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Assessment of Anemia and Thrombopathy in Eastern Sudanese Patients with End Stage Renal Disease

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Abstract: Renal manifestations are becoming a very important health problem in the developing world. In Sudan, the new cases account for about 70-140 thousand of inhabitants per year. Leading to reduced quality of life, these manifestations have negative social and economic impact on the population. This cross-sectional study was conducted in March 2016 to evaluate the anemia and thrombopathy in patients with end stage renal disease (ESRD) in Port Sudan hospital for surgery and hemodialysis, Red Sea State, Sudan. The study enrolled 70 patients, of whom 56 (80%) were males and 14 (20%) were females with the mean age being 51 years along with 70 healthy apparently adult subjects as control group of whom 53 (76%) were males and 17 (24%) were females with the mean age being 31 years. Unlike the control group, 51 (72%) of patients had anemia according to WHO criteria. Severe anemia (Hemoglobin concentration less than 7 g/dl) was detected in 28.6% of patients. Severe anemia has been more frequently (21.4%) in males than in females (7.1%). Likewise, the patient group showed a statistically significant decrease in platelet count (197.700±57.367) as compared to that of the control group (221.357±65.00) ($P<0.024$). In contrast, mean platelet volume (MPV) in the patient group showed a statistically significant increase (11.7±1.66) as compared to that of the control group (10.43±0.98) ($P< 0.006$). Thrombocytopenia was seen in 14.3% of patients. To conclude, this data could indicate that anemia and thrombopathy seen among these patients are attributed to the underlying renal impairment. This study recommends that all patients with unclear cause of anemia and/or thrombopathy should be checked for renal manifestations.

Keywords: Anemia, Thrombopathy, ESRD, Hemodialysis, Sudan

1. Introduction

Port Sudan is a port city in eastern Sudan, and the capital of the State of Red Sea. It has a population of 513,338 residents, according to 2008 estimates. Very limited data are available about the prevalence and causes of renal diseases leading to chronic kidney diseases (CKD) in all States of Sudan, including Red Sea State. Chronic kidney disease is defined as a progressive loss in renal function over a period of months or years, may lead to one or more well recognized complication such as anemia or Bleeding [1]. CKD is a well-known risk factor for end-stage renal disease (ESRD) [2]. The most common causes of CKD are long-term of uncontrolled hypertension, diabetes mellitus as well as polycystic kidney disease. Awareness of the causes of ESRD helps the neurologist to anticipate problems and compilations during renal replacement therapy (RRT) and plan preventive measures for the community [3]. More than 1.1 million patients are approximately estimated to have ESRD worldwide, with an addition of 7% annually. In the USA, the prevalence counts are expected to increase to 85% from 2000 to 2015 [4]. An average incidence of ESRD in the Middle East countries with similar kidney care systems is 93 per million populations [5]. In the developing countries, the evolution of the ESRD population has similar trends [6]. The data reported for new cases in Sudan is about 70–140/thousand inhabitants/year [7]. Anemia and thrombopathy have been considered as predictors of survival in patients with ESRD. Anemic dialysis patients with a hematocrit level of less than 20% have a probability of death [8]. In addition, among the most common complications seen in subjects with ESRD, the anemia, mainly due to little secretion of erythropoietin (EPO) production, abnormalities in white

blood cell (WBC) and platelet (PLT) number and functions [9]. Anemia in CKD is associated with reduced quality of life and increased cardiovascular disease, hospitalizations, cognitive impairment, and mortality. Anemia in CKD is typically normocytic normochromic and hypoproliferative. EPO levels are considered inappropriately low relative to the degree of anemia, because similarly anemic patients with normal kidney function have 10 – 100 times higher EPO levels. In summary, anemia of CKD is a multifactorial process due to relative EPO deficiency, uremic-induced inhibitors of erythropoiesis, shortened erythrocyte survival, and disordered iron homeostasis [10]. Patients with stage 5 CKD exhibit a variety of hemostatic disorders, ranging from increased thrombotic tendency and reduction in the levels of natural inhibitors of coagulation to defective fibrinolysis. Uremic patients show a bleeding diathesis that is mainly due to abnormalities of primary hemostasis; in particular, platelet dysfunction and impaired platelet-vessel wall interaction. Clinically, these changes are associated with the paradoxical observation of thrombotic diathesis as well as the increased bleeding tendency. The mechanism of bleeding in uremia is considered multifactorial. Abnormality in platelet function is partially due to uremic toxins that present in the circulation. Dialysis improves platelet abnormalities and reduces, but does not eliminate the risk of hemorrhage. Hemodialysis can contribute to the bleeding through the continuous platelet activation induced by the interaction between blood and artificial surface. Thrombocytopenia, glomerular thrombosis and thrombi in small arteries and glomerular capillaries are common pathological features in many renal diseases [11]. This study designed to assess the extent of anemia, thrombopathy and limited overview of the etiology of ESRD.

2. Materials and Methods

This was a cross-sectional hospital base descriptive study conducted in March 2016 in Port Sudan hospital for surgery and hemodialysis. The population examined here consisted of seventy patients with end stages of CKD and 70 normal, healthy subjects without knowing renal disease. All patients on regular hemodialysis were interviewed by questionnaire focusing on personal and clinical data including (age, tribe, and cause of ESRD). The medical files of each patient were reviewed to identify the cause of ESRD. Concerning the causes of ESRD, diabetes was diagnosed based on the past medical history and result of the glucose tolerance test, hypertension was diagnosed based on past history of hypertension based on blood pressure of more than 140/90 mmHg. The laboratory parameters including hemoglobin, white cell count, red cell count, red cell distribution width, hematocrit, platelet indices, serum creatinine and urea were evaluated for patients and control.

The hematology parameters are measured by (URIT 3010, E02211 PR China) semi-automated hematology analyzer. Blood samples were collected in tri-potassium ethylene diamine tetra acetic acid (K_3EDTA) and the samples were analyzed within one hour after vein-puncture to avoid the problems occurring when EDTA collected samples are analyzed.

2.1. Inclusion and Exclusion Criteria

We included in this study the hemodialysis patients with ESRD in Port Sudan hospital for surgery and hemodialysis on March 2016. We excluded hemodialysis patients less than 18 years old.

2.2. Definition of Anemia

In this study anemia was defined using The World Health Organization (WHO) criteria, hemoglobin concentration lower than 13.0 g/dl in men and lower than 12.0 g/deal in non-pregnant women defined anemia and hemoglobin < 10 g/dl for men and women was used to define mild anemia, hemoglobin 7.9 -8.9 g/dl for both genders defined moderate anemia and hemoglobin < 7.8 g/dl for both genders defined severe anemia

2.3. Definition of Thrombocytopenia

Thrombocytopenia was defined according to (Shirish M. Kawthalkar) as platelet count below 150,000/µl [12].

2.4. Definition of CKD Stage 5

CKD stage 5 was defined as per National Kidney Foundation/Kidney Foundation's Kidney Dialysis Outcomes Quality Institution (NKF-KDOQI). CKD stage 5 defined as an estimated glomerular filtration rate (EGFR) < 15 CKD patients for renal replacement therapy (Dialysis/Transplantation) [13].

2.5. Statistical Analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS 20.0 version, IBN. Chicago, USA). Results were presented in number, percent, mean and standard deviation.

2.6. Ethical Consideration

All protocols were approved by the ethics committee of the institution (Ethics Committee, Port Sudan Hospital for Surgery and Hemodialysis, Sudan) before the initiation of the study.

3. Results

A total of 70 ESRD patients and 70 healthy subjects participated in the study. The characteristics of the patients are shown in Table 1. The results of this study showed that the mean age of ESRD patients was 51.1±13.6 (years) and 56 (80%) were males and 14 (20%) were females, while the mean age of control subjects was 31.1±13.3 (years) and 53 (76%) were males and 17 (24%) were females. Most of the patients were in advanced stages of renal disease, 100% stage 5. Table 1 also illustrates that the overwhelming majority of renal disease among the Northern Sudan tribe (35.7%),

followed by a Bani Amer tribe (28.6%), and Hadandwa tribe (25.7%).

The etiology of ESRD is shown in Table 2. The most common cause of ESRD in our patients was the hypertension (60%), followed by diabetes mellitus (4.3%), and hypertension with diabetes (4.3%). However, in (31.4%) the cause was unclear.

In patients aged between 21-40 and age > 41 the leading cause of ESRD was hypertension 15.7% and 44.3% respectively. This study showed an insignificant relation between age and etiologies of ESRD (P< 0.806). The hypertension was common cause in older patients.

Prevalence of anemia

Fifty-one participants (72.9%) had anemia as defined by WHO criteria, male being 40 (57.1%) and female 11 (15.7%). A Majority of anemic ESRD patients had severe anemia (28.6%). Males had severe anemia (21.4%) compared to female (7.1%) (Figure 1) severe and moderate anemia was not statistically significant (P< 0.910).

The differences between the mean of RBCs, Hb, Hct, and RDW that occurred in end stage renal disease patients and the Control group were calculated as shown in (Table 3). The RBCs count showed a statistically significant decrease in ESRD patients (3.089±0.807) when compared to that of the Control group (4.652±0.659) (P<0.000). The Hb concentration also showed a statistically significant decrease in ESRD patients (8.89±1.97) when compared to that of the Control group (12.94±2.02) (P<0.000). The Hct level similarly showed a statistically significant decrease in ESRD patients (27.37±6.25) when compared to that of the control group (38.02±4.73) (P<0.000). The RDW-CV level, similar to the indices mentioned above, showed a statistically significant decrease in ESRD patients (10.52±1.19) when compared to that of the Control group (44.44±4.37) (P<0.000). In contrast, the RDW-SD level showed a statistically significant increase in ESRD patients (49.94±8.97) when compared to that of the control group (14.21±1.98) (P<0.000).

The platelet counts also showed a statistically significant decrease in ESRD patients (197.700±57.367) when compared to that of the Control group (221.357±65.000) (P<0.024). In contrast, the indices MPV level showed a statistically significant increase in ESRD patients (11.07±1.66) when compared to that of the control group (10.43±0.98) (P<0.006). However, the indices PDW and PCT levels did not show any statistically significant decrease in ESRD patients when compared to those of the Control group (P<0.305 and P<0.082 respectively). While the indices P-LCR and P-LCC were statistically significant in ESRD patients (17.58±6.21 and 33.57±11.51 respectively) in compared to that of the control group (29.40±7.37 and 64.71±23.92 respectively) (P<0.000). Thrombocytopenia was present in 10 patients, which represent 14.3%. Seven males (10%) and 3 females (4.3%). Thrombocytopenia was not statistically significant with the ESRD (P<0.317).

Table 1. *The characteristics of the patient study population.*

Age (years)	51.1±13.6
Sex	
Male	56 (80%)
Female	14 (20%)
Tribe	
Northern Sudan tribe	25 (35.7%)
Bani Amer tribe	20 (28.6%)
Hadandwa tribe	18 (25.7%)
Western Sudan tribe	5 (7.1%)
Immigrants tribe	2 (2.9%)

Table 2. *Causes of end stage renal disease among study population.*

Hypertension nephropathy	42 (60%)
Unknown	22 (31.4%)
Diabetic nephropathy	3 (4.3%)
DM + HTR	3 (4.3%)
Total	70 (100%)

DM; diabetes mellitus, HTR; hypertension

Table 3. *Comparison of mean differences between ESRD patients and control subjects of the study.*

Parameters	ESRD (n=70) mean±SD	Control (n=70) mean±SD	Median Test	Median Control	Range Test	Range Control	P. Value
WBC x 10^3/µl	5.252±1.720	5.447±1.984	5.0	5.1	2.2-11.6	2.7-12.7	0.537
RBC x 10^9/µl	3.089±0.807	4.652±0.659	3.05	4.61	1.33-5.90	3.37-7.06	0.000
HB gm/dl	8.89±1.97	12.94±2.02	8.9	12.7	4.7-13.6	7.9-16.9	0.000
HCT %	27.37±6.25	38.02±4.73	27.1	37.4	14.5-44	26.6-47.4	0.000
RDW-CV %	10.52±1.19	44.44±4.37	10.1	43.3	8.6-15.4	36.6-61.6	0.000
RDW-SD fl	49.94±8.97	14.21±1.98	46.7	13.6	37.9-77	11.8-22.3	0.000
PLT x 10^3/µl	197.700±57.367	221.357±65.000	200	224	27-367	93-509	0.024
MPV fl	11.07±1.66	10.43±0.98	10.9	10.3	8.4-20.2	8.6-12.6	0.006
PDW fl	13.74±2.53	15.27±12.13	13.3	13.8	9.0-19.8	10-113	0.305
PCT %	0.212±0.05	0.230±0.06	0.215	0.230	.05-0.34	.11-0.52	0.082
P-LCR %	17.58±6.21	29.40±7.37	16.9	28.5	.00-35	15.1-44	0.000
P-LCC x 10^3/µl	33.57±11.51	64.71±23.92	32.0	60.0	.00-65	26.0-148	0.000
Urea mg/dl	133.4±49.5	32.2±37.0	127.5	26.1	52-298	15-68.7	0.000
Creatinine mg/dl	7.59±3.76	0.84±0.28	8.0	0.81	1.7-19.3	0.4-1.6	0.000

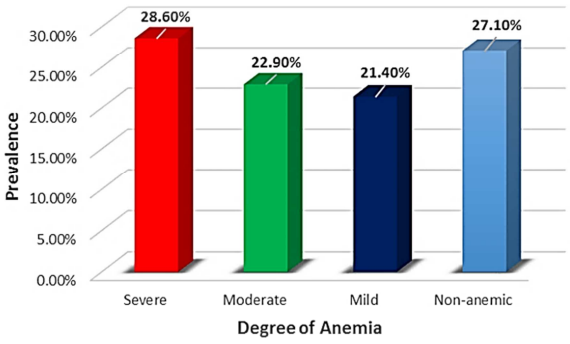

Figure 1. *Overall prevalence of among anemia among ESRD patients (n= 70).*

4. Discussion

Hemodialysis therapy in Sudan is free and powered by the government. There are short limited data on the prevalence and causes of ESRD in Sudan, especially eastern Sudan apart from a few studies. Our results showed that the mean age of ESRD patients is 51 ± 13.1 (years). This indicates that ESRD in Sudan affects the economically productive age group, unlike the situation in other developed countries were the mean age of ESRD patients is generally over 60 years [14]. This average age in this study is on the other hand is another reminder that increasing age is a traditional risk factor for CKD as age, therefore CKD is common in adult as compared to young age.

In the current study, males constitute 80% of ESRD patients receiving hemodialysis therapy, this finding is higher in comparison to other previous studies conducted in Ethiopia and Ivory Coast, where males constituted 61.5% and 61% of ESRD respectively [15, 16].

Hypertension (HTR) is considered to be a common major health problem in sub Saharan Africa (SSA). In our study is a leading cause of ESRD as it is a major cause in many African countries [17]. Previous study conducted in 2009 in central Sudan among 224 patients found that HTR is a common leading cause of ESRD [18]. Osman et al reported that only one-fifth of the Sudanese patients has controlled blood pressure; this may clarify possibly our finding of HTR nephropathy as the leading cause of ESRD [19]. The percentage of the unknown cause of ESRD is increased in our study due to the absence of medical data about the nature of ESRD especially data for kidney biopsies. In addition to HTR and diabetes mellitus (DM), another form of nephropathy like analgesic nephropathy accounted for a significant minority of cases of ESRD in Sudan. This is due to excessive utility of analgesics without physician prescription [20].

The majority of patients were in advanced renal disease stage-5 (70 (100%)). Moreover, the distribution of patients in the early stages was dissimilar in the Nigerian study, which revealed (7.7%) for stage 1, 49 (13.5%) for stage 2, and 66 (18.1%) stage 3. This difference may partly have explained by the fact that Nigerian study had a large sample size compared to our study in addition to that it was a retrospective study [21].

The distribution of patients among CKD stages in this study was different from the reports of other studies done in USA and Indonesia [22, 23], this is due to that in these countries prevention is given priority, as an aggressive screening program of patients especially at risk such as hypertension and diabetes is in place, thereby decreasing progression of CKD.

The present study has demonstrated a high prevalence of anemia in ESRD patients at Port Sudan Hospital for Surgery and Hemodialysis with an overall prevalence of 72.9%, a finding was observed in studies conducted by USA multi-center Survey reported an overall prevalence of anemia 47.8% [22]. Suega, et al in Indonesia and Afshar, et al in Iran also reported the prevalence of anemia to be 73.1% and 75% respectively [23, 24]. In addition, African Nigerian studies revealed 77.5% and 87% prevalence of anemia in ESRD patients [21, 25].

The findings in this study of RBC count, HB, Hct, and RDW levels were similar to the results stated by Costa et al and Pereira et al [26, 27]. Regard to platelet count this study revealed that there was statistically significant decrease in the mean of platelet count, although still within the normal range of ESRD patients. The decreased number in platelet count in ESRD patients may be due to either inadequate platelet proliferation and over-consumption [28] or to reduced thrombopoietin (TPO) secretion from kidney [29]. These findings are consistent with the data obtained by Linthorst et al and Ulusoy et al [30, 31], and inconsistent with data from Erdem et al [32]. Recently, novel platelet indices have been investigated as prospective platelet activation markers which indicates the platelet dysfunction. With respect to the platelet indices MPV, it was increased in this study, a result similar to a recent study which has been documented that the MPV values significantly increased, so the authors claimed that MPV can predict the disease severity [33]. Our study has limitations that need to be taken into consideration. HTR is a leading cause of ESRD, but it was difficult to determine whether it is primary or secondary HTR to the CKD it? This might be for lack of regular medical follow up with our patients. Another point that needs to be discussed is that in our study lack of kidney biopsies from the patients which is needed to make sure that there is no other cause of ESRD and make an exact decision of the etiology of ESRD is hard. This may be too late presentation of the patients and short resources. Unfortunately, due to short facilities EPO, iron profile, and platelet function were not assessed in this study.

5. Conclusion

The findings of this study indicate that most of the hematological values measured in ESRD patients were lowered when compared to control group. Our data showed that the HTR is a leading cause of ESRD in Port Sudan, Red

Sea State. It has been illustrated that the anemia is prevalent among ESRD and the degree of anemia was severe in male as compared to female. Eventually, anemia may be predictive of an increased risk of mortality in ESRD patients. In addition, the increase mean platelet volume could predict platelet dysfunction and the disease severity. To avoid the risk of thrombopathy, platelet indices should be checked periodically.

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