

Kidney Function Tests in Children with Beta-Thalassemia Minor in Zahedan, Southeast of Iran

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There is little information regarding kidney function in patients with beta-thalassemia minor. In this study we investigated kidney function tests in 50 children with beta-thalassemia minor (22 boys and 28 girls). Twenty-four-hour urine samples were collected and analyzed for sodium, potassium, calcium, magnesium, creatinine, phosphate, uric acid, protein, and β 2-microglobulin. Blood samples were obtained for hematologic and biochemical analyses including complete blood count, serum ferritin, sodium, potassium, calcium, phosphate, magnesium, creatinine, and uric acid. This group of children with beta-thalassemia showed some evidence of tubulopathy such as proteinuria (32%), β 2-microglobulin excretion (36%), calciuria (4%), phosphaturia (4%), and uricosuria (20%). Our findings support the existence of renal tubular dysfunction in beta-thalassemia minor. However, further studies in large series are needed to shed light on the possible relation of these two distinct diseases.

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The main adult's hemoglobin, hemoglobin A, is a tetramer of 2 alpha and 2 beta chains. Thalassemia is a hereditary hemolytic anemia resulting from defects in globin chains. The term *beta-thalassemia minor* (also known as *beta-thalassemia trait* and *heterozygotes beta-thalassemia*) is used to explain the existence of beta-thalassemia mutation on a single chromosome.¹ The huge majority of beta-thalassemia minors are asymptomatic, and may be possibly diagnosed by the presence of microcytic hypochromic erythrocytes, with or without minor degrees of anemia. Though, generally, the microcytosis is much more profound, and the anemia is much milder than iron deficiency anemia.² Iran is one of the countries located on the thalassemic belt. On the coasts of Caspian, rate of carriers is approximately 10% and in the other parts of the country, this rate is between 4% and 8%.³

There is little and controversial data regarding kidney function in patients with beta-thalassemia minor.⁴⁻⁷ Prabahar and colleagues found evidence

of renal tubular dysfunction by documenting hypercalciuria, reduced tubular reabsorption of phosphorus, and renal magnesium wasting in a 24-year-old woman with beta-thalassemia minor.⁴ Oktenli and Bulucu found renal glucosuria and tubular proteinuria in a man with beta-thalassemia minor.⁷ Cetin and coworkers showed that 14.6% of their patients with beta-thalassemia minor had signs of tubulopathy such as hypercalciuria, decreased tubular phosphorus reabsorption, renal magnesium wasting, renal uric acid wasting, and tubular proteinuria.⁶ Whereas, no evidence of renal tubular dysfunction was found in patients with beta-thalassemia minor by Kalman and colleagues.⁵

The aim of the present study was to evaluate the renal functions in beta-thalassemia minor in Zahedan, a city in the southeast of Iran. This study was performed from January 2009 to August 2009 on 50 children with beta-thalassemia minor. The diagnosis of beta-thalassemia minor was confirmed by the results of complete blood count, peripheral

smear, serum ferritin level, and hemoglobin electrophoresis. Fasting blood samples were obtained for hematological and biochemical (sodium, potassium, calcium, magnesium, phosphorus, uric acid, urea, and creatinine) analyses. Twenty-four-hour urine specimens were collected for the determination of creatinine, sodium, potassium, calcium, uric acid, magnesium, phosphorus, β 2-microglobulin, and protein levels in urine. Sodium and potassium were assayed by flame photometer (Assel, Rome, Italy). Urine β 2-microglobulin and serum ferritin were assayed by an enzyme-linked immunosorbent assay kit (Orgentic, Diagnostika GmbH, Mainz, Germany), and other biochemical tests were assayed by spectrophotometric methods using available commercial kits.

We assessed tubular function by evaluating fractional excretion ratios of sodium, potassium, uric acid (FE_{UA}), magnesium; tubular phosphorus reabsorption; and urine levels of calcium, phosphate, magnesium, protein, and β 2-microglobulin. Also, we assessed glomerular function by determination of glomerular filtration rate using creatinine clearance which is a good approximation of glomerular filtration rate using the formula:

$$\text{Creatinine Clearance} = (UC \times V / PC) \times (1.73 / A)$$

where UC is urine creatinine (mg/dL); V, urine volume (mL/min), PC, plasma creatinine; and A, body surface area.

The study protocol was approved by the ethics committee of Zahedan University of Medical Sciences and informed consent was obtained from the parents.

Fifty patients (22 boy and 28 girls) with beta-thalassemia minor were included in this study. Their mean age was 13.3 ± 4.7 years (range, 5 to

19 years), and their mean body weight and the body surface were 31.78 ± 10.25 kg (range, 13 to 71 kg) and 1.17 ± 0.30 m², respectively. The levels of hematological parameters are summarized in Table 1. Parameters for glomerular and tubular function are summarized in Table 2. Abnormal fractional excretion ratios for potassium and magnesium were observed in 6% and 2% of the children, respectively. Proteinuria was found in 32% of the patients, β 2-microglobulin in 36%, calciuria in 4%, phosphaturia in 4%, and renal tubular reabsorption of phosphate in 10%.

In this study we found that patients with beta-thalassemia minor had some evidence of tubulopathy such as proteinuria, β 2-microglobulin excretion, calciuria, phosphaturia, and uricosuria. The results suggest tubulopathy evidence supporting the existence of a kidney disorder in beta-thalassemia minor. We also made a comparison of these parameters with those of healthy children ($n = 50$); the results showed that creatinine clearance, fractional excretion of uric acid and potassium, and tubular phosphorus reabsorption were significantly different between beta-thalassemia minor patients and healthy subjects (data are not shown). No significant differences were observed between the groups regarding other parameters of tubular damage.

Oktenli and Bulucu reported renal glucosuria and

Table 1. Hematological Parameters of Children With Beta-Thalassemia Minor

Parameter	Mean Value
Hemoglobin A2, %	4.66 ± 0.57
Mean corpuscular volume, fL	60.98 ± 4.99
Hemoglobin, g/dL	10.97 ± 1.58
Ferritin, ng/mL	66.93 ± 50.02

Table 2. Biochemical Parameters in Blood and Urine of Children With Beta-Thalassemia Minor

Parameter	Value	Reference Range
Creatinine clearance, mL/min/1.73m ²	101.34 ± 23.75	...
Fractional excretion of sodium, %	0.68 ± 0.26	0.3 to 1.6
Fractional excretion of uric acid, %	9.25 ± 7.14	
Fractional excretion of magnesium, %	3.71 ± 1.91	1 to 8
Fractional excretion of potassium, %	7.43 ± 4.09	1 to 15
tubular phosphorus reabsorption, %	92.10 ± 3.98	> 85
Renal tubular reabsorption of phosphate, mg/dL	4.60 ± 0.99	> 3.2
Calciuria, mg/kg/24 h	1.930 ± 1.137	< 4
Phosphaturia, mg/kg/24 h	9.896 ± 4.028	< 15
Proteinuria, mg/m ² /h	4.10 ± 3.16	< 4
β 2-microglobulin, μ g/mL	0.31 ± 0.41	0.03 to 0.3
Uricosuria, mg/dL	0.39 ± 0.26	> 0.53

tubular proteinuria in a man with beta-thalassemia minor.⁷ Cetin and associates investigated 41 subjects with beta-thalassemia minor and found that 6 patients (14.6%) showed indications of tubulopathy, (hypercalciuria, decreased tubular phosphorus reabsorption, renal magnesium wasting, renal uric acid wasting, and tubular proteinuria. They concluded that proximal renal tubular dysfunction is not rare in beta-thalassemia minor patients.⁶ Whereas, no evidence of renal tubular dysfunction was found in patients with beta-thalassemia minor by Kalman and coworkers.⁵

Prabakar and colleagues found nephrocalcinosis with evidence of renal tubular dysfunction such as hypercalciuria, reduced tubular reabsorption of phosphorus, hypomagnesemia, and renal magnesium wasting in a 24-year-old woman with beta-thalassemia minor.⁴

It has been proposed that renal tubular dysfunction in adults with beta-thalassemia minor may be due to inferior hemolysis, decrease erythrocyte life span, tubular iron deposition, oxidative lipid peroxidation, and toxins originated from erythrocytes.^{6,8} There are some studies showing renal dysfunction in patients with beta-thalassemia major.^{4,9-14} In addition, tubular dysfunction has been proposed in patients with iron deficiency anemia.^{15,16}

Our results should be interpreted considering its limitations; we did not determine the N-acetyl- β -D-glucosaminidase which is a marker of renal tubular impairment. In addition, we did not adjust the level of urinary solutes with dietary intake; consequently, the differences in fractional excretion of salts may be owing to variation of dietary intake.

In summary, among our pediatric patients with beta-thalassemia minor, we found evidence of kidney dysfunction. However, further studies in large series are desired to fully reveal whether there is a relationship between these two distinct disorders.

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CONFLICT OF INTEREST

None declared.

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