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Original Article

The Gulf Survey on Anemia Management (GSAM 2005)

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ABSTRACT. We conducted this study to determine the achievements of the current practice guidelines in the management of anemia in the Arabian Gulf Countries. The survey was designed as a retrospective, one day screening of adult patients with end-stage renal disease in six Arabian Gulf countries including Saudi Arabia, Kuwait, Bahrain, Oman, United Arab Emirates and Qatar. Data were collected on patients undergoing chronic dialysis. For random patient sampling, each participating center drew up an alphabetical list of all hemodialysis (HD) or peritoneal dialysis (PD) patients which were 18 years or older and selected every fourth patient on the list. A total of 563 patients from 18 centers were included in the survey. The most common cause of end-stage renal failure was diabetic nephropathy, closely followed by chronic glomerulonephritis. The majority of patients were treated by HD, with only 20% receiving PD. The mean (±SD) hemoglobin (Hgb) concentration was 115 ± 15 g/L (median, 115 g/L; range, 61–159 g/L). The Hgb concentration was ≥ 110 g/L in 28%, ≥ 120 g/L in 38%, and <100 g/L in 16%. Information on their iron status was available for 97% of patients, ferritin levels were available for 97%, and TSAT values for 67% were available. The mean serum ferritin concentration for the study patients was 503 ± 406 ng/ml (median, 390 ng/ml; range, 20.0-2960 ng/ml); 90.5% had a serum ferritin concentration ≥ 100 ng/ml. We conclude that the results of our study demonstrate anemia management in the Gulf countries which is comparable to the European Survey on Anemia Management 2003 (ESAM 2003). However, many patients still have not reached the current recommendation of anemia management.

Keywords: Anemia; Erythropoietin; Dialysis.

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Introduction

Anemia is a major complication of chronic kidney disease (CKD) and has significant effects on the overall prognosis. [1-3] Anemia has also been implicated as a contributing factor in many of the symptoms associated with reduced kidney function. [4] It is also

associated with an increased risk of morbidity and mortality, principally due to cardiovascular disease.[1,3,5]

There is now general agreement, as indicated by recommendations from inter-national expert panels, that partial correction of anemia in patients with end-stage renal disease (ESRD) and CKD reduce mortality and the rate of hospitalization, and results in a quality of life, which is better than in the case of one with severely low hemoglobin (Hgb) levels. [5-9]

The Gulf Survey on Anemia Management in 2005(GSAM 2005) was conducted to evaluate the achievements of the physicians in the Arabian Gulf countries in the management of anemia in light of the current international practice guidelines. The study design was similar to that of the European Survey on Anemia Management 2003 (ESAM 2003) in order to facilitate the comparison with other nations. [10]

Patients and Methods

The survey was designed as a retrospective, one day screening of adult patients with ESRD in six Arabian Gulf countries. The countries participating in this study included Saudi Arabia, Kuwait, Bahrain, Oman, United Arab Emirates and Qatar. Data were collected on CKD patients undergoing hemodialysis (HD) or peritoneal dialysis (PD). The survey was designed to collect data readily available in the dialysis unit without the need to access historical notes, and focused on both individual patient data and the management policies of anemia in the different centers.

For random sampling of the study patients, each participating center prepared an alphabetical list of all HD and PD patients aged ≥18 years and selected every fourth patient on the list. A survey report form was completed with the last patient's dialysis data and included the patient's age and sex, etiology of renal failure, concomitant comorbidities, type of renal replacement therapy, history of blood transfusions, epoetin therapy (dose, route and frequency of administration), iron and vitamin supplementation, concomitant therapies, recent clinical events (within the last 3 months), blood hemoglobin, hematocrit, percentage of hypochromic red cells, reticulocytes, serum C-reactive protein, serum aluminium level, serum ferritin, transferrin saturation (TSAT), serum albumin, immunoreactive parathyroid hormone, and urea pre-/post-dialysis.

In addition, a survey report form was completed for each participating center that included data about the adopted policies for the management of anemia in CKD patients in the corresponding center, such as when to start and how to adjust epoetin doses and how to manage iron supplementation in both HD and PD patients.

For the principal laboratory parameters (hemoglobin, hematocrit, TSAT and serum ferritin), any levels outside the acceptable limits after conversion were queried and re-entered if required; errors were considered if the levels were <12.0% or ≥ 60% for reported hematocrit values, <4.0 g/dl or ≥ 17.0 g/dl for reported Hgb concentrations, < 20 ng/ml or ≥ 3000 ng/ml for reported serum ferritin concentrations, and < 5% or ≥ 60% for TSAT. Any values that remained as outliers were excluded from further analysis.

Table 1. Patients included in GSAM 2005 by country

Country	Centers sampled, n	No of patients, n (%)
KSA	10	268 (47.6)
Kuwait	3	111 (19.7)
UAE	2	56 (9.9)
Oman	1	50 (8.9)
Qatar	1	58 (10.3)
Bahrain	1	20 (3.6)
Total	18	563

Table 2. The characteristics of the study patients

Age, years [a, b.]	
Mean ± SD	53.9±15.4\
Median (range)	56(18-95)
Female/male (%)	48/52
Dry body weight (kg)	
Mean ± SD	65.8 ±17.6
Median (range)	64 (28-145)
Type of renal replacement Therapy (n,%)	
Not recorded	6 (1)
Extra corporeal	443 (79)
Haemodialysis	428 (76)
Hemofiltration	3 (1)
Hemodiafiltration	12 (2)
Peritoneal dialysis	114 (20)
Primary renal disease, n (%)	
Not recorded	7 (1)
Chronic glomerulo-nephritis	96 (17)
Diabetic nephropathy	223 (40)
Renal vascular disease	43 (8)
Chronic interstitial nephropathy	32 (6)
Polycystic kidney disease	17(3)
Other hereditary renal disease	4 (1)
Multiple myeloma	4 (1)
Undefined /other	137 (24)

[a] Age was not reported for 21 patients,
[b.] 14 % of patients were ≤ 70 years

Table 3. The comorbidities [a] in the study patients.

Comorbidity	**n (%)**
Hypertension	480 (89)
Ischemic heart disease	166 (3)1
Congestive heart failure	33 (6)
Cardiac Arrhythmias	29 (5)
Type 1 diabetes	40 (7)
Type 2 diabetes	168 (31)
Hepatitis	111 (21)
Chronic obstructive pulmonary disease	26 (5)
Active neoplasia	5 (1)
Recent allograft rejection	21 (4)
Hemoglobinopathies	3 (1)
Chronic infection /inflammation	24 (4)
Cerebrovascular disease	24 (4)
Peripheral vascular disease	42 (8)

[a] Patients could have more than one comorbidity.

Table 4. Duration of epoetin therapy prior to the survey

Duration	**Patients number**	**(%)**
No epoetin	32	6
<3 months	40	7
3-6 months	56	10
> 6months	435	77
Total	**563**	**100**

We studied 563 patients from 18 centers. The sample sizes varied from country to country, Table 1. The patients in the survey were representative of the general dialysis population in terms of age, sex, body weight and primary cause of renal failure, and dialysis modality, Table 2.

The most common cause of end-stage renal failure was diabetic nephropathy, closely followed by chronic glomerulonephritis. The mean (±SD) systolic blood pressure for the overall group was 147 ± 23.5mmHg (median, 148.5 mmHg; range, 91.0–258 mmHg), while the mean (±SD) diastolic blood pressure was 79.6 ± 13.4 mmHg (median, 80.0mmHg; range, 49.0-127.0mmHg). Hypertension was the most common comorbidity, followed by type 2 diabetes, ischemic heart disease, and viral hepatitis, Table 3.

The overwhelming majority of the study patients were receiving epoetin for >6 months, though nearly 6% did not receive any epoetin, Table 4.

Results

The mean Hgb level was 115 ± 15 g/L (median, 115 g/L; range, 61–159 g/L); 28% had Hgb levels ≥ 110 g/L, 38% had a Hgb levels ≥ 120 g/L, and 16% had Hgb levels <100 g/L. There was a wide variation between countries with regard to the proportion of patients who had a Hgb concentration of ≥ 110 g/dl. When all patients were included, only one country achieved this Hgb level in >75% of patients (Bahrain), while three countries (UEA, Oman

Table 5. Hemoglobin (Hgb) levels by country for patients who had received epoetin therapy for ≥ 3 months.

		Country					
		KSA	**Kuwait**	**UAE**	**Oman**	**Qatar**	**Bahrain**
patients number(n)	558	266	111	54	50	57	20
Mean Hgb g/L	11.45±1.55	115±15	114±14	117±183	109±15	110±15	121±14
Hgb < 110 g/L , n (%)	190 (34)	81 (30)	38 (34)	20 (37)	23 (46)	24 (42)	4 (20)
Hgb ≥110 g/L, n (%)	368 (66)	185 (70)	73 (66)	34 (63)	27 (54)	33 (58)	16 (80)

and Qatar) achieved it in <65% of patients. This was despite the fact that all of centers had stated that their target Hgb concen-tration was ≥ 110 g/L. Overall, 66% of patients receiving epoetin therapy for ≥ 3 months had a hemo-globin concentration ≥ 110 g/L, Table 5.

Information on the iron status of 546 (97%) patients was available. The mean (±SD) serum ferritin levels for these patients was 503 ± 406 ng/ml (median, 390 ng/ml; range, 20.0-2960 ng/ml), and serum ferritin levels were ≥ 100 ng/ml in 90.5% of the patients; serum ferritin levels were not reported for 17 patients, i.e. 3% of the survey population, Table 6.

A large proportion (33.7%) of patients had no recorded TSAT values. For the 373 patients for whom TSAT values were available, the mean (±SD) value was 27.8±14.3% (median, 25.2.0%; range, 5.0–59.0%). Of these patients, 31.0% had TSAT values below 20%. For patients who had received epoetin therapy for ≥ 3 months, only 63.8% were assessed as having adequate an iron status, defined as serum ferritin levels of≥ 100 ng/ml plus a TSAT value of ≥ 20%. It should be noted that serum ferritin levels or TSAT were missing for 151 patients (31%) , Table 7.

Because the majority of peritoneal dialysis patients were treated by the subcutaneous (S.C.) route, they were excluded from any analyses of epoetin dose. There was consi-derable variation in the mean epoetin dose between countries, with the highest mean dose given in Qatar and Kuwait and the lowest in Oman. In all countries, epoetin doses received by patients who did not achieve Hgb levels ≥ 110 g/L were higher than for patients who did achieve these levels, Table 7.

In individual countries, the doses of i.v. and s.c. epoetin were generally quite similar, with the exception of Oman, Bahrain and UAE, where epoetin was administered exclusively via i.v. In HD patients who had received ≥ three months of epoetin therapy, there was no difference in the dose of epoetin administered ia i.v. or s.c., whether the attained Hgb levels were < 110 g/L or ≥ 110 g/L.

In order to identify the factors that may affect epoetin doses and Hgb levels, the study

Table 6. Summary Statistics for Serum Ferretin (ng/ml) by country.

		Country					
		KSA	**Kuwait**	**UAE**	**Oman**	**Qatar**	**Bahrain**
Patients numbers	546	263	106	53	50	54	20
Mean S. Ferritin ng/ml	503± 406	481± 378	419±377	621±427	476±305	474±330	1,073±705
Median S. Ferritin (range) ng/ml	391 (20-296)	408 (20-296)	269 (20-154)	532 (20-152)	409 (29-136)	372 (104-161)	1037 (35-2526)
S. Ferritin < 100 ng/ml (%)	52 (6.5)	29 (11)	15 (14)	3 (6)	4 (8)	0 (0)	1 (5)
S. Ferritin > 100 ng/ml (%)	494 (93.5)	234 (89)	91 (86)	50 (94)	46 (92)	54 (100)	19 (95)

a Excludes any values recorded as < 20.0 ng/ml or ≥ 3000.0 ng/ml

Table 7. Iron status by country of the study patients. [a]

		Country					
		KSA	**Kuwait**	**UAE**	**Oman**	**Qatar**	**Bahrain**
Patients numbers	480	226	92	44	47	52	19
Adequate iron stores(%)	210 (44)	52 (23)	58 (63)	38 (86)	28 (60)	33 (63)	1 (5)
Functional iron deficiency (%)	76 (16)	30 (13)	21 (23)	3 (7)	16 (34)	6 (12)	0 (0)
TSAT missing (%)	151 (31)	121 (54)	0 (0)	0 (0)	0 (0)	13 (25)	17 (89)
Absolute iron deficiency (%)	43 (9)	23 (10)	13 (14)	3 (7)	3 (6)	0 (0)	1 (5)
Mean EPO dose IU/ week	8624	8274	9723	7259	7063	11270	7537

[a] Includes only patients receiving EPO therapy for > 3 months

Definitions of Iron Status**:**

Adequate: Serum ferritin ≥ 100 ng/ml and Transferrin saturation ≥ 20%

Functional deficiency: Serum ferritin ≥ 100 ng/ml and Transferrin saturation < 20%

≥ 100 / TSAT missing: Serum ferritin ≥ 100 ng/ml and Transferrin saturation unknown

Absolute deficiency: Serum ferritin < 100 ng/ml

patients were stratified into two groups on the basis of Hgb levels of <110 g/L (group 1) and Hgb ≥ 110 g/L (group 2). Epoetin doses tended to be higher in group 1 than group 2 (mean EPO dose 11275 and 7299 IU/week, respectively). Epoetin doses were higher in the older age group (p = 0.019), but there was no difference between men and women after adjustment for Hgb levels. The proportions of patients with serum ferritin levels from 200-499 and >500 ng/ml were not significantly different between the two groups. The mean epoetin doses were higher for patients with serum ferritin concentrations < 200 ng/ml and > 500 ng/dl. There was a considerably greater proportion of patients with TSAT < 20% in group1 than group 2 (28% and 16% respectively). In both groups, patients with serum albumin concentrations < 40 g/L responded worse to epoetin therapy than those patients with serum albumin concentrations ≥ 40 g/L. The positive and negative hepatitis status of patients did not have an impact on their average Hgb (114 g/L and 115 g/L, respectively), Serum ferritin (514 and 500 ng/ml, respectively), transferrin saturation (28.7% and 27.6%, respectively). However EPO dose was greater in the patients with no hepatitis (7814 IU/week and 8833, respectively).

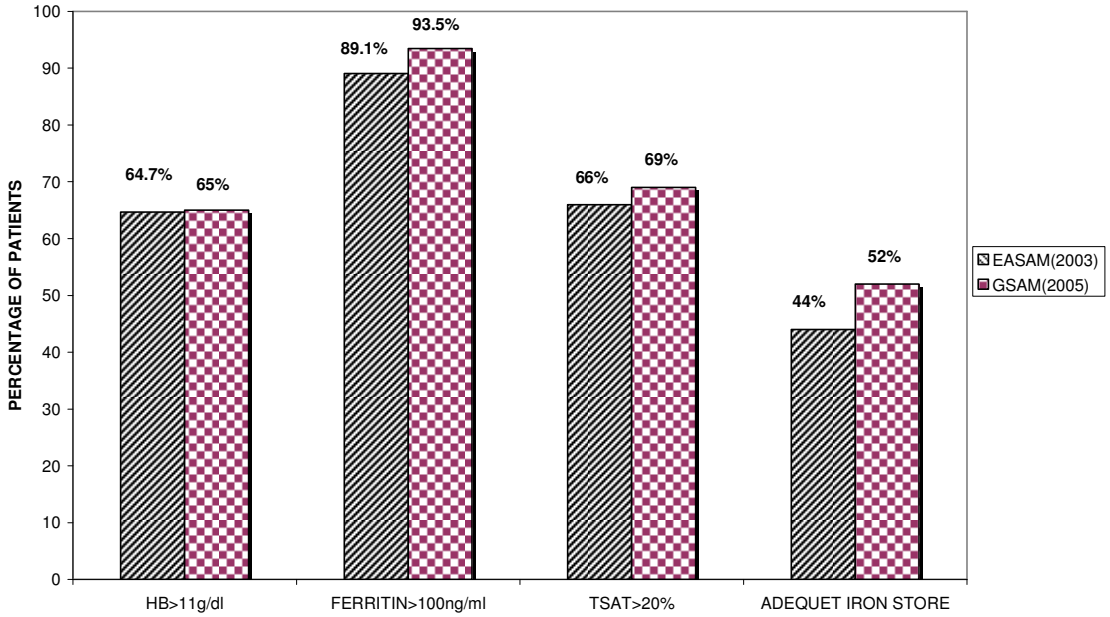
Discussion

Most common dialysis parameters and data regarding anemia management were included in the GSAM 2005. There was a wide variation between countries in the proportion of patients who had a Hgb concentration of ≥ 110 g/L, which is likely to be due to variable sample size from the participating countries.

Most patients had adequate iron stores; however, the unavailable of TSAT for analysis in 33% of patients was a limiting factor.

The mean epoetin dose in the different countries was variable, with the highest mean dose reported from Qatar and Kuwait and the lowest in Oman, while the mean Hgb level

FIGURE 1. PERCENTAGE OF PATIENTS IN GSAM 2005 AND ESAM 2003 WHO REACHED VARIOUS TREATMENT GOALS



was not significant between these countries.

The results of anemia management are comparable to recently published reports of the ESAM 2003, Figure 1. [10] The ESAM was a one day randomized survey conducted to assess anemia management in dialysis patients four years after the introduction of the European Best Practice Guidelines. The survey included 8100 patients. In general, the patient population in ESAM was older than in GSAM. In GSAM, the mean age of the survey population was 53.8 years old compared to 62.5 years old in the ESAM study. Diabetic nephropathy was the most common cause of ESRD in both ESAM and GSAM; however, the rate was significantly higher in the GSAM (40%) comparable to ESAM (24%). This is due the high prevalence of type 2 diabetes in the Gulf countries. It is currently estimated that over 3 million of the general population Saudi (23.7%) have diabetes and that an additional 3 to 5% have either undiagnosed diabetes or impaired glucose tolerance. [11-13]

The overall mean hemoglobin levels were similar for the GSAM, the ESAM, and even the Dialysis Outcomes and Practice Patterns Study (DOPPS). [14] Furthermore, 65% of the patients in the GSAM achieved the target hemoglobin level of 110g/L compared to 64.7% of patients in ESAM. However, the mean weekly epoetin doses were higher in the GSAM (8624 IU) compared to (8506 IU) in the ESAM.

The mean ferritin was 503 ng/ml in the GSAM compared to 468 ng/ml in the ESAM, and the mean TSAT was 25.9% in the GSAM compared to 27.8% in the ESAM. In the GSAM, the proportion of patients with adequate iron status (defined as a serum ferritin concentration of >100 mg/ml and a TSAT value of >20%) was 44% compared to 52% in the ESAM. One third of the surveyed patients in the GSAM had suboptimal Hgb

and iron stores. Most of these patients received intravenous iron and parenteral erythropoietin during the session of in-hospital hemodialysis. Hence, physician-related rather than patient-related barrier is the main contributor to inadequate treat-ment. The potential barriers that may contribute to physician reluctance to follow various anemia management guidelines include the lack of awareness of the guidelines or disagreement with consensus statements. Good management of anemia requires physicians to respond in a timely fashion to indicators of inadequate or ineffective treatment. Similar findings were also noted in the ESAM and DOPPS studies. [14]

The etiology of chronic kidney disease and comorbidities appear to have less effect on the epoetin response in the GSAM, which is similar to what have been noted in ESAM. Suboptimal iron supplementation and monitoring appear to be the main cause of unsatisfactory results in anemia management.

The analysis of the GSAM survey had certain limitations, including the fact that it was a one day cross sectional study and the data were limited to the information readily available without accessing historical notes. Nevertheless, it provides important information about the anemia management in the prevalent dialysis population across the Arabian Gulf countries. The results also reveal that anemia management was comparable to other countries. However, there is a need to collect all data related to the dialysis population in a prospective method in order to get more accurate information.

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