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Evaluation of Bleeding Risk by Hemostatic Parameters in Hemodialysis at the Douala General Hospital: Comparison between Patients on Hemodialysis before 3 Months and after 12 Months

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Abstract

Background: Bleeding disorders are common and may be a life-threating complication among patients with End Stage Kidney Disease (ESKD), especially for those in hemodialysis (HD). Bleeding risk can be evaluated by hemostatic parameter such as platelet count, prothrombine time (PT) or activated prothromplastin time (aPTT) and may be influenced by duration in HD. Objective: Evaluate bleeding risk in HD patients by analyzing some hemostatic parameters according to duration in dialysis. Patients and methods: We conducted a cross sectional study of 3 months (March to May 2022) in the HD center of the Douala General Hospital. All consenting adult patients with ESKD admitted in HD for less than 3 months or more than 12 months were included. Bleeding risk was evaluated by platelet count, PT, aPTT and fibrinogen. Chi-square test and logistic regression were used to compare data and evaluate association with hemostatic disorder. Results: A total of 80 (60% male) patients were included; 30 patients were on HD for less than 3 months and 50 for more than 12 months. Median age was 45 [30 - 60] years in the first group and 43 [30 - 55] years in the second group. Increased bleeding risk was noted in 50% (n = 40) of patients and was similar in both groups. Thrombocytopenia was more common in patients on HD ≥ 12 months (20% (n = 6) vs 44% (n = 22), p = 0.02). Prolong aPTT was more common in HD patients ≥ 3

months (OR = 6.6 [1.88 - 23.5], p = 0.0013) and those with HD catheter (OR = 21.3 [4.6 - 45.7], p < 0.001). Fibrinogen and PT were comparable in both groups. HD catheter was associated with prolong PT (OR = 5.3 CI [1.5 - 8.9], p = 0.03). Conclusion: Increased bleeding risk is common in HD patients. Thrombocytopenia is common in HD patients ≥ 12 months, while prolong aPTT are mainly found in HD patients ≤ 3 months with catheter and may reflect heparin overdose.

Keywords

Thrombocytopenia, Prolongactivated Prothromplastin Time, Hemodialysis, Cameroon

1. Introduction

Bleeding disorders are common complications in end stage kidney disease (ESKD), affecting 50% of patients; it can occur as minor complications such as gingivorrhagiaor epistaxis or can be live-threatening events like gastro-intestinal or intracranial hemorrhage, especially among hemodialysis patients [1] [2] [3]. Many factors can contribute to bleeding in those patients including anemia, lack of erythropoietin, used of heparin, thrombocytopenia and platelet dysfunction associated to uremia [2] [4]. Indeed, structural and functional platelet disorders have been associated with uremia, like decrease in mean platelet volume which lead to decrease platelet mass, modification of the contain of platelet granules (decrease adenosine diphosphate and serotonin) or defect in secretion during platelet activation [4]. Impairment in interaction between platelet and vessel wall is also common and is one of the main causes of bleeding diathesis in uremic patients. The exact mechanism of this lack of adhesion is not fully understood, it may be linked to impaired function of von Willebrand Factor, reduced expression or interaction with platelet GPIIb-III Areceptorinduced by uremic toxins [4]. Hemodialysis, by removing these toxins, can partially correct platelet dysfunction and then reduce the risk of bleeding; and dialysis is recommended as the main therapeutic option to prevent bleeding diathesis [4]. However, chronic activation of platelet by the dialysis membrane and used of heparin can be associated with thrombocytopenia and platelet dysfunction [4]. So long term hemodialysis could lead to increased bleeding risk with more hemostatic disorders than patients who are beginning hemodialysis. At our knowledge, it has never been investigated before. So, we sought to evaluate the bleeding risk in hemodialysis by analyzing some hemostatic parameters according to patient duration in dialysis.

2. Patients and Methods

2.1. Study Design and Patient

We conducted a cross sectional study of 3 months (March to May 2022) in the

hemodialysis center of the Douala General Hospital (DGH), which is the oldest and the biggest center of Cameroon. Adult (>18 years) consent ESKD patient who were admitted in hemodialysis for less than 3 months or more than 12 months were all included. Patient with acute illness, with known hemostatic disorders, on anticoagulant or antiaggregant treatment were excluded.

2.2. Blood Sampling and Measurement

Platelet count, prothrombin time (PT), activated partial thromboplastin time (aPTT) and fibrinogen were used to evaluate bleeding risk. All laboratory tests were performed by the laboratory unit of the DGH. Blood samples were collected at the beginning of the first dialysis of the week, before heparin injection. For full blood count, an EDTA tube was used, and samples were analyzed within 30 - 90 minpost drawing using an URIT 3000 automate. For hemostatic test, citrate whole blood was centrifugated at 3500 U/min for 5 min within 60 minutes post drawing; plasma was then analyzed using a coagulometer.

2.3. Statistical Analysis

Data were summarized as mean ± standard deviation, median [25 - 75 interquartile] or proportion. Comparison among group was done by using Chi-square test. Logistic regression was used to assess relationship between variables and hemostatic disorders. Data were analyzed using the software Epi info version 7.2. The significance level was $p < 0.05$.

2.4. Definition

The following definitions were used:

- Anemia: hemoglobin level < 12 g/dl.
- Thrombocytopenia: platelets number < 150 G/l.
- Prolong PT: PT < 70%.
- Prolong aPTT: ratio patient on control aPTT > 1.2.
- Low fibrinogen: plasma fibrinogen ≤ 2 g/l.
- Increased bleeding risk: patient with thrombocytopenia and/or prolong PT and/or prolong aPTT and/or low fibrinogen.

3. Results

A total of 80 (60% male) patients were included; 30 patients were on HD for less than 3 months and 50 for more than 12 months. Median age was 45 [30 - 60] years in the first group and 43 [30 - 55] years in the second group ($p = 0.7$). Hypertension and diabetes were the main comorbidities. Arterio-venous fistula was the principal vascular access for HD—Table 1. Anemia was more severe in patients on HD ≤ 3 months than in those on HD ≥ 12 months (7.5 ± 1.8 g/dl vs 8.5 ± 1.9 g/dl, $p = 0.02$) and blood transfusion of less than 1 month was more common in patient on HD ≤ 3 months. Increased bleeding risk was noted in 50% (n = 40) of patients and was similar in both groups (HD ≤ 3 months 43.3%

Table 1. Demographic and clinical data.

Variables	HD ≤ 3 months (%) n = 30	HD ≥ 12 months (%) N = 50	p
Sexe (male)	16 (20)	32 (40)	-
Hypertension	21 (70)	35 (70)	-
Diabetes	2 (6.6)	3 (6)	-
Vascular access (fistula)	15 (50)	48 (96)	-
Blood transfusion <1 month	18 (60)	14 (28)	**0.03**

(n = 13), HD ≥ 12 months 54% (n = 27), p = 0.07). Thrombocytopenia was less common in HD patients ≤ 3 months (20% (n = 6) vs 44% (n = 22); p = 0.02)—**Table 2**. Prolong aPTT was more common in new patients (HD ≤ 3 months 36.7% (n = 11) vs HD ≥ 12 months 8% (n = 4); p = 0.001) with an OR of 6.6 (CI [1.88 - 23.5], p = 0.0013). Prolong aPTT was also associated with hemodialysis catheter (OR 21.3, CI [4.6 - 45.7], p < 0.001) and recent blood transfusion (<1 month)—**Table 3**. Fibrinogen and PT were comparable in both groups. Hemodialysis catheter was associated with prolong PT (OR = 5.3, CI [1.5 - 8.9], p = 0.03).

4. Discussion

The aim of this study was to evaluate bleeding risk in hemodialysis patient with hematologic parameter according to duration in HD. We found that increased bleeding risk is common in hemodialysis patients. Low aPTT is frequent inpatient starting HD with catheter while thrombocytopenia is more common after 12 months in dialysis; and HD catheter is also associated with low PT.

Thrombocytopenia was frequent in our study and HD patients of more than 12 months had an increased risk of 6.6 compared to HD patients of less than 3 months. Kaze and al, in Cameroon found thrombocytopenia in 24% of non-dialysis chronic kidneydisease (CKD) patients [5]. Gäckler and al in Germany also noted thrombocytopenia in 30% of ESKD patients [6]. Thrombocytopenia have been reported to be more prevalent in hemodialysis patients, including long term hemodialysis patient compared to patients in peritoneal dialysis or non-dialyzed ESKD patient [7]. It is estimated that platelet count can drop of up to 15% during hemodialysis session with recovery to normal after end of treatment due to the platelet adhesion and complement activation by dialyzer materiel [7] [8]. However, persistent thrombocytopenia with mild degree of predialysis thrombocytopenia has also been ported [7] [8]. Although chronic activation of platelet by hemodialysis membrane, including polysulfone (which is the main membrane used in our center), used of electron-beam sterilized hemodialysis membranes and heparin have been implicated, the exact mechanism of this hemodialysis related thrombocytopenia remains unknown [7] [8] [9].

Table 2. Laboratory data.

Variables	HD ≤ 3 months (%) n = 30	HD ≥ 12 months (%) n = 50	p
Hemoglobin (g/dl)			**0.03**
≤6	5 (16.7)	4 (8)	
]6 - 9[	20 (66.6)	27 (54)	
]9 - 12[	5(16.7)	15 (30)	
≥12	-	4 (8)	
Platelet (G/l)			**0.02**
<150	6 (20)	22 (44)	
≥150	24 (80)	28 (56)	
PT (%)			0.46
Normal	26 (86.7)	56 (92)	
Prolong	4 (13.3)	4 (8)	
aPTT			**0.001**
Normal	19	46	
Prolong	11 (36.7)	4 (8)	
Fibrinogen			0.94
Low	1 (3.3)	3 (6)	
Normal	29 (96.7)	47 (94)	

Table 3. Factors associated with hemostasis disorders.

Variables	OR	Confidence interval	p
Thrombocytopenia			
Hemodialysis duration (≤3 months)	0.31	0.11 - 0.9	**0.02**
Vascular access (catheter)	2	0.58 - 6.8	0.26
Blood transfusion < 1 month	1.04	0.4 - 6	0.9
Prolong aPTT			
Hemodialysis duration (≤3 months)	6.6	1.88 - 23.5	**0.0013**
Vascular access (catheter)	21.03	4.6 - 45.7	**<0.001**
Blood transfusion < 1 month	0.25	0.03 - 0.56	**0.01**
Prolong PT			
Hemodialysis duration (≤3 months)	1.7	0.4 - 7.6	0.4
Vascular access (catheter)	5.3	1.5 - 8.9	**0.03**

Low aPTT was found in 19% of our patients and it was more common in HD ≤3months and patients with hemodialysis catheter. Momudu and al in Nigeria noted that prolong aPTT was also frequent in CKD compared to healthy control [10]. However, prolong aPTT is usually found in post dialysis and it is associated with the used of heparin [11] [12]. So, it may reflect heparin overdose in some of

our patient since non fractioned heparin is usually start at the same standard dose for every patient and then adjusted with time according to bleeding or coagulation events during the HD session. Moreover, high dose heparinized catheter locked solution had been associated to increased aPTT [13], reflecting systemic heparinization and also suggest heparin overdose.

PT was normal in most of our patient as noted in other studies [6] [11] [12]. Prolong PT was only associated with hemodialysis catheter. As previous noted, heparin overdose due to heparinized catheter locked solution may explain this result.

Low fibrinogen was uncommon in our population like previous reported in CKD and hemodialysis patients [6].

5. Strength and Limitation

The main limitation of this study is the lack of platelet functional test such as platelet function analyzer test, platelet aggregability test or clotting time. However, to our knowledge, it is the first study in our context assessing hemostatic disorder in hemodialysis patient according to their duration in dialysis. It then provided some data on the evolution of hemostatic disorder in these patients with time.

6. Conclusion

Thrombocytopenia and prolong aPTT are frequent in hemodialysis in our context. Thrombocytopenia is more common after 12 months while prolong aPTT is usually found in new hemodialysis patient using catheter and may reflect heparin overdose.

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Ethics Approval and Consent to Participate

This study received administrative authorization from the DGHand the Faculty of Medicine and pharmaceutical Sciences of the University of Dschang. It was also approved by the National Ethic Committee of Research for Human Health. All participants provided a written informed consent before enrolment.

Consent for Publication

All authors gave their approval for publication.

Authors' Contribution Statement

Study conception—FMEHD, DTE, NDE
Clinical data collection and supervision—DTE, FMEHD, NDE, AN
Acquisition and validation of the biological data—EL, DTE, NBVJ
Data analysis—DTE, NBVJ, AN

Data interpretation—EL, FMEHD,
Manuscript drafting—FMEHD, NDE, HMP
Critical revision of the manuscript—FMEHD, EL, HMP NDE

Availability of Data and Materials

Data and materials are available with corresponding author which is the principal investigator. They can be consulted at any time upon request. However, the ethical clearance and the inform consent form did not mention that patient data could be shared to a third part.

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] Pavord, S. and Myers, B. (2011) Bleeding and Thrombotic Complications of Kidney Disease. *Blood Reviews*, **25**, 271-278. https://doi.org/10.1016/j.blre.2011.07.001

[2] Lutz, J., Menke, J., Sollinger, D., Schinzel, H. and Thürmel, K. (2014) Haemostasis in Chronic Kidney Disease. *Nephrology Dialysis Transplantation*, **29**, 29-40. https://doi.org/10.1093/ndt/gft209

[3] AlvesRios, D.R., Carvalho, M.D.G., Lwaleed, B.A., Silva, A.C.S., Borges, K.B.G. and Dusse, L.M.S. (2010) Hemostatic Changes in Patients with End Stage Renal Disease Undergoing Hemodialysis. *Clinica Chimica Acta*, **411**, 135-139. https://doi.org/10.1016/j.cca.2009.11.022

[4] Özkan, G. and Ulusoy, S. (2013) Bleeding Diathesis in Hemodialysis Patients. Intech, Singapore. https://doi.org/10.5772/52926

[5] Kaze, F.F., Kowo, M.P., Wagou, I.N., Maimouna, M., Fouda, H.D. and Halle, M.P. (2020) Hematological Disorders during Chronic Kidney Disease Stages 3 to 5 Non-Dialysed in Cameroon. *Open Journal of Nephrology*, **10**, 61-72.

[6] Gäckler, A., Rohn, H., Lisman, T., Benkö, T., Witzke, O., Kribben, A. and Saner, F.H. (2019) Evaluation of Hemostasis in Patients with End-Stage Renal Disease. *PLOS ONE*, **14**, e0212237. https://doi.org/10.1371/journal.pone.0212237

[7] Daugirdas, J.T. and Bernardo, A.A. (2012) Hemodialysis Effect on Platelet Count and Function and Hemodialysis Associated Thrombocytopenia. *Kidney International*, **82**, 147-157. https://doi.org/10.1038/ki.2012.130

[8] Duayer, I.F., Lima, M.J.C., Araújo, N., Nihei, C.H., Barcelos, M.A.F., Braga, O., Britto, Z.M.L. and Elias, R.M. (2022) Dialysis-Related Thrombocytopenia: A Case Report. *Brazilian Journal of Nephrology*, **44**, 116-120. https://doi.org/10.1590/2175-8239-jbn-2020-0109

[9] Kiaii, M., Djurdjev, O., Farah, M., Levin, A., Jung, B. and MacRae, J. (2011) Use of Electron-Beam Sterilized Hemodialysis Membranes and Risk of Thrombocytopenia. *JAMA*, **306**, 1679-1687. https://doi.org/10.1001/jama.2011.1499

[10] Momodu, I., Dahiru, J.A. and Liman, H.M. (2018) Assessment of Some Coagulation Parameters in Chronic Kidney Disease Patients Attending Specialist Hospital in Sokoto. *Journal of Blood Disorders and Treatment*, **1**, 14-16.

[11] Hernaningsih, Y., Widodo, W. and Aprianto, K. (2019) Comparison of PPT and APTT in Pre and Post-Hemodialysis Patients as the Heparin-Exposed Effect. *Folia*

Medica Indonesiana, **55**, 166-170. https://doi.org/10.20473/fmi.v55i3.15491

[12] Khan, M.Z., Akhtar, S.Z., Pervez, S.N., Khan, M.S. and Malik, A.A. (2014) Coagulation Profile in Pre and Post Hemodialysis Patients of End Stage Renal Diseases. *The Kaohsiung Journal of Medical Sciences*, **7**, 33-36.

[13] Thomson, P.C., Morris, S.T. and Mactier, R.A. (2011) The Effects of Heparinized Catheter Lock Solutions on Systemic Anticoagulation in Hemodialysis Patients. *Clinical Nephrology*, **75**, 212-217. https://doi.org/10.5414/CN106460