

Research article

Non-Traumatic Subdural Hematoma in Patients on Maintenance Hemodialysis: A 10 Year Audit of a Center in Sub-Saharan Africa

L'Hématome Sous-Dural non-Traumatique chez les Patients Hémodialysés Chroniques : Audit d'une Décennie de Pratique dans un Centre en Afrique Sub Saharienne

Ashuntantang GE¹, Kaze F¹, Halle MP², Menanga AP¹, Tatah G¹, Ze Minkande J³, Njamnshi AK¹, Eyenga VC³

¹ Department of Internal Medicine & Specialties, Faculty of Medicine & Biomedical Sciences, University of Yaoundé 1.

² Department of Clinical Sciences, Faculty of Medicine & Pharmaceutical Sciences, University of Douala.

³ Department of Surgery & Specialties, Faculty of Medicine & Biomedical Sciences, University of Yaoundé 1.

Corresponding author: Dr Gloria E. Ashuntantang: maglo09@hotmail.com

ABSTRACT

INTRODUCTION:

Non-traumatic subdural hematoma (SDH) is a rare but grave complication of maintenance hemodialysis (HD), with recent data suggesting a doubling of the annual incidence rate in the USA. With geographic variations in the clinical profile of the ESRD population, we sought to study the pattern of non-traumatic SDH in a Sub-Saharan African hemodialysis setting.

METHODOLOGY

We conducted a retrospective review of medical records of patients treated by maintenance hemodialysis diagnosed by brain CT scan at the Hemodialysis unit of the Yaoundé General Hospital from November 2002 to November 2012 to identify patients with non-traumatic subdural hematoma occurring after a period of at least 3 months on maintenance HD. Relevant data were collected for analysis.

RESULTS

A total of two cases of non-traumatic SDH were identified from the 464 patient records (cumulative incidence of 0.43% in 10 years). These were males with end stage renal disease from malignant nephrosclerosis. The mean age was 52 years. None was receiving prophylactic anti-thrombotic agents. Headaches and neurological deficits were the main clinical features. Treatment was surgical with a mortality rate of. Large interdialytic weight gain, excessive ultrafiltrates and uncontrolled hypertension were common findings.

CONCLUSION

The frequency, clinical presentation, and prognosis of non-traumatic SDH in this study, is consistent with recent reports from Europe and the USA. However, contrary to the latter, non-traumatic SDH occurred in young males without prophylactic antithrombotic agents. Early diagnosis through a high index of suspicion and increased access to brain CT scan may reduce diagnostic delays and improve outcome.

KEY WORDS

Non-traumatic subdural hematoma, maintenance hemodialysis, management, outcome

RESUME

INTRODUCTION

L'hématome sous-dural (HSD) non-traumatique est une complication rare et grave de l'hémodialyse chronique (HDC). Les données récentes suggèrent que l'incidence annuelle a doublé au cours de la dernière décennie aux Etats Unis. Avec les variations géographiques des profils cliniques des hémodialysés chroniques, nous avons entrepris d'étudier le profil de l'HSD non-traumatique en Afrique Sub-saharienne.

METHODOLOGIE

Il s'agit d'une analyse rétrospective des dossiers médicaux d'hémodialysés chroniques depuis au moins trois mois, ayant présenté un HSD non-traumatique diagnostiqué au scanner cérébral dans l'unité d'hémodialyse de l'Hôpital Général de Yaoundé pendant la période allant de Novembre 2002 à Novembre 2012. Les données cliniques importantes étaient relevées.

RESULTATS

Sur 464 dossiers médicaux recensés, deux cas d'HSD non-traumatique ont été identifiés, soit une incidence cumulative de 0,43% en 10 ans. Il s'agissait de sujets de sexe masculin, d'âge moyen de 52 ans, en insuffisance rénale chronique terminale secondaire à une hypertension artérielle maligne, ne recevant aucune prophylaxie anti-thrombotique et présentant des céphalées associées aux déficits neurologiques. Le traitement a été chirurgical avec un taux mortalité de 50%. La prise importante de poids interdialytique, l'ultrafiltration excessive et l'hypertension artérielle non contrôlée étaient les principales retrouvées cliniques

CONCLUSION

La fréquence, la présentation clinique et le pronostic de l'HSD non-traumatique reportés dans cette étude sont similaires aux données européennes et américaines. Cependant, dans notre série, HSD non-traumatique survient chez des sujet jeunes, en absence de traitement anti-thrombotique prophylactique. Le diagnostic précoce par une suspicion clinique et l'accès au scanner cérébral pourraient améliorer son pronostic.

MOTS CLÉS

Hématome sous-dural non-traumatique, hémodialyse chronique, traitement, pronostic.

INTRODUCTION

Non-traumatic subdural hematoma (SDH) is a rare but grave complication of long-term hemodialysis (HD), which clinically mimics the more frequent neurological complications such as stroke and the disequilibrium syndrome in this patient population (1–4). Recent studies from Europe and the USA show an incidence rate of about 190 cases per 100,000 dialysis patients per year (3,4), representing a 20-fold increase compared to the general population (3). Furthermore, the USA study demonstrated a doubling of the incidence within the last decade (3). Advanced age, use of anti-thrombotic agents, the platelet dysfunction of uremia and hemodialysis-related factors have consistently been reported as risk factors of this condition (1,3). It has been suggested that intracranial hemodynamic fluctuations created by hemodialysis and venous hypertension resulting from chronic volume overload create fissures in the small bridging veins of the dura which subsequently bleed in the presence of the platelet dysfunction of uremia, and anticoagulation during HD (4–6). The high incidence of non-traumatic SDH now reported in developed countries has been attributed to the increasing use of prophylactic antithrombotic agents to maintain patency of vascular grafts or cardiovascular disorders in the aging HD population. (3,7).

In Cameroon, like other sub-Saharan African countries, the dialysis population is young with a relatively limited survival on dialysis (8–10). Furthermore, arteriovenous grafts are rarely used as permanent vascular access in our center (11); thus rendering the use of prophylactic antithrombotic agents for access patency unlikely. However, most patients in sub-Saharan Africa can only afford two dialysis sessions per week at best (8–10), with consequent long interdialytic intervals, chronic volume overload, uncontrolled hypertension and excessive ultrafiltrates. We therefore sought to determine the cumulative incidence and factors associated with non-traumatic SDH in a hemodialysis facility of a tertiary hospital in Cameroon.

METHODS

This retrospective study was designed to determine the cumulative incidence and factors associated with non-traumatic SDH during long-term hemodialysis. The cohort was made up of patients with end-stage renal disease (ESRD) admitted into the Hemodialysis Unit of the Yaounde General Hospital between 20th November 2002 and 30th November 2012, and who had spent at least 90 days on hemodialysis. Patients' records from the hemodialysis, radiology and neurosurgery departments

were reviewed for a diagnosis of non-traumatic SDH. Relevant patient data including comorbidities and dialysis parameters were noted. The records of patients with SDH were further analyzed for the clinical presentation, management of SDH as well as patient outcome. Non-traumatic SDH was defined as SDH occurring in the absence of a known history of trauma within one year preceding diagnosis.

Descriptive statistics is expressed as means \pm standard deviation or median (25th–75th interquartile range).

The small number of events precluded further statistical analysis to look for associated factors.

Study setting: The Yaoundé General Hospital is a tertiary health structure, with CT scan and neurosurgical facilities. Its HD unit, which was created in November 2002, cares for about one third of the maintenance HD population in Cameroon. The medical staff has not changed since its creation. Patients typically undergo two weekly dialysis sessions of four hours each. Conventional HD is performed through polysulfone dialyzers using bicarbonate dialysate. Only standard heparin at a loading dose of 2500 IU and a maintenance dose of 500 IU/hour is used for anticoagulation. Hemodialysis is subsidized by the state.

RESULTS

A total of 464 patients who met the study criteria were identified. Men constituted 67% of the study population. The mean age was 46 ± 14.36 years (14–72 yrs). Hypertension, chronic glomerulonephritis and diabetes were the main known underlying renal diseases. The mean dialysis duration was 20.65 ± 14.86 months (range 3–81). Most (97%) of the patients were on 2 weekly HD sessions while 3% mostly children, had 3 sessions per week.

A total of 2 cases of non-traumatic SDH occurred among the 464 patients during the study period giving a cumulative incidence of 0.43%. The case histories are presented below, with a summary of patient data shown in Table I.

Case Histories

Case 1

Mr. Y was a 45 years old salesman, who had been on maintenance hemodialysis for 6 months following end stage renal disease consequent on malignant nephrosclerosis. He was brought to the emergency room for sudden onset of right hemiparesis and aphasia. His past medical history was unremarkable for trauma and other chronic illnesses.

TABLE I. SUMMARY OF DATA OF PATIENTS WITH NON-TRAUMATIC SDH

Parameters	Patient No. 1	Patient No. 2
Age	45	59
Sex	M	M
Underlying renal disease	Malignant nephrosclerosis	Malignant nephrosclerosis
HD vascular access	Native arteriovenous fistula	Native arteriovenous fistula
Duration on dialysis (months)	6	36
Total dialysis heparin dose	5000 IU	5000 IU
Interdialytic weight gain (kg)	5	6
Perdialytic ultrafiltrate (L)	5	5
Mean dialysis blood pressure (mmHg)	170/115	160/100
Prophylactic antithrombotic drug use	None	None
Mean BP on admission (mmHg)	165/100	190/100
Clinical manifestations	Headaches, aphasia, right hemiparesis	Headaches, photophobia, unilateral mydriasis
Diagnostic delay (weeks)	3	4
Treatment	Burr hole under local anesthesia	Burr hole under local anesthesia
Outcome	Alive, 6 years post-operation	Died 6 hours post-operation

Systemic review revealed headaches which were made worse by head movements, and associated with intermittent vomiting, for which he had consulted his doctor three weeks prior this admission. His last dialysis was performed 24 hours before admission. His dialysis regimen consisted of 2 four hour sessions of hemodialysis per week, through a left forearm native arteriovenous fistula. Standard heparin at a total dose of 5000 IU was used for anticoagulation during dialysis sessions. He had never used parenteral erythropoiesis stimulating agents. His medications consisted of nifedipine 20 mg twice daily, labetalol 200mg thrice daily, and Calcium carbonate 1000mg three times a day during meals. Blood transfusions were used for anemia correction as needed. He had experienced no acute complications of hemodialysis. He was non-compliant to treatment and had an average interdialytic weight gain of 5 kg. The mean intradialytic blood pressure was 170/115mmHg with a mean pre-dialysis blood pressure of 178/120mmHg. There were no episodes of intradialytic hypotension. The patient was anuric. Physical examination on admission, revealed a blood pressure of 165/100 mmHg and a regular heart rate of 62 beats per minute. He was conscious but aphasic. A right pyramidal syndrome with central facial paralysis was noted. There were no other abnormalities detected. A provisional diagnosis of hemorrhagic stroke was made; but an unenhanced brain CT scan revealed a left fronto-parietal subdural hematoma causing a 10 mm shift of the midline with herniation of the cingular gyrus (Fig.1). Laboratory results were unremarkable but for normocytic normochromic anemia of 8 g/dl. The prothrombin time, the activated partial thromboplastin time and bleeding times were normal at 10 seconds (90% of control), 28 seconds (normal range 27-35 seconds) and 7 minutes(normal value <9 minutes) respectively.

The patient underwent three heparin-free hemodialysis sessions with blood transfusions to correct his anemia prior to surgery. Hematoma was drained eight days later through a left posterior parietal burr hole under local anesthesia. Heparin free hemodialysis sessions were continued thrice weekly for another two months. Follow-up was uneventful and he was discharged from hospital after eight days post-operatively with complete recovery of neurologic deficits. He is alive on maintenance HD six years post-operation.

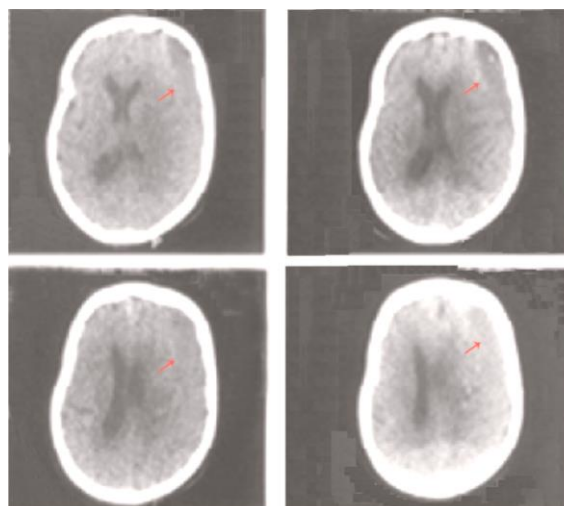


Figure.1: Non-enhanced CT Scan of the brain showing a crescent-shaped iso-dense lesion on the left fronto-parietal region with a 10mm shift of the midline and Cingular herniation

Case 2

Mr. F is a 59 years old accountant, who had been on maintenance hemodialysis for 36 months following end stage renal disease (ESRD) caused by malignant nephrosclerosis. He consulted for worsening headaches of 4 weeks duration. The headaches were throbbing generalized, permanent, non-radiating, and associated with photophobia and drowsiness. There was no vomiting. There was no recent history of trauma. He had taken increasing doses of paracetamol with no improvement. Apart from hypertension and ESRD, there was no other significant past medical history. His usual medications included 50mg of extended-release nicardipine twice a day, clonidine 150mg three times a day, labetalol 200mg three times a day, and calcium carbonate 1000mg twice daily during meals. He had never received recombinant erythropoietin, intravenous iron, oral anticoagulants or antiplatelet agents. His hemodialysis regimen consisted of 2 sessions of 4 hours each per week. Standard heparin at a cumulative dose of 5000 IU was used at each session. His average interdialytic weight gain was 6 kg with a mean ultrafiltration volume of 5 liters per dialysis session. A left radio-cephalic arteriovenous fistula was used for vascular access. Physical examination on admission, noted an anxious man, in agonizing pain. Glasgow coma score was 11/15, and the right pupil was dilated. There were no other motor or sensory deficits detected. Blood pressure was 190/100 mmHg and the rest of the physical examination was unremarkable. A provisional diagnosis of hemorrhagic stroke was entertained. An unenhanced CT scan of the brain revealed a left posterior parietal subdural hematoma with compression of the lateral ventricle and cerebral falx (Fig. 2).

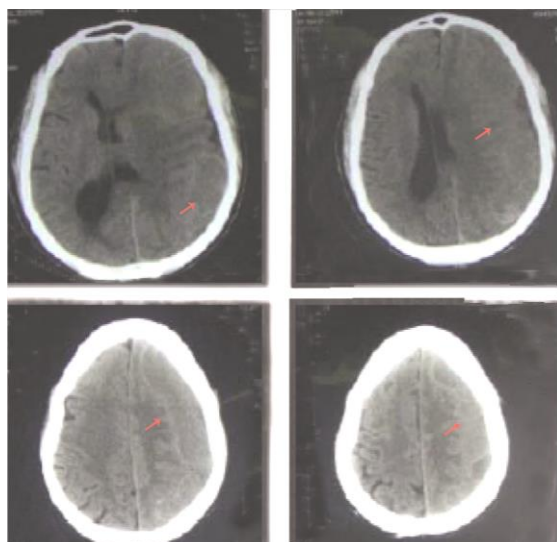


Figure 2: Non enhanced CT scan showing a left posterior parietal crescent shaped hypodense lesion overlying the parietal brain convexity with mass effect on the adjacent structures

Apart from a hemoglobin level of 7.8 g/dl, no other laboratory abnormalities were present. The prothrombin time was 11 seconds (94 % of control), the activated partial thromboplastin time was 29 seconds (normal range 27-35 seconds) and the bleeding time was 6 minutes (normal value <9 minutes). He was placed on 10% mannitol to reduce cerebral oedema, and intravenous nicardipine to control blood pressure. Pre-operatively, anemia was corrected with blood transfusions while hemodialysis was modified to three times a week without heparin. On day 7 of hospitalization, hematoma was evacuated through a left posterior parietal burr hole under local anesthesia. Patient died 6 hours post -operatively from iatrogenic hyperkalemia.

DISCUSSION

This single center study revealed a cumulative incidence of non-traumatic SDH of 0.43% during a 10 year period in a HD facility in sub-Saharan Africa. SDH occurred in two young men who had no risk factors of SDH such as the use of antithrombotic agents, history of trauma or an abnormal coagulation profile. They both had large interdialytic weight gain, high ultrafiltration rates during HD and uncontrolled hypertension. Surgical evacuation of hematoma through a burr-hole was performed under local anesthesia in both. One patient died in the immediate post-operative period from hyperkalemia, while the outcome was uneventful in the other who is alive after 6 years.

There is a dearth of information on non-traumatic SDH in the dialysis population of in sub-Saharan Africa. Limited access to HD and other renal replacement therapies, low patient survival rates on HD, and the unavailability of CT scan in many parts of the region may explain this rarity(8,10,12,13). The cumulative incidence in this study was comparable to the 0.4% observed by Power et al in the UK among 2542 patients on maintenance HD(2). These figures are however much lower than the 3.3% cumulative incidence reported in a single center four decades ago in the USA (1). The improvement in hemodialysis technology with a need for less anticoagulation during therapy may explain this difference. Recent reports show a similar incidence of about 190 cases of SDH per annum per 100,000 patients on hemodialysis in both Europe and the USA, While the incidence of non-traumatic SDH appears high but stable in the European HD population, there has been a two-fold increase in incidence over the last decade in the USA (3). Sood et al reported an increase from 90 cases in 1991, to 191 cases in 2002 per 100,000 patients per year(3). These incidence rates far exceed the incidence rates in the general population which is estimated at 3-58 cases per 100,000 patients annually in developed countries(4). How the cumulative incidence of 0.43% in the present study compares with rates in the general

Cameroonian population is unknown. Dongmo et al reported an incidence of 13 cases of SDH annually among the 12 million inhabitants of Cameroon in 1995 (14). This rate was certainly an underestimate as diagnosis was based on CT scan findings during an era where access to CT scan was very limited; with only one CT scan for the entire nation.

Factors associated with non-traumatic SDH could not be evaluated in this study due to the small number. Advanced age, extracellular volume overload, excessive intradialytic ultrafiltrates, uncontrolled hypertension anticoagulant use and the platelet dysfunction of uremia have been suggested as risk factors for SDH in this patient group (1–4, 15–17). In addition to the venous hypertension induced by volume overload, excessive ultrafiltrates may worsen intracerebral hemodynamic fluctuations created by hemodialysis (3, 5, 6). Some authors have suggested the increasing use of warfarin and antiplatelet agents especially for cardiovascular diseases and vascular graft patency in an elderly ESRD population as the major risk factor in recent years (3, 7). None of the patients in the present study was using oral anticoagulants or antithrombotic agents. In conformity with other studies (2, 4), the coagulation profile including the bleeding time was normal at the time of diagnosis of SDH in the 2 cases. However, chronic volume overload, high ultrafiltration rates and uncontrolled hypertension which were reported as risk factors for SDH in the hemodialysis population over four decades ago (1, 2, 15), are quite frequent in our HD population as illustrated by the two cases. Whether these factors contributed to SDH in this study, is not known. The impact of these and other risk factors such as advanced age could not be evaluated in this study due to the small number. The mean age of patients with non-traumatic SDH was 71 years in the UK HD population (4), while 68% of the patients in the USA study were above 65 years old (3), compared to 52 years in this study. Advanced age is a well-known risk factor of SDH in the general population (14, 18). The elderly patient on HD is particularly at risk since he is more likely to be placed on prophylactic antithrombotic agents to maintain patency of prosthetic vascular grafts and for cardiovascular diseases such as atrial fibrillation (3, 7).

The clinical presentation of non-traumatic SDH in this study, was similar to reports in both the HD and non-dialysis population, with increasing headaches and neurological deficits being the major symptoms (1–4, 14–17). Unlike developed countries, there was a long delay in diagnosis, which was estimated at 4 and 3 weeks respectively in this study. The non-specificity of symptoms, the low index of suspicion and the high cost of CT scan may account for this delay. The more frequent hemorrhagic stroke was the provisional diagnosis made in both cases. The diagnosis of non-traumatic SDH is thus quite challenging in the absence of affordable brain imaging techniques.

Both patients in this study underwent burr-hole craniotomy under local anesthesia coupled with heparin-free HD pre-operatively and for a further 2 months post-operatively for the one who survived. In the recent UK study, only 27% of participants underwent surgery; while the rest were unfit for surgery due to severe comorbid conditions associated with advanced age (4). The mean age of the patients in the UK study was 71 years with 45% being diabetics. Treatment is often surgical; however medical therapy with corticosteroids (16) or tranexamic acid (19) alone or as an adjunct to surgery have shown promising results. Surgical evacuation of hematoma through a burr-hole coupled with heparin-free dialysis is the usual therapeutic strategy (1, 4, 15, 17, 19). The criteria for surgical evacuation although not validated in the ESRD population, are same as for the non-HD population (4, 16). One of the 2 patients in this study died post-operatively. The prognosis is gloomy in this population compared to their non-dialysis peers (1–4). Survival rates of 15 to 34% are reported in several studies (1–4). The 30-day mortality was 39% and 46% in the recent US and European studies respectively (3, 4). Reconstitution of hematoma which is a very common post-surgical complication reported in the literature was not observed in this study (1, 3, 4).

This study has some limitations: the cumulative incidence of non-traumatic SDH may be underestimated in this study since brain CT scan is not routinely performed for all HD patients with headaches and neurological deficits. Secondly, potential risk factors could not be determined due to the small number of cases. Despite these limitations, we believe our results reflect the epidemiology of this pathology in the hemodialysis population of Cameroon.

The cumulative incidence, clinical presentation, management and prognosis of non-traumatic SDH in this study is consistent with reports from developed countries. However, in contrast to those countries, non-traumatic SDH occurs in middle-aged males, who are not receiving prophylactic anti-thrombotic agents and without coagulation abnormalities. Early diagnosis through a high index of suspicion and increased access to brain imaging techniques will reduce diagnostic delays and perhaps improve prognosis in this setting.

REFERENCES

1. Leonard A, Shapiro FL. Subdural hematoma in regularly hemodialyzed patients. *Ann Intern Med.* 1975 May;82(5):650–8.
2. Bechar M, Lakke JP, van der Hem GK, Beks JW, Penning L. Subdural hematoma during long-term hemodialysis. *Arch Neurol.* 1972 Jun;26(6):513–6.
3. Sood P, Sinson GP, Cohen EP. Subdural hematomas in chronic dialysis patients: significant and increasing. *Clin J Am Soc Nephrol CJASN.* 2007 Sep;2(5):956–9.

4. Power A, Hamady M, Singh S, Ashby D, Taube D, Duncan N. High but stable incidence of subdural haematoma in haemodialysis--a single-centre study. *Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc*. 2010 Jul;25(7):2272–5.
5. Stefanidis I, Bach R, Mertens PR, Liakopoulos V, Liapi G, Mann H, et al. Influence of hemodialysis on the mean blood flow velocity in the middle cerebral artery. *Clin Nephrol*. 2005 Aug;64(2):129–37.
6. Hata R, Matsumoto M, Handa N, Terakawa H, Sugitani Y, Kamada T. Effects of hemodialysis on cerebral circulation evaluated by transcranial Doppler ultrasonography. *Stroke J Cereb Circ*. 1994 Feb;25(2):408–12.
7. Bennett WM. Should dialysis patients ever receive warfarin and for what reasons? *Clin J Am Soc Nephrol CJASN*. 2006 Nov;1(6):1357–9.
8. Naicker S. Burden of end-stage renal disease in sub-Saharan Africa. *Clin Nephrol*. 2010 Nov;74 Suppl 1:S13–16.
9. Kaze FF, Ashuntantang G, Kengne AP, Hassan A, Halle MP, Muna W. Acute hemodialysis complications in end-stage renal disease patients: the burden and implications for the under-resourced Sub-Saharan African health systems. *Hemodial Int Int Symp Home Hemodial*. 2012 Oct;16(4):526–31.
10. Bello BT, Raji YR, Sanusi I, Braimoh RW, Amira OC, Mabayoje OM. Challenges of providing maintenance hemodialysis in a resource poor country: Experience from a single teaching hospital in Lagos, Southwest Nigeria. *Hemodial Int Int Symp Home Hemodial*. 2013 Jul;17(3):427–33.
11. Fokou M, Teyang A, Ashuntantang G, Kaze F, Eyenga VC, Chichom Mefire A, et al. Complications of arteriovenous fistula for hemodialysis: an 8-year study. *Ann Vasc Surg*. 2012 Jul;26(5):680–4.
12. Ashuntantang GE, Njouom R, Kengne AP, Ngemhe AN, Kaze FF, Luma HN, et al. Incidence and potential risk factors for seroconversion to Hepatitis C positivity in patients on Maintenance Hemodialysis in Sub-Saharan Africa: A single center study. *Health Sci Dis [Internet]*. 2013 [cited 2014 Jan 24];14(1). Available from: <http://www.hsd-fmsb.org/index.php/hsd/article/view/74>
13. Bower JH, Zenebe G. Neurologic services in the nations of Africa. *Neurology*. 2005 Feb 8;64(3):412–5.
14. Dongmo L, Juimo A, Eloundou N, Njamnshi A, Adeeva V, Tiyou C. [Hematome sous-dural chronique au Cameroun: Aspects cliniques, radiologiques et thérapeutiques a propos de 43 cas]. *Médecine Afr Noire*. 1999;46(3):157–60.
15. Nakashima H, Tomita S, Yoshino K, Norikane H, Baba Y, Doi A, et al. [A case of chronic subdural hematoma in a hemodialyzed patient]. *No Shinkei Geka*. 1986 Apr;14(5):675–9.
16. Inzelberg R, Neufeld MY, Reider I, Gari P. Non surgical treatment of subdural hematoma in a hemodialysis patient. *Clin Neurol Neurosurg*. 1989;91(1):85–9.
17. Tietjen DP, Moore J Jr, Gouge SF. Hemodialysis-associated acute subdural hematoma. Interim management with peritoneal dialysis. *Am J Nephrol*. 1987;7(6):478–81.
18. Djientcheu V, Esiene A, Yangoue T, Tchaleu B, Minkande JZ. Surgical treatment and outcome of 195 cases of non acute subdural haematoma at the Youndé Central Hospital: The need for landmarked burr holes. *Afr J Neurol Sci [Internet]*. 2011 [cited 2014 Jan 24];30(2). Available from: <http://www.ajol.info/index.php/ajns/article/view/77314>
19. Vujkovic B, Sabovic M. Treatment of subdural and intracerebral haematomas in a haemodialysis patient with tranexamic acid. *Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc*. 2000 Jan;15(1):107–9.