Red blood cell count is associated with glomerular filtration rate and albuminuria in normoalbuminuric type 1 diabetic patients with normal or mildly impaired renal function

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INTRODUCTION

Anemia is a common feature in diabetic patients with chronic kidney disease (CKD). Anemia in diabetic patients develops earlier than in subjects with renal disease from other causes and those with reduced hemoglobin have higher risk of progressive renal disease and have a more rapid decline in glomerular filtration rate (GFR). Reduced hemoglobin levels, even within the normal range, identify diabetic patients with an increased risk of cardiovascular morbidity and mortality. Although previous studies demonstrated that anemia is associated with reduced GFR and increased albuminuria in patients with established renal disease, little is known about the relationship between red blood cell count (RBC) and change in renal function among individuals with normal or mildly impaired renal function. The aim of this study was to investigate relationship between RBC and renal function parameters in type 1 diabetic patients (T1DM) with normal or mildly impaired renal function.

SUBJECTS AND METHODS

Study included 313 normoalbuminuric (urinary albumin excretion rate (UAE) <30 mg/24h based on median UAE of at least two 24-h urine collections) T1DM with normal or mildly decreased (eGFR > 60 mlmin-11.73m2) renal function and before any interventions with statins, ACE inhibitors or angiotensin II receptor blockers. eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula. Microalbumin was measured spectrophotometrically by turbidimetric immuno-inhibition. Complete blood count was determined on an automatic blood counter (Advia 120, Siemens Diagnostic Solutions, USA).

RESULTS

Mean/median values of BMI, waist to hip ratio (WHR), HDL cholesterol, triglycerides, hemoglobin (Hb), erythrocytes (E), serum iron, ferritin, serum creatinine, UAE, eGFR as well as blood pressure were within the normal range for patients with diabetes, with slightly elevated HbA1c and LDL cholesterol levels. Serum creatinine was significantly associated with Hb, hematocrit (Hct), E, serum iron and ferritin, with Hb showing the strongest correlation (r= -0.42, p<0.001). eGFR was significantly associated with Hb, Hct and E, with Hct showing the strongest correlation (r=0.18, p=0.001). However, UAE did not significantly correlated with RBC. Stratifying RBC for the degree of serum creatinine, trends across quartiles of serum creatinine for Hb, Hct, E, serum iron and ferritin were statistically significant (all p<0.001). Subjects in the 4th quartile of serum creatinine had significantly lower Hb, Hct, E, serum iron and ferritin levels compared to subjects in 1st, 2nd, and 3rd quartiles. Stratifying RBC for degree of UAE, trends across quartiles was statistically significant only for Hb and Hct (p=0.03). Stratifying RBC markers for the degree of eGFR, trends across different groups for Hb, Hct and E were statistically significant (all p≤0.01). Subjects with eGFR ≥ 125 mlmin-11.73m-2 had significantly higher levels of Hb, Hct and E than subjects with an eGFR below 125 mlmin-11.73m-2.

Table 1: QUARTILES OF URINARY ALBUMIN EXCRETION RATE

	1st quartile (<6.8 mg/24h)	2nd quartile (≥6.8<11.0)	3rd quartile (≥11.0<16.7)	4th quartile (≥16.7 mg/24h)
Hemoglobin (g/L)	140±14	139±16	143±15	135±17*
Hematocrit (L/L)	0.41±0.04	0.40±0.04	0.42±0.04	0.40±0.04*
E (x10^{12}/L)	4.7±0.4	4.6±0.5	4.7±0.4	4.6±0.4
Iron (μmol/L)	15 (3-46)	17 (3-40)	17(2-62)	16 (2-46)
Ferritin (μg/L)	60 (5-335)	52 (8-460)	76(5-697)	40 (7-374)

E – Erythrocytes; *-P<0.05 for trend

Table 2: LEVELS OF RED BLOOD CELL COUNT DEPENDING ON LEVEL OF ESTIMATED GLOMERULAR FILTRATION RATE

Variable	eGFR ≥60<90	eGFR ≥90<125 ml min^{-1} 1.73m^{-2}	eGFR ≥125	P
Hemoglobin (g/L)	133±20	141±14	140±13	0.01
Hematocrit (L/L)	0.38±0.05	0.41±0.04	0.41±0.03	0.001
Erythrocytes(x10^{12}/L)	4.4±0.5	4.7±0.4	4.7±0.3	0.003
Iron (μmol/L)	15 (2-29)	17 (2-62)	14 (3-46)	0.1
Ferritin (μg/L)	33 (7-413)	66 (5-697)	54 (13-194)	0.07

eGFR - estimated glomerular filtration rate.

DISCUSSION

Anemia is a common finding in T1DM associated with cardiovascular risk and progression of renal disease. Significant associations between RBC and renal function parameters even in T1DM with eGFR >60 ml/min and UAE <30 mg/24h suggest that the interplay between RBC and renal function exist in the absence of nephropathy. Since progression to chronic renal disease, as a main predictor of all-cause mortality in T1DM, is likely to occur in majority of diabetic patients, there is a need to further explore the role of risk factors such as anemia.