed complication in a recent publication in the North-central part of the country (7). Despite the fact that femoral access is the commonly used for haemodialysis in our environment with a gradual shift towards other central vessels, there is paucity of data on the prevalence of deep venous thromboses affecting femoral vein (3,4).

It is important therefore to carry out clinicalevaluation of this procedure in our facility to highlight the frequency of deep venous thromboses of the central vessels and its associated peculiarities to reduce its occurrence if possible and to allow for effective preparedness to attend to this complication if and when it arises. This study aims to highlight the incidence of femoral vein thromboses in patients undergoing haemodialysis in ourfacility and its associated peculiarities where femoral vessel use for dialysis is still common with a gradual shift towards internal jugular access creation.

MATERIALS AND METHODS

This was a prospective observational study involving ninety-six (96) patients who had femoral venous cannulation done for haemodialysis between January 1st 2021 to December31st 2021.Approval for this study was obtained from the Ethics and Research Committee of Osun State University Osogbo, Osun State. Consecutive patients for central vascular cannulation were adequately counselled and written informed consent obtained. Data was extracted using structured questionnaire from the case note, dialysis charts, record book and interviews. Information extracted included the demographic attributes of the patients, portal of admission, past history of thromboses, clinical diagnosis, aetiology of kidney disease, biochemical profile at initiation of dialysis, site ofcatether insertion, type of vascular access, catheter size, frequency of dialysis, session of dialysis, duration of dialysis, frequency of catheter change,type of dialyzer , clotting profile, occurrence of deep vein thrombosis, site of thrombosis and presence of doppler ultrasound evidence of deep venous thrombosis. Uncooperative patients, failure to give informed consentandexistence of coagulopathies were reasons for exclusion from vascular route creation.

Niprol Surdial X machines which uses bicarbonate dialysate with dialysate flow rate of 500mls/min and blood flow rate ranging between 200-400mls/min depending on the type of accesswere used for dialysis in this study. Elisio 17H synthetic one-time use polynephron dialyzer with a surface area of 1.7m^2 was used for dialysis

in all the patients. After obtaining informed consent, patients were cleaned and sterile drape applied with strict observance of asepsis. Dialysis catheters were inserted after site for access establishment has been chosen. After local infiltration with plain 1% lidocaine, catheter was introduced into thefemoral vein at the mid-point between the anterior-superior iliac spine and pubic tubercle beneath the inguinal ligament medial to femoral artery pulsation. Vascular access into the right internal jugular vein was done after the patients were placed in the Trendelenburg position with the internal jugular vein localized at the apex of the triangle formed by the two heads of the sternocleidomastoid muscle lateral to the common carotid artery pulsation. Modified Seldinger method was adapted to advance the catheter over the guide wire.

Data obtained was analysed using Statistical Productand ServiceSolutions (SPSS) version 20. Continuous data was expressed as mean (standard deviation)or as median (interquartile range) where appropriate. Categorical data was summarized using frequencies and percentages. Continuous variable was analysed using student T-test while categorical variable was analysed using chi-square. Analysis of Variance (ANOVA) was used to compare variablesbetween more than two (2) groups. Multi variate regression analysis was utilized to identify the various predictors of femoral deep venous thromboses.A p-value of <0.05 was regarded as statistically significant.

RESULTS

A total of 98 patients had central venous cannulation in the year under review. Thirty-six patients (n=36,36.7%) were males and sixty-two patients (n=62, 63.3%) were females with a maleto female ratio of 1:1.7. The age ranged between 16 to 87 years with a mean age of 48.32 ±16.63 years. The age and gender stratification of the patients_is shown in Table1.The peak age of presentation varied across gender although overall it was between ages 45 and 64 years. The commonest age group affected in AKI were ages 18-44 while CKD was more frequently encountered among the middle age group (45-65). Twenty-nine (29.6%), twenty-two (22.4%), twenty-one (21.4%), nineteen (19.4%) and seven (7.2%) patients were traders, civil servants, artisan, unemployed and students respectively. Majority of the study population (82.7%) were married while the single and widowed constituted 14.2% and 3.1% respectively. Haemodialysis was initiated on an emergency basis in all the patients. The distribution of the diagnosis across gender is tabulated in Table 2.

Twenty-nine (29.6%) patients comprising nine males (25%) and twenty females (32.3%) had CKD from multiple ($p \geq 2$) aetiologies. The source of referral for haemodialysis is shown in Figure 1. Majority of the patients (n=46, 46.9%) were admitted via the accident and emergency unit of the hospital.The total number of haemodialysis sessions was 508 with a mean value of 5.18 ± 0.41. All the patients had dialysis using 12Fr x 15 cm double lumen catheter which was either curved or straight. The total sessions for AKI and CKD were 49 (3.27±1.80) and 459 (5.53±0.46) respectively with patients with CKD having more exposure to haemodialysis than those with AKI. Sepsis was the commonest precipitant of acute decompensation in CKD patients (n=35, 42.2%) closely followed by accelerated hypertension (n=24, 28.9%) with each having a female preponderance. The gender distribution of the other precipitants is shown in Table 3. Only one patient with CKD had more than 1 precipitant of acute decompensation.

The clinical characteristics of the respondent based on their clinical diagnosis is shown in Table 4. The highest number of patients requiring dialysis were seen in October of the year under review (n= 15.15.5%) while the least was seen in January and June (n=3, 3.1%). Femoral vein was the most used vascular access for haemodialysis accounting for 94.9% which is remotely followed by non-tunnelled jugular venous access (3.6%).

The median duration on cannulation was 4 days. Deep venous thromboses (DVT) of the femoral vein was observed more in patients with CKD (n=7, 7.1%) when compared to AKI (n=1, 1.02. %) with a total incidence of 8.2%. The mean packed cell volume (PCV) before commencement of dialysis was higher in males (25.48±7.99) than females (23.67±6.07). Features of DVT were seen in all the patients after in-dwelling femoral catheter had stayed for > 7 days although this was not statistically significant (P-value=0.187). None of the patients that developed DVT had a prior occurrence.

The gender variation in the occurrence of DVT is shown in Figure 2. There was no patient with thrombosis of the internal jugular vein. Arteriovenous fistula was used for dialysis in only 1 patient which was created from the referral centre after initial dialysis with tunnelled internal jugular access. Chronic Kidney Disease patients

who had acute decompensation of their renal function from sepsis had more incidence of femoral deep venous thrombosis although this was not statistically significant (P-value=0.557). A statistically significant relationship was found between AKI and occurrence of DVT (X^2= 15.00, P-value = < 0.02). The development of DVT was not statistically influenced by the number of precipitants as well as presence of multiple aetiologies of CKD (X^2=0.09, P-value=0.764).

The characteristics of the study population according to the presence or absence of central vascular access DVT is shown in Table 5. It was statistically evident that deep venous thromboses was more likely to affect the Iliofemoral veinthan the superficial femoral vein (P-value < 0.0001). In this study the occurrence of DVT following central venous catheterization was not related to age, packed cell volume at the initiation of dialysis, frequency of catheter change, type of dialyzer used, number of attempts at catheterization and site of vascular access on regression analysis. (See Table 5)

DISCUSSION

Temporary or permanent vascular route established in the central vessels of the thigh, neck or utilization of arteriovenous fistula allows for therapy optimization in patients with renal failure while awaiting transplantation for those with progressive decline in kidney function(6). Majority of the study population were of the female gender which is in contrast to previously documented finding by Okunola et al (9) in the same centre and recent finding in the North-central part of the country with equal gender distribution(3). This may be linked to better health seeking attitude in female compared to their male counterparts. It could also be due to a skewed referral system.

A mean age of 48.3±16.6 yearswas seen similar to previous finding in our centre and other parts of the country (3,7,9). The increasing occurrence of kidney disease in the younger age distribution compared to the western world where it is commoner in the elderly may be due to interplay in environmental, socio-economic and genetic factors not excluding increasing burden of infectious aetiology in our environment (5,10). Chronic kidney disease (CKD) accounted for 84.7% of the diagnostic indication for vascular routeestablishment for haemodialysis which is similar to previous finding in Nigeria and Sub-Saharan Africa (3,4,7,9).

The skewness of the diagnostic indication for vascular access creation for haemodialysis towards CKD as opposed to AKI has also been reported in the Western world (10). Hypertension, obstructive uropathy and glomerulonephritis were the most frequently encountered aetiology of CKD while sepsis accounted for approximately 50% of the causes of AKI in the study population. This observation is in accord with previously documented report in the centre as well as finding in some parts of the country which is in contrast to previously reported glomerulonephritides preponderance (3,4,9,11). Accelerated hypertension was the most frequently encountered precipitant of acute decompensation in patients with CKD whichcould emanate from the underlying aetiology, poor health seeking attitude, low socio-economic status limiting access to blood pressure lowering medications, dietary indiscretion, ignorance and lack of abundant health budgetaryallocation for all the populace.

Femoral venous access was used for haemodialysis initiation in more than 90% of the studied population. This is similar to the findings in most of the previous studies in Nigeria with a recent shift towards internal jugular cannulation although a few centers used subclavian vein (3,7,9). The predominant use of femoral venous access could be due to late presentation resulting in emergency initiation of haemodialysis, low nephrologist/patients' ratio as well as financial constraint on the part of the patients due to lack of effective national health coverage (3,4,12.13). The utilization of permanent vascular route for dialysis in our study which was low (1%) has been reported in previous studies in the countryand may be due to, low/ none existence of pre dialysis care, late nephrologist referral, high financial implication of AV fistula creation as well as unequal distribution of clinical experts in that field (4,9,12,13). This is in contrast to report from Ethiopia where close to 50% of patients were dialyzed via AVF (14).

The prevalence of deep venous thromboses in this study was 8.2% which was similar 8.9% reported by Dada et al (15) in South-West Nigeria. This is however lower than 11.2% reported by Joynt et al[16] in China and 34% reported by Durbec et al[17]in his prospective evaluation of use of femoral catether in critically ill medical and surgical patients. Affectation of iliofemoral vein which accounted for 67.5% of the cases of DVT in this study (p-value= <0.0001) further supports earlier report of increased affectation of this vessel by lower limb thrombosis (16). As demonstrated in our study, occurrence of DVT was not related to the

frequency of placement trial, presence of blood collection following damage to the adjoining artery, coagulation profile of the patient and how long the catheter was used for dialysis or drug administration (17).

Deep venous thrombosis can begin on the first day of cannulation although all the patients with DVT in this study showed clinical symptoms after being on catether for more than 7 days. In a recently published study in Indonesia, all four patients developed DVT after a month on bi- luminal femoral catheter (18). The likely explanation for the DVT observed may be due to low catheter vessel ratio (CVR) which was not measured although latest guideline proposed > 45% CVR (19). The development of thrombus is usually due to interplay between local and pro thrombotic factors. Utilization of double lumen catheters for HD has been documented to cause damage to the vascular endothelium as well as reduction in the lamina flow with resultant stasis and its sequelae (20). In conclusion, although the occurrence of central vascular access related DVT was seen in 8.6% of patients who had haemodialysis in this study with predilection for the femoral veins, further studies will be needed to unravel the peculiarities enabling its occurrence.

The study was limited due to inability to do doppler ultrasound of the femoral vessels prior to the commencement of renal replacement therapy to discover those with risk factors for latter occurrence of femoral DVT as well as those with asymptomatic DVT and inability to measure the catheter vessel ratio (CVR) in all the patients that had femoral vein cannulation most importantly in those who later developed femoral vein DVT.

Conflict of Interest: None declared.

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Table 1: Age and gender stratification of patients

Agegroup(yrs.)	Male n (%)	Female n (%)	Total n (%)	X^2	P-value
< 18	1 (2.8)	0 (0)	1 (1.0)		
18-44	17 (47.2)	19 (30.6)	36 (36.7)		
45-64	13 (36.1)	30 (48.4)	43 (43.9)		
=65	5 (13.9)	13 (21.0)	18 (18.4%)		
Mean ±SD	51.1± 15.6	43.5 ± 17.5	48.3 ± 16.6	4.83	0.185

Table 2: Gender stratification of diagnosis of the study population according to underlying aetiology

Diagnosis	Male n (%)	Female n (%)	Total n (%)	X^2	P-value
CKD	27 (75.0)	56 (90.3)	83 (84.7)		
AETIOLOGY					
Hypertension	10 (27.8)	29 (46.8)	39 (39.8)		
DM	4 (11.1)	5 (8.1)	9 (9.2)		
Obstructive Uropathy	5 (13.9)	15 (24.2)	20 (20.4)	10.064	0.073
Glomerulonephritis					
ADPKD	8 (22.2)	6 (9.7)	14 (14.3)		
	0 (0)	1 (1.6)	1 (1.0)		
AKI	9 (25.0)	6 (9.7)	15 (15.3)		
AETIOLOGY					
Sepsis	4 (66.7)	3 (33.3)	7 (46.7)		
Hypovolemia	0 (0)	3 (33.3)	3 (20.0)		
Pre-eclampsia	0(0)	1(11.1)	1 (6.7)		
Malignancy	0 (0)	1 (11.1)	1 (6.7)	7.857	0.249
Herbicides	0 (0)	1 (11.1)	1 (6.7)		
Ruptured Viscus	1 (16.7)	0(0)	1 (6.7)		
Nephrotoxins	1 (16.7)	0 (0)	1 (6.7)		

CKD- Chronic kidney disease, AKI- Acute kidney injury, DM- Diabetes Mellitus,
ADPKD- Autosomal Dominant Polycystic Kidney Disease

Table 3: Precipitant of acute decompensation across gender in patients with CKD

Precipitant	Male n (%)	Female n (%)	Total n (%)	X^2	P-value
Sepsis	12 (44.4)	23(41.1)	35 (42.2)		
Sepsis& Accelerated HTN	1(3.7)	0 (0)	1(1.2)		
Nephrotoxins	5 (18.5)	10(17.9)	15(18.1)		
Accelerated HTN	5(18.5)	19(33.9)	24 (28.9)		
Unknown	4 (14.8)	4 (7.1)	8 (9.6)		
Total	27 (32.6)	56 (67.4)	83 (100)	4.736	0.315

Table 4: Clinical characteristics of the study population across diagnostic stratification

Parameters	Total n (%)	CKD n (%)	AKI n (%)	X^2	P-value
Access type					
Femoral	93 (94.9)	78 (94)	15(100)		
IJC	1 (1.0)	1 (1.2)	0		
AVF/Tunnel	1(1.0)	1(1.2)	0	0.952	0.813
Femoral& IJC	3 (3.1)	3 (3.6)	0		
Cannulation Frequency					
Once	58 (59.2)	45 (54.2)	13 (86.7)		
Twice	25 (25.5)	24 (28.9)	1 (6.7)	5.626	0.131
Thrice	14 (14.3	13 (15.7)	1 (6.7)		
>3times	1 (1.0)	1 (1.2)	0		
Symptom of Thromboses					
Swelling	6 (6.1)	5 (6.0)	1 (6.7)	0.372	0.829
Pain	2 (2.0)	2 (2.4)	0		
No symptom	90 (91.8)	76 (91.6)	14 (93.3)		
Cannulation Duration(days)					
1-5	15 (15.3)	10 (12.0)	5 (33.3)		
6-10	48 (49.0)	40 (48.2)	8 (53.3)		
11-15	15 (15.3)	13 (15.7)	2 (13.3)	7.488	0.187
16-20	10 (10.2)	10 (12.0)	0		
21-25	6 (6.1)	6 (7.2)	0		
>25	4 (4.1)	4 (4.8)	0		
Prior cannulation					
Yes	3 (3.1)	3(3.6)	0	0.599	0.455
No	95 (96.6)	80 (96.4)	15 (100.0)		
Nos of attempt					
1	58 (59.2)	45 (54.2)	13 (86.7)		
2	25 (25.5)	24 (28.9)	1 (6.7)	5.626	0.131
3	14 (14.3)	13 (15.7)	1 (6.7)		
4	1 (1.0)	1 (1.2)	0		
DVT					
Yes	8 (8.2)	7 (8.4)	1 (6.7)	0.053	0.818
No	90 (91.8)	76 (91.6)	14 (93.3)		
Type of DVT					
Acute	6 (75.0)	5 (71.4)	1 (100.0)	0.381	0.537
Sub-acute	2 (25.0)	2 (28.6)	0		
Vessel affected					
Iliofemoral vein	5 (62.5)	5 (71.4)	0	1.143	0.285
SFV	3 (37.5)	2 (28.6)	1 (100.0)		

DVT = Deep Venous Thromboses; SFV = Superficial Femoral Vein;
CKD = Chronic kidney disease; AKI = Acute kidney Injury.

Table 5: Stratification of the study population characteristics according to the presence or absence of DVT

Parameters	All Patients	Presence of DVT n (%)	Absence of DVT n (%)	P-value
	98	8 (8.2)	90 (91.8)	
Mean age	48.32 ±16.6	48.00 ±12.86	48.34±16.99	0.956
Gender				
Male	36 (36.7)	4 (50.0)	32 (35.6)	0.417
Female	62 (63.3)	4 (50.0)	58 (64.4)	
Frequency of Cannulation				
Once	58 (59.2)	3 (37.5)	55 (61.1)	
Twice	25 (25.5)	4 (50.0)	21 (23.3)	0.416
Thrice	14 (14.3)	1 (12.5)	13(14.4)	
>3 times	1 (1.0)	0	1 (1.1)	
Number of Precipitant				
1	97 (98.9)	8 (8.2)	89 (91.8)	0.764
=2	1 (1.1)	0	1 (100.0)	
Clinical Diagnosis				
CKD				
AKI	83 (84.7)	7 (8.4)	76 (91.6)	0.557
	15 (15.3)	1 (6.7)	14 (93.3)	< **0.02***
Vessel affected				
Iliofemoral vein	5	5 (62.5)		
SFV	3	3 (37.5)	90	<**0.0001***
Others	0			

DVT = Deep Venous Thromboses; CKD = Chronic kidney disease; AKI = Acute kidney injury; SFV = Superficial femoral vein; *Statistically significant at a P-value of < 0.05.

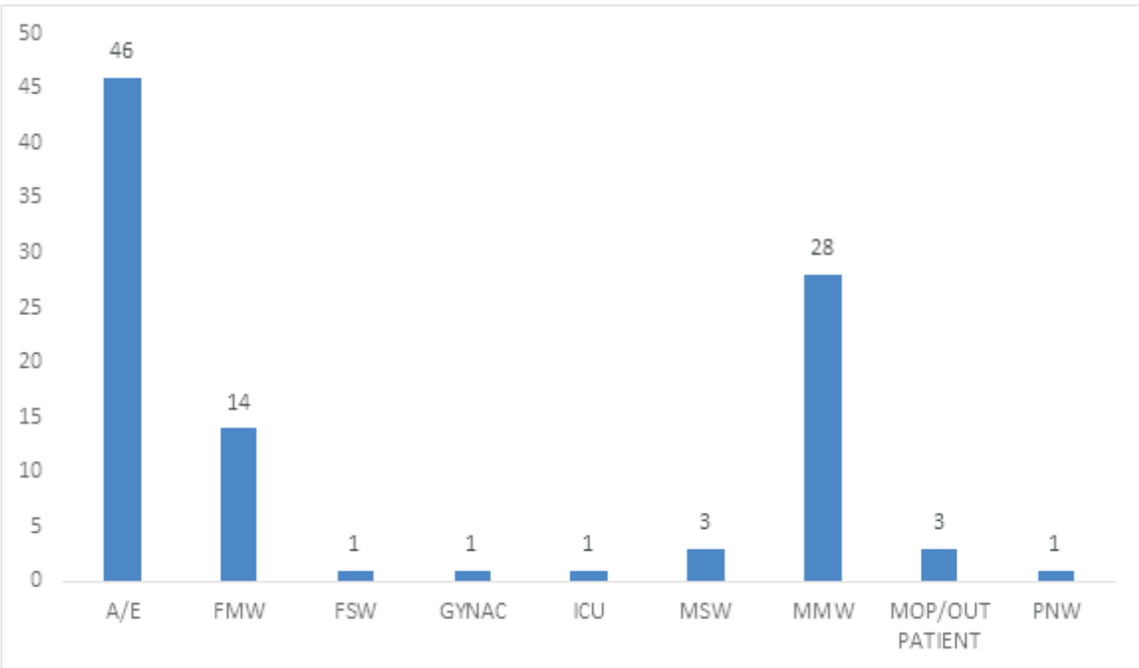

Figure 1: Showing source of the distribution of the patients who had haemodialysis across the wards A/E = Accident and Emergency, FMW = Female Medical Ward, FSW = Female Surgical Ward, GYNAC = Gynecology Ward, ICU = Intensive Care Unit, MMW = Male Medical Ward, MSW = Male Surgical Ward, MOP/OUTPATIENT = Medical Out Patient. PNW = Post Natal Ward.

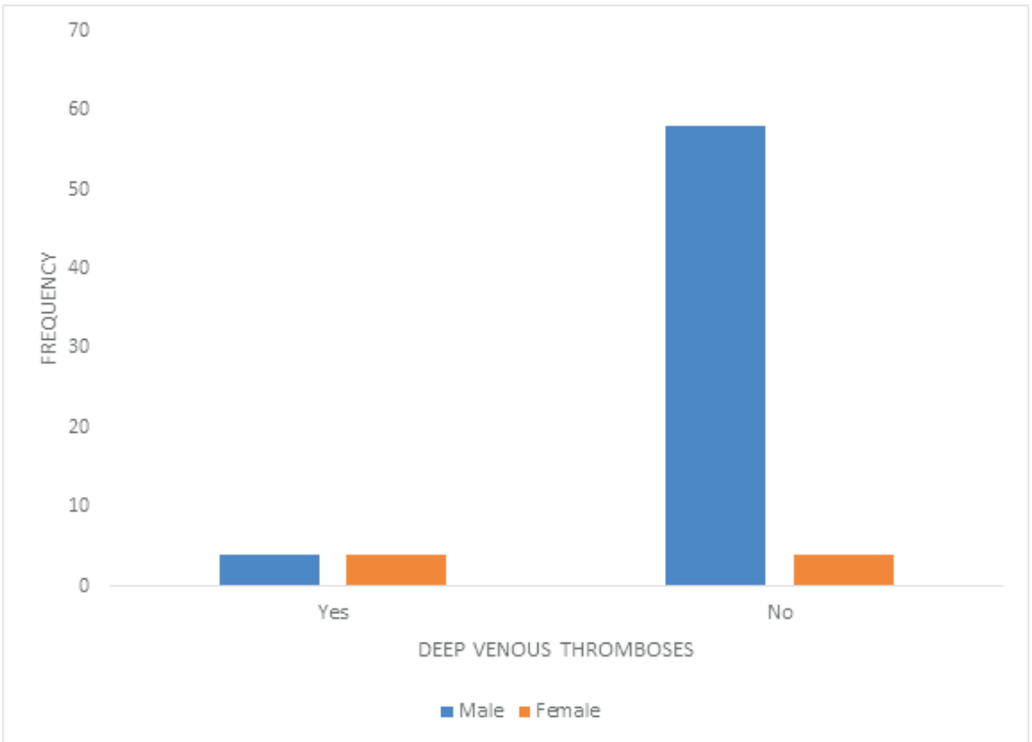

Figure 2: Showing Gender distribution of Deep Venous Thromboses among the study population.