ANEMIA IDENTIFIED ONE MONTH AFTER RENAL TRANSPLANTATION IS PREDICTIVE OF ANEMIA IDENTIFIED AFTER TWELVE MONTHS

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Abstract

The aim of this study was to evaluate whether anemia identified earlier than 3 months postengraftment in modern era could be predictive of anemia at 12 months. Cross-sectional and cohort studies based on retrospective analysis of existing clinical records were performed. Data on recipient's age at transplantation, follow-up serum creatinine (SCR) and hemoglobin (Hb) on day 7 (D7), at month 1 (M1) and at month 3 (M3) postengraftment were collected. Outcome was anemia identified at 12 months (M12) postengraftment. There were 75 patients on D7, 74 at M1 and 61 at M3. Multiple linear regression model that included recipient's age at transplantation, Hb and creatinine on D7 and tested the risk for anemia at M12 retained only the age in the model, with the coefficient of 0,84 (P=0,001). The same model at M1 retained Hb and age, with the coefficients of 0,26 (P=0,03) and 0,81 (P=0,0002), respectively and at M3 it retained Hb and age, with the coefficients of 0,41 (P=0,004) and 0,70 (P=0,003), respectively. Anemia identified at M1 after renal transplantation is predictive of anemia at M12.

KEY WORDS: renal transplantation, anemia, regression analysis

Introduction

Anemia is common after renal transplantation and is frequently under-treated (1,2). Prevalence of anemia is the highest by the time of transplantation because the target hemoglobin (Hb) levels in the end-stage renal disease between 11-12 g/100 cm³ are already within the anemic range, as defined by the criteria of World Health Organisation. By three months post-transplant, hemoglobin levels rise and then subsequently fall in those with progressive allograft dysfunction. At one year post-transplant about 40% of patients are anemic (3). Thus, it takes 3 months after renal transplantation to evaluate renal anemia because non-renal reasons, such as perioperative blood loss, frequent phlebotomies and fluid shifts interfere with its proper evaluation up until 3 months postengraftment (4). We conducted this study to evaluate whether anemia identified earlier than 3 months postengraftment in modern era could be predictive of anemia at 12 months.

Methods

We conducted cross-sectional and cohort studies based on retrospective analysis of existing clinical records at the University-based Internal medicine hospital in the town of Tuzla, Bosnia and Herzegovina.
Inclusion criteria
Data were collected from the records of patients transplanted and followed up at Tuzla transplant clinic from 1999 - 2008 and from the records of patients transplanted elsewhere from 1982 - 1998, but followed up at Tuzla transplant clinic thereafter. Patients with incomplete or unavailable charts were excluded from the study. The study was approved by a local ethics committee. Anemia identified at 12 months (M12) postengraftment was the outcome variable.
Predictors
Recipient's age at transplantation, follow-up serum creatinine (SCR) and hemoglobin (Hb) on day 7 (D7), at month 1 (M1) and at month 3 (M3) postengraftment.
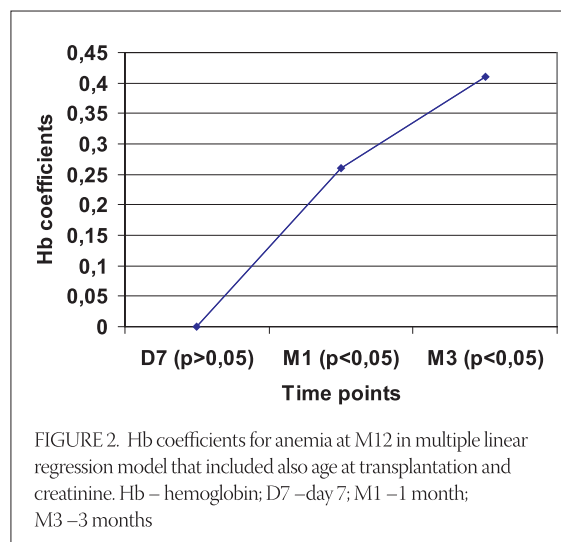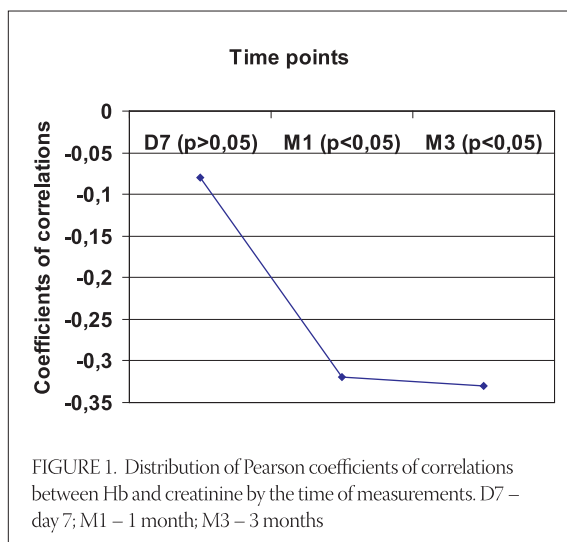*Measurements*
Measurements were done on D7, at M1, M3, and M12. Anemia was expressed as decreased qualitative variable of hemoglobin (Hb) identified at M12. As recommended by the American Society of Transplantation, it was considered present if the Hgb concentration was ≤ 13 g/100 cm³ in men or ≤ 12 g/100 cm³ in women. Recipient's age at transplantation, Hb and SCR were represented by quantitative variables in years, g/dm³ and μmol/dm³, respectively.
Statistical analysis
The degree of association between Hb and serum creatinine on each measurement was assessed by a correlation analysis using Pearson coefficient after a log-transformation to correct for a lack of normality, where appropriate. Linear regression analyses were done to test the crude associations between Hb on each measurement before M12, and Hb at M12. Multiple linear regression prognostic model was applied on each measurement before M12 to identify the independent risk factors for anemia at M12, using forward selection technique with a selection criterion of P<0,05.

Results

There were 75 patients on D7, 74 at M1 and 61 at M3. Three patients were on erythropoietin therapy. Pearson coefficients of correlations r between Hb and creatinine on D7 was -0,08; CI -0,30 to 0,16; (P=0,52), at M1 -0,32; CI -0,52 to -0,10 (P=0,005) and at M3 -0,33; CI -0,54 to -0,08(P=0,01) (Fig.1).

FIGURE 1. Distribution of Pearson coefficients of correlations between Hb and creatinine by the time of measurements. D7 – day 7; M1 – 1 month; M3 – 3 months

FIGURE 2. Hb coefficients for anemia at M12 in multiple linear regression model that included also age at transplantation and creatinine. Hb – hemoglobin; D7 –day 7; M1 –1 month; M3 –3 months

Regression coefficient of the association between Hb on D7 and Hb at M12 was 0,21 (P=0,21) between Hb at M1 and Hb at M12 it was 0,19 (P=0,13). When the patients who were transplanted in recent years, since 2002 until now were selected, regression coefficient was 0,59 (P=0,014). Regression coefficient of the association between Hb at M3 and Hb at M12 was 0,41 (P=0,005). Multiple linear regression model that included recipient's age at transplantation, Hb and creatinine on D7 and tested the risk for anemia at M12 retained only the age in the model, with the coefficient of 0.84 (P=0,001). The same multiple regression model at M1 retained Hb and age in the model, with the coefficients of 0,26 (P=0,03) and 0,81 (P=0,0002), respectively and at M3 it retained Hb and age, with the coefficients of 0,41 (P=0,004) and 0,70 (P=0,003), respectively. Summary of Hb coefficients in its association with Hb at M12 in multiple linear regression model is shown in the Figure 2.

Discussion

In the early post-transplant period anemia assessment that can be attributed to renal reasons is not reliable because the perioperative blood loss, frequent phlobotomies and fluid shifts interfere with its proper evaluation (5). Therefore, the studies that evaluate the impact of anemia on various outcomes usually start with anemia assessment performed only 3 months after transplantation (6). Prominent risk factors for anemia in kidney transplant recipients (KTR) is impaired kidney function (7). Because the kidney function is the main predictor of anemia (8,9,10,11,12), we first tested the correlation between serum creatinine and Hb on each measurement before M12 (D7, M1 and M3) to identify the earliest time when creatinine and anemia could be related to each other and we found the significant correlation coefficient the earliest at M1 (Figure 1).

The crude association between Hb values before M12 and anemia identified at M12 was significant only after 3 months, with regression coefficient of 0,41 (P=0,005). However, when the patients who were transplanted in recent years, since 2002 until now were taken into account, the significant association was established already at M1. Another important risk factor for anemia in kidney transplant recipients is recipient's age (13). Therefore, other than kidney function, we adjusted the analysis also for recipient's age in multivariate linear regression model in order to control the confounding variables. Thus, the first follow-up measurement that identified in multivariate linear regression model the significant association between Hb values before M12 and Hb at M12 was performed at M1, in contrast to the experience accumulated so far indicating the M3 as the earliest time for establishing such an association (Figure 2). We believe that shift of the earliest time from M3 to M1 may be the reflection of an improved postoperative management in recent years, which decreased significant perioperative blood loss, the frequency of phlobotomies and established proper fluid balance earlier than at M3.

Conclusion

There is no correlation between anemia and renal function seven days after renal transplantation.
Correlation between anemia and renal function exists one month and 3 months after renal transplantation
Anemia identified one month after renal transplantation can be predictive of anemia at twelve months.
Other than anemia at one month, the independent risk factor for anemia at twelve months is the recipient's age.

List of Abbreviations

Hb	-	hemoglobin
D7	-	7 days after transplantation
M1	-	1 month after transplantation
M3	-	3 months after transplantation
M6	-	6 months after transplantation
M12	-	12 months after transplantation
SCR	-	serum creatinine

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