Prevalence and factors predicting anemia in sudanese hemodialysis patients

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Research article

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Abstract

Background: Anemia is a deleterious complication of end stage renal disease (ESRD). It is highly prevalent in sub-saharan Africa. The predictors of control of hemoglobin levels in ESRD patients in Sudan are unknown.

Methods: A prospective observational study was conducted to evaluate the prevalence of anemia and factors affecting the control of hemoglobin levels in ESRD patients. A standardized data collection form was used for collecting patient information. A total of 1015 hemodialysis patients were recruited from twelve centers.

Results: The 534 (52.6%) patients were included in the final analysis. Those were excluded, including, 194 (19.1%) patients were transferred to other centers before completion of the study, 165 (16.3%) died, 38 (3.7%) underwent renal transplantation and 84 (8.3%) were lost to follow-up. Among the patients who included in the final analysis, 307 (57.5%) were males and the mean age was 48.7±16.1 years. All the analyzed patients were anemic (hemoglobin level<12 g/dL), 67% had a hemoglobin level <10 g/dL. In multivariate analysis the variables which had statistically significant associations with hemoglobin levels equal or higher than 10 g/dL were insured patients [OR = 1.53, 95% CI (1.04–2.25)]; and two drug combinations: "Erythropioesis simulating agent (ESA), intravenous (IV) iron, oral iron, and vitamins" [OR = 1.87, (1.27–2.76)] and "ESA, oral iron and vitamins" [OR = 6.67, (2.98–14.94)]. While, a family history of ESRD [OR = 0.57, (0.35–0.94)] and duration of hypertension for "6-9 years" [OR = 0.47, (0.25–0.87)]; Female patients were identified as being more likely to have lower hemoglobin in both univariate and multivariate analyses.

Conclusion: There was suboptimal treated anemia requiring attention in this population. Patients with a family history of ESRD and duration of hypertension for "6-9 years" were predicted to have lower hemoglobin levels. More concern should be paid to uninsured patients and anemia drugs, including the ESA and iron preparations. The results of this study increase our knowledge about the prevalence of anemia and the factors that contribute to control of hemoglobin levels in Sudan.

Keywords: Prevalence, Anemia in ESRD, Hemodialysis, Erythropioesis Stimulating Agents, Hemoglobin Level, Health Insurance, Hypertension, Family History of ESRD, Sudan, Khartoum.

Background

Chronic kidney disease (CKD) is a global public health problem [1]. End stage renal disease (ESRD) is the irreversible loss of kidney function, and has been defined by the Kidney Disease Improving Global Outcomes (KDIGO) Anemia Work Group as CKD stage 5 (G5, A3) with GFR < 15 ml/min/1.73 m^2 and albuminurea > 300 gm/mmol [2]. The incidence of ESRD has been rising in Sudan and the prevalence was estimated at 106 ESRD patients per million people in 2009 [3]. Anemia in ESRD is a complex disorder that is largely caused by erythropoietin deficiency [4], which in turn is related to CKD burden [5]. Other contributory factors include reduced red blood cell life span, iron deficiency, nutritional deficiencies,

vitamin B_{12} and folic acid deficiency, and toxins [6, 7]. The condition is defined, in adults and children older than 15 years with CKD, as hemoglobin (Hb) concentration < 13.0 g/dl (< 130 g/l) in males and < 12.0 g/dl (< 120 g/l) in females [2]. Studies conducted elsewhere have reported differing prevalence and factors associated with anemia in ESRD patients [8–13]

Despite the high burden of ESRD and its complications in Sudan, there is a scarcity of published information regarding the prevalence of, and risk factors for, anemia in people with ESRD in the country. The study provides baseline information about the status of anemia in ESRD patients undergoing HD in Khartoum State and the factors affecting the control of Hb levels.

Methods

Study design and data collection

A multi-center prospective observational study was conducted at public hemodialysis (HD) centers in Khartoum from August 1, 2012 to July 31, 2013. Adult (≥ 18 years) patients who attended dialysis sessions were identified, told about the study and asked to sign forms giving informed consent for participation.

The power and sample size (PS) software [14] was used to calculate the sample size for the objectives for detection of differences between two binomial probabilities. Those patients who were dialyzed for ≥ 4 months at one of twelve major centers, randomly selected out of 24 centers distributed across Khartoum town, were included. Only those centers, which visited by more than 20 patients per day were included in the study. Each center provided 85 patient representatives of the HD patients. Patients were followed until transfer to other centers, renal transplantation, and loss to follow-up, the end of the study or death. Using non-probability convenient sampling, patients were selected from each center. Patients who had other chronic diseases such as malignancy or rheumatoid arthritis were excluded.

Cumulative registration records were used to identify patients in the HD centers. Selected patients, who satisfied the eligibility criteria and agreed to participate, were identified and followed-up at the dialysis centers. The centers provide dialysis for patients twice per week, with each session lasting four hours.

A standardized data collection form was used to collect information on socio-demographic factors such as age, sex, race, height and dry weight (i.e., the weight of the patient at the time of recruitment, information that is necessary for the performance of well-tolerated dialysis sessions without hypotension). Social factors, including insurance status, education level, employment status, monthly income, and marital status were also recorded, along with social habits such as smoking and alcohol consumption. Patients' medical records were reviewed for clinical information such as comorbidities, the etiology of their ESRD and its duration, and laboratory data.

In addition, information was obtained on anemia medications and other concomitant drugs.

Each patient's body mass index (BMI) was computed as their weight in kilograms divided by the square of their height in meters, and categorized into the five standard groups. The Modification of Diet in Renal Diseases (MDRD) equation [15] was used for the estimation of glomerular filtration rates (eGFR).

Outcomes Measurement

The main study outcome was the prevalence of anemia among HD patients. In this study anemia was defined, based on the 2012 KDIGO definition, as Hb level < 13.0 g/dL (< 130 g/L) in males and < 12.0 g/dL (< 120 g/L) in females. A hemoglobin level < 10, versus ≥ 10 g/dL, threshold was used to identify factors affecting control of Hb level. This Hb cut-off was based on the KDIGO Anemia Work Groups suggestion for the initiation of ESA when Hb level < 10 g/dL in ESRD HD patients [2]. Patients whose Hb fell below 10 g/dL were considered as patients with lower Hb concentrations.

Statistical analysis

The Statistical Package for Social Sciences (SPSS) version 22.0.1 [16], was used for the analysis of the data. The statistical significance of variables was taken as $p < 0.05$.

Categorical variables were presented as frequencies and percentages, and continuous variables were presented as means (± SD). Multiple logistic regression was used to predict factors associated with control of Hb levels < 10 vs. ≥10 g/dL. All independent variables were considered for inclusion in the multivariate models. Independent variables which had a p-value < 0.025 in the previous multivariate analysis were included in the final model.

Results

One thousand and fifteen patients were enrolled in the study. Out of them 194 (19.1%) transferred to other centers, 165 (16.3%) died, 38 (3.7%) received renal transplants, and 84 patients (8.3%) were lost to follow-up. A total of 534 patients (52.6%) were included in the analysis. Mean age of the included patients was 48.7 ± 16.1 years. Baseline socio-demographic and clinical characteristic of the patients are given in Table 1. Vascular fistula (A.V) was used in 80% of patients. All 534 patients were suffering from normochromic normocytic anemia. 67% of patients had Hb < 10 g/dL. The baseline mean Hb level of overall patients was 7.89 ± 1.24 g/dL. It was 9.37 ± 0.96 g/dL at the end of follow-up.

Predictors affecting control of Hb levels < 10 vs. ≥10 g/dL

All independent variables with p-value less than 0.025 in a multivariate model (Table 3) were entered into the final multivariate model. After adjustment, the variables with statistically significant associations with higher Hb level (≥ 10 g/dL), were insured patients [OR = 1.53, 95% CI (1.04–2.25)], drug pattern of "ESA, IV iron, oral iron, and vitamin" [OR = 1.87, (1.27–2.76)], and a drug combination of "ESA, oral iron and

vitamin" [OR = 6.67, (2.98–14.94)]. While the factors associated with lower Hb level (< 10 g/dL), were family history of ESRD [OR = 0.57, (0.35–0.94)], and duration of hypertension of "6–9 years" [OR = 0.47, (0.25–0.87)].

Discussion

This study highlights the prevalence of anemia among HD patients and the factors that associated with control of Hb levels. It follows the 2012 KIDGO Work Group definition of anemia as Hb level < 12.0 g/dL. All the patients enrolled in this study had Hb levels below this threshold. Normocytic normochromic anemia was seen in all the patients during the study period.

In contrast to former data, this study disagrees with the lowest prevalence, of 33.5–53.4% [9, 17, 18], that have been reported by US studies. The finding of this study is also very different from the Dialysis Outcomes and Practice Patterns study (DOPPS) international study, which reported a range of anemia prevalence from 23–77% in the studied countries [10]. However the present study is in agreement with the finding of earlier studies which found anemia in all studied patients [19]. It does also identify a greater prevalence of anemia in African descent patients that is inconsistent with the 67.5% found by a Brazilian study [20].

Furthermore, the current study result is consistent with reported ranges of prevalence from studies in similar African regions [11–13]. The disparity in prevalence of anemia has been suggested by [21] to relate to deficiencies in several aspects of HD patient care such as inadequate dialysis doses and anemia management in Sudan HD centers. This could be explained by the variability in anemia management in the HD centers and fits with a study [22] finding, at Khartoum HD centers, a lack of adherence to anemia practice guidelines with delayed work-up of samples and the infrequent monitoring of iron status. That could be expected to result in the delay of anemia drug monitoring and dose adjustment for ESA and iron preparations. All these problems may relate to financial constraint and the lack of universal insurance coverage, as well as all medications having to be bought by patients and therefore often having their availability interrupted. Late arrival of patients to nephrologists or the hospital, and most of them being admitted and initiating HD at the time of diagnosis of ESRD using a catheter are other possible explanations that are supported by previous data [23]. However, the high prevalence of anemia in this study may also be partially due to racial and genetic factors in Sudanese patients; previous studies have documented poorer anemia control in people of African descent than white patients with HD [20, 23]. In addition, inadequate hemodialysis routines of two sessions per week, resulting from financial constraints, less than recommended by guidelines, could be an extra component.

In this research, insured patients were found to have a strong association with increase odds of higher Hb concentration in both the unadjusted and adjusted models. No other data were available about association of insurance status with ESRD-related anemia. The finding of the current study agrees with previous data, where uninsured patients with chronic diseases were found less likely to receive their medications than insured patients [24]. A previous study showed that the uninsured patients were at

higher risk of ESRD and mortality than patients with private insurance [25]. The present study result is also partially consistent with American data that showed insured nonelderly American people were found to have better access to healthcare than those who were uninsured [25]. Another study [26] found a significant segment of Medicare covered patients with suboptimal anemia management. This variation could possibly be explained by the greater affordability and availability of medicines for the management of ESRD and its complications, such as anemia, for insured patients rather than the uninsured counterparts.

In this research, the data revealed that patients with a family history of ESRD were had decreased odds of higher Hb level in both unadjusted and adjusted regression models. This study finding in agreement with previous data from a prospective study that showed an increased risk of ESRD in populations with family histories of ESRD [27]. This suggests that the effects of a family history of ESRD may be related to both genetic and environmental factors. Environmental risk factors for ESRD, such as socioeconomic status (SES), can be shared among family members. Those of lower SES are probably more likely to experience ESRD due to insufficient or not affordable health care for diabetes, high blood pressure, and the early symptoms and phases of kidney damage [28–30]. The present study results, consistent with a Korean study reported that family history of chronic renal faliure (CRF) may be a risk factor for malnutrition in patients undergoing HD [31]. Accordingly, all these factors may lead to lower Hb levels, though that is in agreement with result of this study that a family history of ESRD may be associated with having a lower Hb level.

The results of this study also reveal that duration of hypertension of between six and nine years was significantly associated with lower Hb level than those of people with less than three years of hypertension (reference group). The findings of the present research in agreement with previous data [32], that identified hypertension and DM as leading causes of epidemic renal disease. This finding consistent with that previous Sudanese study having found hypertension to be the leading cause of ESRD in 14.3% of the patients [33]. That may suggest progression to worse complications that lead on to lower Hb level.

The findings of this study in agreement with the results of the Kidney Early Evaluation Program (KEEP) study [7]. That identified hypertension as risk factor increasing the odds of anemia. Their conclusions may be supported by previous Sudanese studies, which revealed hypertension to be a contributing cause of ESRD in HD patients [33, 34], and affect economically productive younger age groups within the population [34]. The effects of a long duration of hypertension, which may produce a decline of Hb level, are another possible explanation of this finding. This association may only be explainable by the correlation of hypertension, DM and CVD with a lack of economic resources [35–37]. Furthermor, increased mortality risk only after 3 years among HD patients, when baseline predialysis systolic blood pressure (SBP) was ≥ 170 mmHg, which may related to lower Hb level [38], although baseline blood pressure (BP) may also affect subsequent changes in serum albumin concentrations, Hematocrit (Hct), Kt/V, and BP. Morover, the association of higher SBP in ESRD patients with higher rate of complication and comorbidites may be another explanation for this result [39].

The result of this study found that patients on the drug combination "ESA and IV iron, oral iron with vitamins" and "ESA and oral iron with vitamins" had a higher likelihood of elevated Hb levels than those on drug pattern "IV iron and oral iron with vitamin". It is interesting to note that ESA was experienced by 61% of the present study patients (data not shown).This finding is somewhat similar to that reported by [40], in the European Survey on Anemia Management (ESAM) study that identified significant improvement in anemia management, despite, many patients remaining below the target Hb levels. Hence, ESA was received by 65.7% patients when assessed after three months, in contrast to the 61% of current study patients over one year. Furthermore, another study [41] produced results that were similar to finding of this study. They found less than 50% of patients had an Hb value within the recommended ranges of the National Kidney Foundation-Disease Outcome Quality Initiative (NKF-DOQI) guidelines. This contrasted with the 20% of this study patients who achieved the target recommended Hb level after one year. The current research differed from the findings of the DOPPS study in that the proportion of the European DOPPS patients with Hb < 10 g/dL decreased from 30–23%. This proportion was 67% in the present study. Moreover, a large percentage of patients, 38–89% received IV therapy across DOPPS countries [10], compared with 87% in this research. One possible explanation for this disparity is the difference in the race and ethnicity of the patients, though it is also probably related to differences in adherence to clinical practice guidelines and protocols for the treatment of anemia and a lack of regular monitoring of patients' iron statuses.

In this research, despite the female sex being found to be significant in the univariate and multivariate regression models, it lacks predictive power in the final model. Female patients were found to be more likely to have a lower Hb level than males. This result matches the results of a Spanish study where female sex was associated with uncontrolled Hb values [42]. Similarly, this study result is consistent with the DOPPS finding that female sex was associated with lower Hb value [10]. There was no difference in erythropoietin levels between the sexes, suggesting this may be a direct effect of physiological phenomena relating to estrogen and androgen hormones [43]. However, finding of present research disagrees with that of the KEEP study where, according to the KDOQI definition, anemia was more predominant in men than women [7]. This variation may be explained by differences in ages, with female patients being older than male patients: mean age (49.19 ± 15.94 years) vs. (48.66 ± 16.05 years). Another possible explanation is that a great proportion of females were found with lower (SES). The majority of them were unemployed, with lower education levels and monthly income. Lower SES has been considered as a contributing factor to malnutrition in HD patients [29, 30], as it is related to low food intake and poor food intake characteristics [44].

Advanced age was consistently associated with the lower Hb level in previously documented studies [8, 10, 45]. However, patient's age did not have the statistical power to demonstrate a significant effect on an Hb level in this study. This may be due to the study data having a relatively small number of patients presenting with lower Hb level in the age subgroups.

Several limitations of this study need to be acknowledged. First, the observational nature of the study limits it to demonstrating associations rather than causality. Second, iron status, folate and vitamin B_{12}

values were not obtained because they are not routinely measured in these clinics. Third, the presence of comorbidities and recent clinical events may affect Hb levels. Despite these limitations, the study had several strong points worth mentioning. First, a large sample size was collected from multiple representative centers across the state; the study focused on one ethnic group, as the majority of participants were Sudanese, and thus can lead to result generalizability. Second, the observational prospective nature of the study provides several important pieces of information relevant to the health care system in Sudan.

Conclusion

In conclusion, the findings of this study in Sudanese hemodialysis patients call attention to the high prevalence of anemia, despite considerable use of ESA with anemia medication. Universal health insurance coverage and accessibility of anemia medication, including ESA could contribute to the improvement of anemia management. Patient's family history of ESRD and hypertension need more attention. Better adherence by health care professionals to practical guidelines and protocols should enhance anemia control.

Abbreviations

CKD:Chronic kidney disease; ESRD:End stage renal disease; Hb:hemoglobin; Hemodialysis:HD; KDIGO:Kidney Disease Improving Global Outcomes; GFR:Glomerular filtration rate; BMI:Body mass index; MDRD:Modification of Diet in Renal Diseases; eGFR:estimation of glomerular filtration rates; SPSS:Statistical Package for Social Sciences; SD:Standard deviation:OR:Odds ratios; CI:Confidence interval; HTN:Hypertension; DM:Diabetes mellitus; ESA:Erythropoiesis stimulating agents; IV:Intravenous; SDG:Sudanese pound; DOPPS:Dialysis Outcomes and Practice Patterns study; SES:Socioeconomic status; KEEP:Kidney Early Evaluation Program study; CVD:Cardiovascular disease; CRF:Chronic renal faliure; BP:Blood pressure; SBP:Systolic blood pressure; Hct:Hematocrit; NKF-DOQI:National Kidney Foundation-Disease Outcome Quality Initiative guidelines; ESAM:European Survey on Anemia Management study.

Declarations

Ethics approval

This study was approved by the National Center for Kidney Diseases and Surgery, Ministry of Health, Republic of Sudan and other approvals were obtained from the centers for patient screening.

Consent to participate

The patients who fulfilled eligibility criteria and were approved to participate by written informed consent.

Consent for publication

Not applicable

Availability of data and material

The datasets generated during and/or analysed during the current study are not publicly available due to [it is PhD study and not published yet], but are available from the corresponding author on reasonable request.

Competing interests

No conflicts of interest

Funding

No funding was used in this study.

Authors' contributions

O.A, H.K and M.B made important contributions to the conception and design of the study. H.K and M.B were involved in the supervision of the study. O.A was involved in the data collection, literature search, analysis and interpretation of data. U.A contribute in editing of the manuscript. All authors read and approved the final manuscript, and are accountable for all aspects of the work.

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Tables

Due to technical limitations, Tables 1-3 are provided in the Supplementary Files section.

Supplementary Files

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- STROBEchecklistv4.doc
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