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Prolonged Bleeding Following Removal of Arterio-Venous Fistula Needles after Hemodialysis Therapy

Chacha M. Makuri[1*], Omary Minzi[1], Alphonce Marealle[1], Paschal Ruggajo[2,3]

[1]Department of Clinical Pharmacy and Pharmacology, MUHAS, Dar Es Salam, Tanzania.
[2]Renal Unit, Muhimbili National Hospital.
[3]Department of Internal Medicine, School of Medicine, Muhimbili University of Health and Allied Sciences, Dar Es Salam, Tanzania.

***Corresponding author:**

Chacha M. Makuri

Muhimbili University of Health and Allied Sciences

P. O. Box 65001

Dar es Salaam, Tanzania

Email: cmmakuri@gmail.com

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Abstract

Background
Bleeding at fistula sites in patients with end stage renal disease (ESRD) is a common and potentially serious complication that contributes to blood loss (anemia). This study aimed to determine the factors that influence prolonged bleeding at fistula puncture sites following removal of fistula needles.

Methods
This was a descriptive cross-sectional study. We consecutively enrolled patients who underwent maintenance hemodialysis between May and October 2017 at Muhimbili National Hospital and Access Dialysis Centre in Dar es Salaam, Tanzania. A case report form (CRF) was used for data collection.
Prolonged bleeding was assessed by measuring activated partial thromboplastin time (aPTT) and compression time (CT). Descriptive statistics and regression analysis were used to assess the association between factors and tease out the independent factors associated with prolonged bleeding at fistula puncture site. A two-tailed p-value <0.05 was used as a cut-off for statistical significance.

Results
One hundred and fifteen patients were recruited for the study whereby 81(70.4%) of participants had elevated aPTT (> 31 seconds) and 4 (3.5%) had prolonged compression time (> 15 minutes). The mean aPTT and compression time of the participants were 42 ± 17.6 seconds and 5 ± 2.9 minutes respectively. Over half of participants 67(58.2%) had normal compression time (≤ 15 minutes). Elevated serum urea levels (> 7.4mmol/L) was the only factor significantly associated with elevated aPTT (OR=4.143 95% C.I (1.021-16.810), p=0.047).

Conclusion
The findings have demonstrated that elevated serum urea levels are significantly associated with prolonged bleeding time following removal of Arterio-Venous fistula needles after completion of a hemodialysis therapy session. This study suggests that, in hemodialysis procedure where a fixed dose of heparin is generalized to all patients there is a chance of exceeding the individual's requirements.

Recommendations
Serum urea levels should be factored in when gauging the individual risk of arterio-venous fistula site bleeding for patients using heparin for anticoagulation during hemodialysis. Further studies with large sample sizes are recommended to elucidate how other predisposing factors may affect A-V fistula bleeding.

Keywords: Hemodialysis, heparin, prolonged bleeding, urea reduction ratio, A-V Fistula, aPTT, Compression time, blood urea.

Introduction

End stage renal failure (ESRF) is a total and permanent kidney failure with estimated glomerular filtration rate (eGFR < 15mL/min/1.73m^2 (1). End stage renal disease is becoming common ailments in Tanzania with prevalence of 7 to 14% among adults by 2015(2, 3). The growth of ESRD population keeps increasing parallel to the rising incidence of diabetes mellitus, hypertension and aging population which are the major risk factors (2 -6).

Patients with end stage renal disease (ESRD) are managed with hemodialysis (HD) in which heparin is added (7, 8). Heparin is used as a blood thinning agent to facilitate blood flow, prevent thrombosis and clotting of the dialyzer (9, 10). It has a half-life of 30-120 minutes in health individual and is increased in renal failure patients as 35% of heparin is excreted via the kidneys (9,10).

Following parenteral administration, approximately one-third of the molecules present in UFH bind to anti-thrombin III, and provide the anticoagulant properties by activating the serine protease inhibitor anti-thrombin III that inhibits conversion of prothrombin to thrombin and factors Xa and IXa (11-12). The remaining two-thirds of the heparin molecules bind to endothelial cells and macrophages (monocytes cells) and cleared from the circulation (11 - 12).

Monocytes and endothelial cells

Monocytes and endothelial cells have ability to clear circulating heparin and affect its pharmacokinetics and pharmacodynamics. There is a decrease of monocyte counts in ESRD patients because the presence of blood urea and other toxins impairs endocytosis ability of monocytes and monocytes-derived dendritic cells. Lim et al, reported that there is a decrease in monocytes and endothelial cells mass that affects extent of UFH binding following intravenous infusion in ESRD patients (13,14). Furthermore, in 2006, Pena and colleagues conducted a study on the relationship between the vascular endothelial function and body weight among normal, overweight and obese children and revealed that vascular endothelial

function and monocytes cells are primarily determined by body weight / BMI. Overweight patients are rich in monocyte counts (extra-vasculature) and endothelial cells that predict the need of a larger heparin dose (15, 16).

Blood urea levels and urea reduction ratio of ESRD Patients during hemodialysis

There is elevation of blood urea nitrogen (BUN) in patients with ESRD. Blood urea levels result to platelet dysfunctions leading to prolonged bleeding (17, 18). Urea Reduction Ratio (URR) is the principal measure of hemodialysis dose. Adequate hemodialysis dose is achieved, if URR is greater than 65%(19 - 25).

$$URR = \frac{\text{Predialysis urea level - Postdialysis urea level (mg/dL)}}{\text{Pre-dialysis urea level}} \times 100\%$$

Body Mass Index (BMI) of ESRD Patients during hemodialysis

Heparin (UFH) is dosed based on BMI during hemodialysis. However, many studies demostrated that prolonged bleeding measured by aPTT was not a significant affected by BMI (26 – 32).

Bleeding at fistula sites of ESRD Patients during hemodialysis

In hemodialysis procedure where a fixed dose of heparin is generalized to all patients there is a chance of exceeding the individual's requirements resulting to excessive bleeding (33 - 37). The bleeding effect of heparin blood concentration is measured by activated partial thromboplastin time (aPTT) and compression time for clot formation under controlled conditions (38 - 42). Bleeding at fistula sites in patients with ESRD is a common and potentially serious complication that leads to blood loss (anemia) and difficult in achieving optimum compression time (1-15minutes) and aPTT (≤31 seconds) (43 - 45). The cause of bleeding diathesis in patients with ESRD is multifactorial (46- 48).

Problem statements

In hemodialysis procedure where a fixed dose of heparin is generalized to all patients there is a chance of exceeding the individual's requirements resulting to excessive bleeding (33 - 42).

Bleeding at fistula sites in patients with ESRD is a common and potentially serious complication that leads to blood loss (anemia) and difficult in achieving optimum compression time (1-15minutes) and aPTT (≤31 seconds) (43 - 45). The cause of bleeding diathesis in patients with ESRD is multifactorial (46- 48). Prolonged bleeding at fistula puncture sites following removal of fistula needles can be influenced by several factors such as body mass index, monocyte counts, and heparin and blood urea levels.

Rationale

The findings from this study may help Clinicians to design heparin dosing protocol and dose adjustments in relation to bleeding parameters influenced by body weight, monocyte counts, and heparin and blood urea levels.

Research questions

1. What is the effects of body mass index, monocyte counts and blood urea levels on compression time and activated partial thromboplastin time (aPTT) at the end of hemodialysis, HD?

Specific objectives

1. To determine the effects of body mass index, monocyte counts and blood urea levels on compression time and activated partial thromboplastin time (aPTT) at the end of hemodialysis, HD?

Methods and study subjects

Study design & subjects

This was a descriptive cross-sectional study conducted among patients ESRD attending maintenance hemodialysis at Muhimbili National Hospital and Access Dialysis Centre in Dar es salaam City, Tanzania, between May and October 2017.

Patient recruitment

Convenient sampling procedure was employed during recruitment based on the inclusion and exclusion criteria. In this sampling procedure subjects were selected because of their convenient accessibility and proximity to the researcher. Inclusion criteria included: those above 18 years of age and who consented to be part of the study. The exclusion criteria included: those HD patients under regular uses of anti-platelets therapy, serious ill patients and those with congenital coagulopathy like hemophilia.

Data collection

This study used a Case Report Form (CRF) to capture required information and data for variables, such as social-demographic information, patient's medical history, and hemodialysis status and laboratory values. The routine procedure at the dialysis unit was followed during data collection. The eligible patients were followed from zero hour to the end of hemodialysis session (maximum of 4 hours). Demographic data and laboratory values were collected based on a checklist in the CRF. Age, sex, BMI, co-morbidities, complete blood count (CBC), pre-blood urea, potassium and calcium were performed prior to commencement of the procedure, while post-blood urea levels, aPTT and compression time were collected at the end of hemodialysis.

About 2.5 to 5ml of blood was collected in their respective collecting tube such as Sodium citrate-tube for coagulation studies, lithium-heparin- *tube for blood urea* and EDTA-K2/EDTA-K3-tube for CBC. The collected blood samples were processed within 15 minutes at Muhimbili-National-Hospital and Access-Dialysis-center

laboratories. Prolonged bleeding was assessed by measuring coagulation parameters such as aPTT and compression time at the end of HD procedure.

Compression time (≤ 15 minutes) after removal of the A-V fistula were measured by applying gently compression of the fistula needle site to avoid oozing of blood buying time for natural in vivo clotting and coagulation process to take place so as to close the fistula. Stop watch was used to record time in minutes.

The activated partial thromboplastin time (aPTT) with a normal range of ≤ 31 seconds according to MNH setting standard with reference to supplied aPTT reagent set. A laboratory test to measure heparin blood concentration.

Statistical analysis

Demographic and laboratory data were analyzed using the Statistical Package for Social Sciences (SPSS V-20.0). Dependant variables in this study were compression time and aPTT and independent variables were BMI, monocyte count and blood urea levels. The influences of independent variables were assessed to elucidate how they affected compression time and aPTT). Prolonged bleeding was assessed by measuring aPTT and compression time and correlated with dependant variables. The association between dependant and independent variables were analyzed using descriptive statistics and logistic regression analysis. Univariate analysis was used for quantitative variables such as compression time, age, BMI, blood urea levels, monocytes counts and aPTT. Proportion(s) was applied for categorical data such as sex, categorized variables such as BMI. Linear relationship was used for quantitative variables such as BMI, urea levels or monocytes counts and compression time. The results were of statistical significance when P-value was <0.05.

Ethical approval

The study was approved by Muhimbili University of Health and Allied Sciences (MUHAS) Research Publications Committee and conducted according to good clinical practice. The purpose of the study and its procedures were clearly explained

to all study participants. A written informed consent was obtained from all participants prior to enrolment.

Results

Demographic and clinical characteristics of participants (pre-dialysis data)

Data were collected from 115 patients with a mean age of 51±14.485 years (**Table 1**). The majority of patients were males (68.7%) and normal BMI (65.2%). Hypertension was the most common comorbidity (34.8%), followed by diabetes (23.5%), co-existing hypertension & diabetes (19.1%), and infections (22.6%)**.**

Blood count, electrolyte panel, aPTT and Compression time

The mean value of hemoglobin level was 9.93 ± 2.43g/dL. Twenty-six patients (22.6%) had Hgb values less than 8g/dL and eighty-nine patients (77.4%) had Hgb values more than 8g/dL the target range recommended by the *European Best Practice Guidelines (EBPG), 2002*.

The study participants stopped bleeding between 3 to 20 minutes after removal of the needle with a mean compression time of 5.72 ± 2.984 minutes. More than a half, 67(58.2%) of participants achieved homeostasis within normal compression time (5 – 15 minutes). Few of them 4(3.5%) experienced prolonged compression time (>15 minutes) and the rest achieved compression time for not more than 5 minutes.

Furthermore, the mean values of platelet count, monocytes count, white blood cell counts hematocrit, potassium levels, Calcium levels and aPTT were 226 ± 80.62K/uL, 9.54 ± 2.45%, 6.09 ± 3.459K/uL, 29.6 ± 10.82%, 5.53 ± 0.95mmol/L and 2.118 ± 0.202 mmol/L and 42.077 ± 17.639 seconds, respectively as shown in **Table 2.**

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Table 1: Demographic characteristics of the Study participants (N =115)

Characteristics	Frequency (n)	Percent (%)	Mean ± SD
Age Groups : (yrs)			51 ± 4.485
≤ 35	21	18.3	
36 - 55	43	37.4	
> 55	51	44.3	
Sex			
Male	79	68.7	
Female	36	31.3	
BMI (kg/m^2) (kg/m^2)			
Below Normal (<18.5)	6	5.2	23.66 ± 3.87
Normal (18.5-24.9)	75	65.2	
Overweight (25-29.9)	25	21.7	
Obese (>30)	9	7.8	
Co-Morbidities			
Hypertension	40	34.8	
Diabetes	27	23.5	
Hypertension& Diabetes	22	19.1	
Infections*	26	22.6	

**includes Bacterial infections, HIV & Malaria.*

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Table 2: Blood count, electrolyte panel, aPTT & compression time

Blood count panel	Frequency	Percent	Mean ±SD
HB Level (g/dl)			
Below (<8g/dL)	26	22.6	9.93 ± 2.43
Above (>/=8g/dL)	89	77.4	
Monocyte count (%)			
Normal (< 10 %)	71	61.7	9.54 ± 2.45
High (≥ 10 %)	44	38.3	
Platelet Count (K/uL)			
Low (<150 K/Ul)	11	9.6	226 ± 80.62
Normal (150 - 410 K/Ul)	102	88.7	
High (>410 K/Ul)	2	1.7	
Potassium Level (mmol/L)			
Low (<3.5mmol/L)	3	2.6	5.53 ± 0.95
Normal (3.5 - 5.1mmol/L	46	40.0	
High (>5.1mmol/L)	66	57.4	
Calcium Level (mmol/L)			
Low (<2.1mmol/L)	38	33.0	2.118 ± 0.202
Normal (2.1-2.55mmol/L)	77	67.0	
White Blood Cell (K/uL)			
Low (<4 K/Ul)	20	17.4	6.09 ± 3.459
Normal (4 - 10 K/Ul)	88	76.5	
High (>10 K/Ul)	7	6.1	
Haematocrit (%)			
Low (<36%)	90	78.3	29.6 ± 10.82
Normal (36 - 46%)	25	21.7	
Post-aPTT (seconds)			
Normal aPTT (≤31)	34	29.6	42.077 ± 17.639
Prolonged aPTT (>31)	81	70.4	
Compression Time: CT(minutes)			
Normal CT (≤15)	111	96.5%	5.72 ± 2.984
Prolonged CT(>15)	04	3.5%	

Univariate analysis for effect of BMI, blood urea levels and monocyte count on compression time

Table 3 below shows that, the increase of blood urea level and monocyte count is not associated with prolonged compression time. Only five patients had prolonged compression time, however, the association was insignificant, p=0.328 and p=0.287 respectively.

Table 3: Effect of BMI, blood urea and monocyte counts on Compression

	Compression Time (CT) (minutes)			
	Frequency (%)			
Body Mass Index	Normal CT≤15	Prolonged CT >15	Total	P-Value
Below(<18.5)	5(83.3%)	1(16.7%)	6(100.0%)	0.243
Normal (18.5-25)	71(94.7%)	4(5.3%)	75(100.0%)	
Overweight (25-30)	25(100.0%)	0(0.0%)	25(100.0%)	
Obese (>30)	9(100.0%)	(0.0%)	9(100.0%)	
Blood Urea Levels (mmol/L)				
Normal(< 3.2 – 7.4)	82(71%)	5(29%)	86(100.0%)	0.328
Above (> 7.4)	28(100.0%)	0(0.0%)	28(100.0%)	
Monocyte counts (%)				
Normal (≤10)	67(97.1%)	2(2.9%)	69(100.0%)	0.287
High (>10)	44(95.7%)	2(4.3%)	46(100.0%)	

Univariate analysis for Effect of BMI, blood Urea Levels and Monocyte Count on aPTT

Table 4 below shows that, high blood urea was significantly associated with prolonged aPTT four times when compared to patients with normal urea level (OR=4.143 95%C.I (1.021-16.810), p=0.047). Furthermore, high monocyte count is less likely to cause elevated aPTT when compared to normal Monocyte count

(OR=0.576 95%C.I (0.244-1.361), p=0.208), but the risk was not statistically significant. Body mass index was not statistically associated with aPTT (Table 4)

Table 4: Effect of BMI, blood Urea Levels and Monocyte Count on aPTT

	aPTT (seconds)				
Urea Levels (mmol/L)	Frequency (%)				
	aPTT≤31	aPTT> 31	Total	OR:(95%C.I)	P-Value
				Reference	
Normal 2.5 – 7.4	27(31.3)	52(68.7)	79(100)	2.19(0.632-7.598)	2.190
Above > 7.4	7(19.4)	29(80.6)	36(100)	4.143(1.021-16.810)	0.047
Monocyte Count					
Normal≤10 %	24(33.8)	47(66.2)	71(100.0)	Reference	
High (>10%)	10(22.7)	34(77.3)	44(100.0)	0.576(0.244-1.361)	0.208
Body Mass Index					
Below(<18.5)	1(16.7)	5(83.3)	6(100.0)	1.696(0.186-15.452)	0.639
Normal (18.5-25)	19(25.3)	56(74.7)	75(100)	Reference	
Overweight (25-30)	11(44.0)	14(56.0)	25(100)	0.432(0.168-1.112)	0.082
Obese (>30)	3(33.3)	6(66.7)	9(100.0)	0.679(0.154-2.982)	0.608

Association of hemodialysis dose (URR) on aPTT and compression time

From **table 5** below, there was no association between urea reduction ration (URR) and compression time p = 0.608. About 76.9% of participants with inadequate dialysis had elevated aPTT, however, the difference was not statistically significant (p=0.388).

Table 5: Proportion of Urea Reduction Ratio on compression time and aPTT

	Compression Time (CT) (minutes)			
	Frequency (%)			
URR	Normal CT (≤15)	Prolonged CT (>15)	Total	p-value
Inadequate dialysis (<65%)	37(94.9%)	2(5.1%)	39(100.0%)	0.608
Adequate dialysis (≥65%)	74(97.4%)	2(2.6%)	76(100.0%)	
	aPTT (seconds)			p-value
	Frequency (%)			
URR	aPTT ≤31	aPTT> 31	Total	
Inadequate dialysis (<65%)	9(23.1)	30(76.9)	39(100.0)	0.388
Adequate dialysis(65% and above)	25(32.9)	51(67.1)	76(100.0)	

Discussion

The overall results revealed that the frequency of prolonged bleeding assessed by compression time and aPTT was 3.5% and 70.4%, respectively. Mean compression time of 5.72 ± 2.984 minutes and mean aPTT of 42.077 ± 17.639 seconds were observed during the study. The reported frequency of prolonged aPTT was 70.4%

which is higher when compared to what reported by previous studies (20,23,24) as 55% and 50% in the study by Butt et al and Lutz et al, respectively. The post-dialysis mean aPTT of 42.077 ± 17.639 seconds in our study was likely similar to what has reported by earlier studies, who reported aPTT mean of 46.54 seconds (35 - 42).

Compression time is the time taken for fistula sites to achieve hemostasis (blood clotting) by allowing natural in vivo clotting and coagulation process to take place. From the table 3 below, the study participants were stopped bleeding between 3 to 20 minutes after removal of the needle with a mean compression time of 5.72 ± 2.984 minutes. More than a half, (58.2%) of participants was achieved homeostasis within normal compression time (5 – 15 minutes). Few of them 4(3.5%) experienced prolonged compression time (>15 minutes) and the rest were achieved compression time not more than 5 minutes. This is consistent with what have reported by Bachtell et al, 8 – 12 minutes, Hodde et al, 5 – 10 minutes, Boulanger et al, 10 minutes and British Renal Agency guideline 2015, 5 – 15 minutes as normal compression time (43 - 45)

In this study the effects of body weight, body mass index, blood urea levels, monocyte counts and urea reduction ratio (URR) on compression time was assessed and revealed that few participants (3.5%) were experienced prolonged compression time *(Table 3)*. The reason for this observation could be explained by other factors such as vascular stenosis, poor needle insertion, blood pressure variability, blood viscosity, blood flow rate, number of hemodialysis sessions and individual variation in pharmacokinetics and pharmacodynamic of heparin (46 - 48). No any similar study that has been reported on the influence of body weight, BMI, blood urea levels, monocyte counts and URR on compression time that can compare to our study. In future, there is a need of well-structured structured studies on compression time and heparin dose on how it can be affected by body weight, BMI, blood urea levels, monocyte counts and hemodialysis dose (URR)

Activated partial thromboplastin time (aPTT) is the most commonly used laboratory test to monitor heparin blood concentration (38 - 42).
In our study the effects of body mass index, blood urea, monocyte counts and urea reduction ratio on aPTT has been determined *(Table 4)*.

Body Mass Index

The findings have shown that there was no significant association among overweight patients to achieve optimal and reduced aPTT compared to patients with low BMI, this is inconsistent with what have been reported by earlier studies that there is a safe use of body weight or BMI while dosing heparin to achieve optimal hemostasis, and dosing of heparin based on body weight or BMI could help to minimize prolonged bleeding, however, in the earlier studies, they anticipate that the use of actual weight, especially in obese patients, would result in higher initial aPTT values, potentially exposing patients to unwarranted bleeding risks. In the earlier studies the association was not statistically significant due to the fact that variation in aPTT may be secondary to pharmacodynamic variability instead of the patient's weight (26 – 31).

Monocytes cells affects heparin activity, they bind heparin and cleared it from blood circulation (13 - 16). In this study, the effects of monocyte counts were assessed and revealed that participants with low monocyte counts (*Table 4*) experienced insignificant prolonged aPTT compared to high monocyte counts. This is not consistent with what was reported by Pena et al and Mahdieh et al, that there is a positive correlation between body weight and white blood cell counts (monocytes) which obviously affects heparin clearance via the fast saturable pathway, resulting into over-dose that increase the bleeding risk in such patients due to heparin-platelets dysfunctions() (). Thissuggesting that patients that are rich in monocyte counts (extra-vasculature) may need a larger dose (13 - 16)

Blood urea

The excess of blood urea impair platelet functions leading to prolonged bleeding (17 - 25). Assessment of blood urea levels (*Table 4*) has revealed that urea above normal level (>7.4mmol/L) is significantly associated to elevated aPTT fourfold when compared to urea below normal level. This is in agreement with what have been reported by Park *et al &* Butt et al. Both reported that excess of uremia and serum-heparin cause platelet dysfunctions leading to elevated aPTT. The statistical significant can be explained through platelets impairments that affect clotting systems. This is in agreement with what was reported by others (17 - 25), that in renal failure patients, about 35% of heparin dose accumulates and impair platelets functions leading to prolonged bleeding. In the study conducted in South Korea by Park et al, suggested that uremia causes platelet dysfunction that potentiating the effects of heparin. Lim et al (2007) also reported that blood urea and other toxins among ESRD patients decreases the endocytosis ability of monocytes and monocytes-derived dendritic cells, as a result heparin accumulation leading to prolonged bleeding (17 - 25).

Hemodialysis dose (URR)

Furthermore, the association between hemodialysis dose and aPTT at the end of hemodialysis in *Table 5,* revealed that participants with inadequate dialysis (< 65%) had prolonged aPTT (> 31 seconds). This is in agreement with what have reported by the previous studies that inadequate dialysis affects the bleeding due high urea levels and that, those patients with low uremic state have shown normal bleeding profile when compared to those with high uremic toxins (17 - 25).

Hematological changes during hemodialysis

In additional, (*Table 2)* there is a possibility of a patient to develop heparin related side effects such as anemia (22.6%), thrombocytopenia (9.6%), hyperkalemia (57.4%) and osteoporosis (33%). This is consistent with what has been reported by the previous (49 - 58). In additiona form our findings revealed that mean Hb was 9.93 ± 2.43g/dL in which 22.6% had < 8g/dL (anemia). From, the *EBPG, 2002*

recommended the target range of > 8g/dL as criteria for hemodialysis patients to reduce morbidity. Attention is highly recommended to perform Hb levels before ESRD patients start the procedure. Mean potassium 5.53±0.95 and 57.4% had >5.1mmol/L had hyperkalemia, similarly Bengalorkar; et al (India) 2010 has reported hyperkalemia in HD patients. Mean platelet counts of 226 ± 80.62 and 9.6% had low K (<150 K/uL) had thrombocytopenia similar with Liu Z, et al. (China) (2014) reported a decreased platelet count in HD patients. Mean calcium levels of 2.118 ± 0.202 and 33% had low Ca (<2.1mmol/L) had osteoporosis that supported by Miller et al reported abnormalities of calcium, phosphorus, parathyroid hormone and vitamin D metabolism in renal failure patients (49 -58).

Discrepancy of our study from earlier studies

The observed difference in our study compared to earlier studies can be explained by inclusion criteria, assessment methods, sample size, race, patient's types, patients' conditions and post-blood sampling time to measure aPTT, the individual variation in body weight, BMI, monocyte counts, blood urea and co-morbidities, heparin dose. The reduction in the time duration of the dialysis session and use of more sophisticated and detail set of coagulation parameters can also explain this discrepancy.

Conclusion

The findings have demonstrated that elevated serum urea levels are significantly associated with prolonged bleeding time following removal of Arterio-Venous fistula needles after completion of a hemodialysis therapy session. Other risk factors such as BMI, heparin dose, body weight, monocytes count and hemodialysis dose were not associated with prolonged bleeding at fistula site punctures.

Recommendations

Serum urea levels should be factored in when gauging the individual risk of arterio-venous fistula site bleeding for patients using heparin for anticoagulation during hemodialysis. Further studies including large sample sizes are recommended to

elucidate how other predisposing factors such as heparin dose, BMI, body weight, monocytes count and hemodialysis dose affect A-V fistula bleeding.

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