Anemia and Survival in Thai Hemodialysis Patients: Evidence from National Registry Data

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Background: *Anemia is a major contributor to morbidity and mortality in chronic dialysis patients. The K/DOQI guideline recommends the target hemoglobin of 11-12 g/dl (hematocrit of 33-36%). However, the appropriate hematocrit level for Thai hemodialysis patients has been controversial.*
Objective: *To investigate the influence of anemia on mortality in Thai chronic hemodialysis patients who initiated their dialysis from 1999 through 2003.*
Material and Method: *The data from the Thailand Renal Replacement Therapy Registry who has conducted an annual report of chronic dialysis patients throughout Thailand since 1997 was used. Data of twice- and thrice-weekly hemodialysis patients who had recorded hematocrit from 1999 through 2003 were processed and confirmed before final analysis. Records of 3,211 hemodialysis patients from 301 centers were included.*
Result: *The original kidney diseases were diabetes mellitus (31.5%) and hypertension (20.9%). Most patients received twice-weekly hemodialysis (86.3%). The mean hematocrit was 29.3 5.5%. Most patients (72.8%) had hematocrits of less than 33%. Kaplan-Meier analysis showed patients with hematocrit of ?33% or more had better survival than patients with hematocrits of less than 33% (p <0.01). Patients with hematocrits of less than 27, 27-29.9, 30-32.9 and 36% or more had mortality risks of 1.90 (95% CI: 1.31-2.76, p <0.01), 2.10 (95% CI: 1.42-3.09, p <0.01), 1.74 (95% CI: 1.18-2.56, p <0.01) and 1.174 (95% CI: 0.73-1.90, p = 0.51) respectively, compared to those with hematocrit of 33-35.9%.*
Conclusion: *The best survival can be achieved in Thai patients with hematocrits of at least 33%.*

Keywords: *Anemia, Hemodialysis, Mortality*

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It is known that patients with end-stage renal disease (ESRD) suffer from anemia due to an erythropoietin deficiency. The correction of anemia with recombinant human erythropoietin (rHuEPO) has been shown to improve quality of life, exercise capacity, cognitive function, sleep disturbances and ameliorates left ventricular hypertrophy, which is a major contributor to cardiac mortality and morbidity in ESRD patients[1-5]. Although the benefits of correction of anemia have been proven, the optimal target hemoglobin (Hb) / hematocrit (Hct) for ESRD patients has remained unestablished. The National Kidney Foundation : Kidney/Dialysis Outcomes Quality Initiative (K/DOQI) guideline recommended the target Hb of 11-12 g/dl (Hct of 33-36%)[6-7] and the European Best Practice Guidelines recommended the target Hb of at least 11 g/dl (Hct of at least 33%)[8]. Since the costs of renal replacement therapy and rHuEPO are high, few patients can afford the treatment, particularly patients in developing countries like Thailand. To know the cost-benefits of rHuEPO

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therapy, especially in terms of quality of life, it is essential to know the appropriate Hct level in Thai patients who are treated with hemodialysis.

Thus, the objective of the present study was to investigate the impact of anemia on mortality in Thai patients who initiated chronic hemodialysis from 1999 through 2003.

Material and Method

This was a retrospective, longitudinal study of ESRD patients in the Thailand Renal Replacement Therapy (TRT) Registry database. The Nephrology Society of Thailand has conducted the registration of patients who have been on chronic dialysis and published annual report since 1997. The data have been reported voluntarily to The Nephrology Society of Thailand by all dialysis units in Thailand. The selection for analysis was restricted to Thai patients who initiated hemodialysis from January 1st, 1999 to December 31st, 2003 and had records of Hct levels from 1999 through 2003. All data were confirmed by each contributing institution before the final analysis. Data were available for patient demographic characteristics, hemodialysis prescription, hematocrit level and dates of initiation and termination of hemodialysis treatments. Survival analysis was confirmed using all records with date of initiation and present status as of December 31st, 2004.

Continuous variables were reported as mean SD. Patient's survival was analyzed by Kaplan-Meier method and the Log-rank test was used to compare the survival curves. Multivariate Cox regression analysis was used to determine independent predictors of survival. A p-value of less than 0.05 was considered statistically significant. Analyses of data were performed using SPSS for Windows release 11.0 (SPSS Inc., Chicago, Illinois, USA).

Results

Records of 3,211 hemodialysis patients from 301 centers were included. Basic characteristics of the population are shown in Table 1. The mean age of the studied population was above 50 years. Males were approximately half of the patients. The two most common causes of underlying kidney disease were diabetes mellitus and hypertension. Most patients received twice-weekly hemodialysis. The averaged weekly spKt/V and percentage of urea reduction ratio (URR) were used to determine adequate compliance with the K/DOQI guidelines. The mean Hct level was less than 30%. The overall 1- and 5-year survival rates were 95.8% and 59.2%, respectively (Fig. 1).

As shown in Table 2, patients were stratified into 5 groups by mean Hct (less than 27%, 27-29.9%, 30-32.9%, 33-35.9% and 36% or more groups) and the group of patients with Hct of less than 27% was the largest. Most patients (72.8%) were anemic and had Hct of less than 33%. The duration of hemodialysis treatment and weekly spKt/V were similar across all strata of Hct levels. In comparison to patients with Hct of 35-35.9%, patients with Hct of less than 33% were significantly younger, but the ages of patients with Hct of 36% or more were not different. Although patients with Hct of 33% or more were older than patients with Hct of less than 33%, they had better survival than those with Hct of less than 33% ($p<0.01$) based on the Kaplan-Meier analysis (Fig. 2). Multivariate Cox regression analysis showed that patients with Hct of less than 27%, 27-29.9%, 30-32.9% and 36% or more had higher mortality risks compared to those with Hct of 33-35.9% (Table 3).

Discussion

Anemia is a common complication of chronic kidney disease, especially in dialysis patients[9]. The impact of anemia on morbidity and mortality in hemodialysis patients has been explored. An inverse association of Hct level with mortality in hemodialysis patients has been previously reported[10]. The association be-

Table 1. Patient characteristics

Characteristic	(mean SD)
Number of patients	3,211
Male : Female (%)	50.2 : 49.8
Age (years)	54.0 15.5
Body weight (kgs)	55.3 11.3
Height (cms)	160.3 8.6
Cause of ESRD (%)	
DM : HT : CGN	31.5 : 20.9 : 9.4
Duration of HD (years)	2.2 1.3
HD session per week (%)	
2 HD/wk : 3 HD/wk	86.3 : 13.7
HD time per session (hours)	4.17 0.3
Weekly spKt/V	3.8 1.1
URR (%)	75.3 9.0
Hematocrit (%)	29.3 5.5

HD = Hemodialysis, DM = Diabetes mellitus, HT = Hypertension, CGN = Chronic glomerulonephritis, URR = Urea reduction ratio

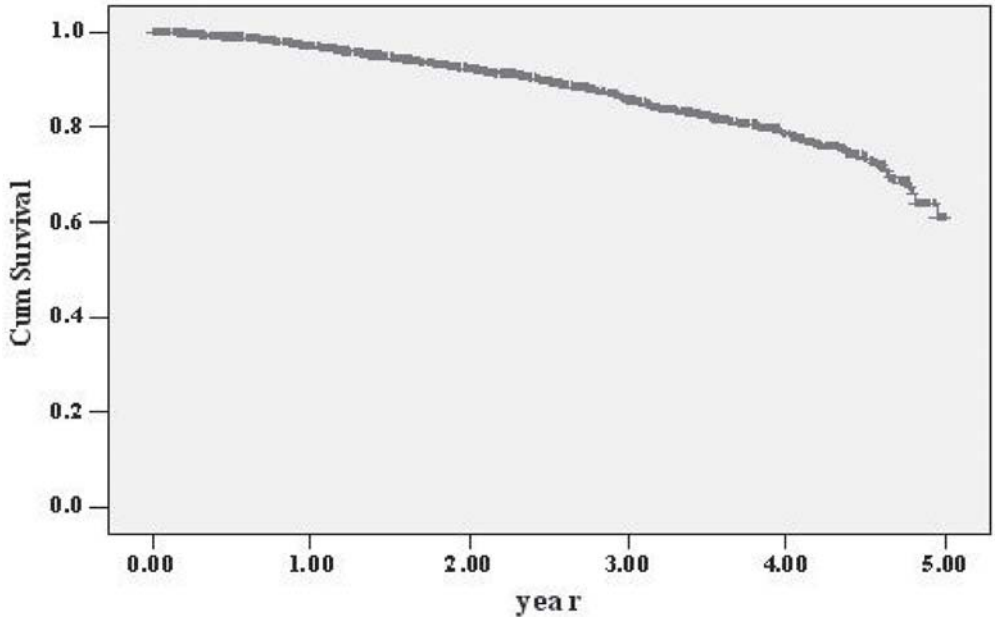

Fig. 1 Kaplan-Meier survival of all patients (N = 3211)

Table 2. Age, duration of hemodialysis and weekly spKt/V in patients with different levels of hematocrit (N = 3211)

Hct (%)	< 27	27-29.9	30-32.9	33-35.9	≥36
N	981	620	736	492	382
(%)	(30.6)	(19.3)	(22.9)	(15.3)	(11.9)
Age X SD	49.6 15.93*	54.0 14.89*	55.6 14.82*	57.6 14.32	57.9 14.95
Years of HD X SD	2.19 1.28	2.19 1.29	2.23 1.29	2.31 1.32	2.24 1.23
Weekly spKt/V X SD	3.79 1.11	3.78 1.19	3.84 1.14	3.96 1.23	3.82 0.96

* $p < 0.05$ as compared to the Hct 33-35.99% group

Table 3. The effect of hematocrit level on mortality (N = 3211)

Hct (%)	Hazards ratio	95% CI	p-value
< 27	1.90	1.31-2.76	< 0.01*
27-29.9	2.10	1.42-3.09	< 0.01*
30-32.9	1.74	1.18-2.56	< 0.01*
33-35.9	1.00		
> 36	1.17	0.73-1.90	0.51

*Significantly higher than patients with Hct of 33-35.9%

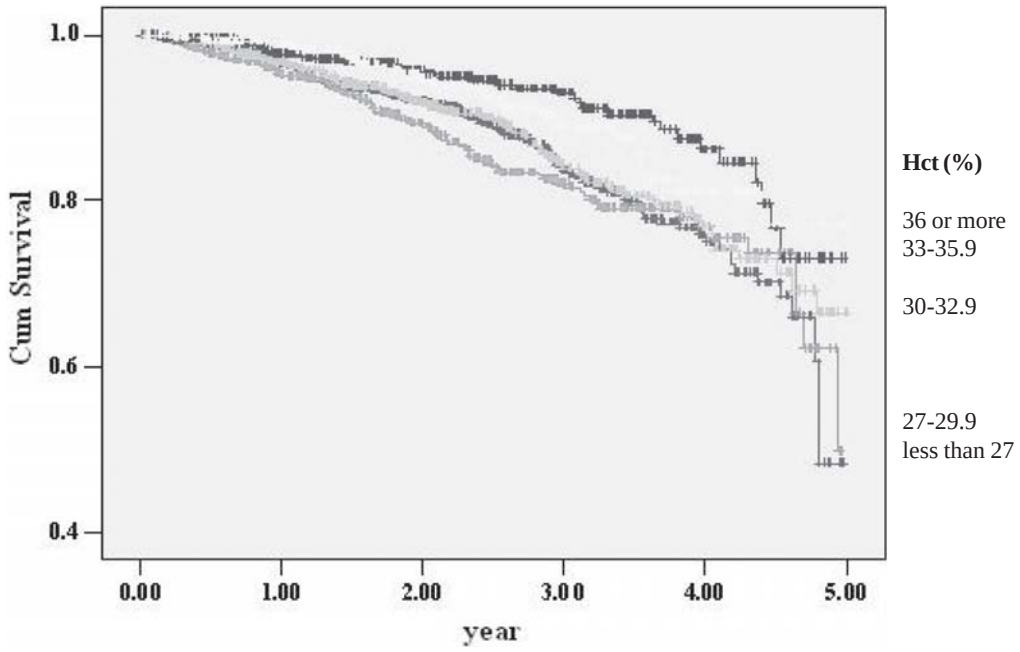

Fig. 2 Kaplan-Meier survival of patients with different levels of hematocrit (N = 3211)

tween anemia and mortality risk may be mediated through the effects on cardiovascular diseases. Anemia is considered to be an important risk factor in the development of left ventricular hypertrophy, a major contributor to cardiac mortality and morbidity in ESRD patients[11]. Correction of anemia by using rHuEPO ameliorates left ventricular hypertrophy and other cardiovascular complications in hemodialysis patients[4,11-12]. The K/DOQI guideline recommends a target Hb of 11-12 g/dl (Hct of 33-36%). Such a recommendation requires supporting information for Thai patients because of differences in race and dialysis conditions. As discussed earlier, the high cost of rHuEPO therapy limits its usage in Thailand.

The mean Hct level of Thai patients was 29.3 5.5%. This was lower than that in most developed countries[13]. The majority of the Thai ESRD patients who were on hemodialysis had Hct of less than 27% and approximately 70% of the total patients had Hct of less than 33% compared to 40% in developed countries[13]. Patients with Hct of 33% or more were older but had better survival than those with Hct of less than 33%. Multivariate Cox regression analysis showed that Hct of less than 33% was an independent predictor of survival in hemodialysis patients. Moreover, patients with Hct of 36% or more seem to also have better but not statistically significantly better survival. The survival benefit from Hct of 33% or more was not influenced by the patient's age. Thus, the present results support the guideline that recommends a target Hb of 11-12 g/dl (Hct of 33-36%) in hemodialysis patients.

Regarding underlying kidney disease, the most common causes were diabetes mellitus and hypertension, which reflects a similarity to other countries. While most US, European and Japanese patients receive standard thrice-weekly hemodialysis, most Thai patients receive only twice-weekly hemodialysis due to resources and financial constrains. Nevertheless, they achieved the minimum recommended dialysis adequacy measured by mean weekly spKt/V of 3.8 1.1. Although many unfavorable factors were found to exist, Thai patients had comparable survival to those reported in most developed countries. From the presented data, the 5-year survival of patients with Hct of 33-35.9% was almost 75%. Thus, it is quite feasible to attain a greater likelihood for survival if the majority of Thai patients can achieve recommended target Hb/Hct, particularly with standard thrice-weekly hemodialysis. Unfortunately, there were several limitations to the present study. It was a retrospective descriptive study based on the nature of the registry. Data were not completed and not available for co-morbid conditions, hospitalizations, causes of anemia, iron status and details of rHuEPO therapy.

In conclusion, most Thai hemodialysis patients (72.8%) had Hct of less than 33%. Patients with Hct of 33% or more had better survival than those with Hct of less than 33%. This is comparable to findings in most developed countries. Results confirm that the best survival can be achieved in Thai patients with hematocrit of at least 33%.

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ภาวะโลหิตจาง และการรอดชีวิตในผู้ป่วยฟอกเลือดชาวไทย: หลักฐานจากข้อมูลการลงทะเบียนการรักษาทดแทนไตในประเทศไทย

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ภาวะโลหิตจางเป็นปัจจัยที่มีบทบาทสำคัญต่อการเจ็บป่วยและการเสียชีวิตของผู้ป่วยโรคไตวายเรื้อรังระยะสุดท้ายที่ได้รับการฟอกเลือด จาก K/DOQI guideline แนะนำระดับ hemoglobin ที่เหมาะสมเท่ากับ 11-12 g/dl (hematocrit เท่ากับ 33-36%) ซึ่งอาจมีความยุ่งยากในการรักษาสำหรับผู้ป่วยคนไทย การศึกษานี้มีวัตถุประสงค์ต้องการผลของภาวะโลหิตจางที่เกี่ยวข้องกับการเสียชีวิตของผู้ป่วยคนไทยที่เริ่มการฟอกเลือดในช่วง พ.ศ. 2542 ถึง พ.ศ. 2546 การศึกษานี้อาศัยข้อมูลการลงทะเบียนการรักษาทดแทนไตสำหรับผู้ป่วยโรคไตวายเรื้อรังระยะสุดท้ายในประเทศไทยที่ได้ดำเนินการมาตั้งแต่ปลายปี พ.ศ. 2540 จนถึงต้นปี พ.ศ. 2549 โดยคัดเลือกข้อมูลของผู้ป่วยที่ฟอกเลือดสัปดาห์ ละ 2-3 ครั้งที่มีระดับของ hematocrit ในช่วง พ.ศ. 2542 ถึง พ.ศ. 2546 และได้รับการตรวจสอบความถูกต้องของข้อมูลจากสถานพยาบาลเดิมของผู้ป่วยแล้วพบว่ามีข้อมูลของผู้ป่วยฟอกเลือดที่สามารถนำมาวิเคราะห์จำนวน 3,211 คนจากสถานพยาบาล 301 แห่ง สาเหตุของโรคไตวายเรื้อรังระยะสุดท้ายส่วนใหญ่เกิดจากโรคเบาหวาน (31.5%) และโรคความดันโลหิตสูง (20.9 %) ผู้ป่วยส่วนใหญ่ได้รับการฟอกเลือดสัปดาห์ละ 2 ครั้ง (86.3%) และมีระดับ hematocrit เท่ากับ 29.3$\pm$5.5% ผู้ป่วยส่วนใหญ่ (72.8 %) มีระดับ hematocrit ต่ำกว่า 33% จาก Kaplan-Meier analysis พบว่าผู้ป่วยที่มี hematocrit สูงกว่าหรือเท่ากับ 33% จะมีอัตราการเสียชีวิตน้อยกว่าผู้ป่วยที่มี hematocrit ต่ำกว่า 33% (p <0.01) โดยผู้ป่วยที่มี hematocrit น้อยกว่า 27, 27-29.9, 30-32.9 และ มากกว่า 36% จะมี mortality risks เท่ากับ 1.90 (95% CI: 1.31-2.76, p <0.01), 2.10 (95% CI: 1.42-3.09, p <0.01), 1.74 (95% CI: 1.18-2.56, p <0.01) และ 1.174 (95% CI: 0.73-1.90, p = 0.51) ตามลำดับเมื่อนำไปเปรียบเทียบกับผู้ป่วยที่มี hematocrit เท่ากับ 33-35.9% สรุปการศึกษานี้พบว่าผู้ป่วยคนไทยควรมีระดับ hematocrit อย่างน้อย 33% เพื่อลดอัตราการเสียชีวิต