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Research Article

The Efficacy of Urine Sodium Versus Serum Creatinine for Prediction of Renal Tubular Dysfunction in the pediatric patients with B Thalassemia

Soad Abd ElMoaty Salah[1]*, Ebtesam Mohamed Mahmoud Selema[1], Asmaa Abdelfattah Ganna[1]

[1]Department of Pediatric, Shebin El-Kom Teaching Hospital, Shebin El-Kom 32511, Menoufia, Egypt.

***Corresponding Author:** Soad Abd ElMoaty Salah, Department of Pediatric, Shebin El-Kom Teaching Hospital, Shebin El-Kom 32511, Menoufia, Egypt.

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Abstract

Background: Beta-thalassemia syndromes are inherited disorders caused by defective synthesis of beta-globin chains, leading to ineffective erythropoiesis and severe microcytic hypochromic anemia, particularly in β-thalassemia major. Thalassemia intermedia represents an intermediate clinical form with moderate anemia that does not usually require regular blood transfusions. Although thalassemia is associated with significant cardiopulmonary and systemic complications, renal involvement has been relatively under-recognized. Therefore, accurate estimation of glomerular filtration rate (GFR) is essential for proper evaluation and management of renal function in children with β-thalassemia, as traditional markers such as creatinine may yield inaccurate results.

Methods: Fifty children of Beta thalassemia (major and intermedia) disease participated in the present study. Their age ranged from 3 to 20 years with mean age 10.27 ± 4.24 years. Patients were selected from the outpatients attending the pediatric outpatient's clinic of Shebein Elkom Teaching Hospital.

Results: there is highly positive significant correlation between Serum creatinine, age, S urea, B2M, Na, Ca and Ph($P<0.001$), positive significant difference with K ($P<0.05$), and highly negative significant correlation with C Cr 24 urine collection and There is highly positive significant correlation between Na in urine& age, ferritin, S urea, S Cr, B2 M ,K, Ca & Ph ($P<0.001$),and highly negative significant correlation with Hb and C Cr by 24hour urine ($P<0.001$).

Conclusion: Urine sodium is a significant important marker of renal tubular dysfunction especially in young thalassemic patients as compared to serum creatinine, Urine sodium had more sensitivity (92%), specificity 81.3% at area under curve 0.89 with the best predictive cutoff value 300 as compared to serum creatinine which recorded lowest sensitivity 69% and specificity 10%, with area under curve 0.55. Finally, urine sodium has the best diagnosis efficiency value "regarding sensitivity, specificity and positive predictive value" when compared with serum S Cr.

Keywords: Renal tubular dysfunction, β thalassemia, Urine sodium, Pediatric patients, glomerular filtration rate.

Key Message

- Renal involvement in children with beta-thalassemia is often under-recognized and requires early and accurate assessment.
- Urine sodium is a sensitive and reliable marker for detecting renal tubular dysfunction in pediatric beta-thalassemia patients.

- Urine sodium demonstrates higher diagnostic accuracy than serum creatinine, making it a superior tool for early renal evaluation in thalassemic children.

Introduction

Beta thalassemia syndromes, including β thalassemia major and intermedia, are inherited hemoglobinopathies caused by defective β globin chain synthesis, resulting in chronic anemia, iron overload, and ineffective erythropoiesis. In pediatric patients, β thalassemia major typically presents with severe anemia that necessitates lifelong regular blood transfusions and iron chelation therapy, whereas β thalassemia intermedia manifests with milder anemia and less frequent transfusion requirements [1].

Advances in medical care have significantly improved survival, yet they have also unmasked a spectrum of organ complications, including alterations in renal function that may be clinically silent in early stages. Multiple studies have documented evidence of both glomerular and tubular dysfunction in children with β thalassemia major and intermedia, including abnormalities such as proteinuria, increased urinary excretion of low molecular weight proteins, and elevated urinary electrolyte ratios, despite normal serum creatinine and estimated glomerular filtration rate (eGFR) values [2].

These findings underscore that routine assessments may fail to detect early renal injury, necessitating more sensitive biomarkers for early detection of renal involvement in thalassemic children. For instance, elevated urinary Na/Cr ratios and other urinary biochemical markers have been reported in up to 41% of pediatric β thalassemia patients, reflecting tubular impairment that may precede overt changes in traditional renal parameters. Consequently, urinary markers such as urine sodium and other early indicators have been explored as superior predictors of renal tubular dysfunction compared to serum creatinine, which often remains within normal ranges until later stages of renal injury [3]. This highlights the importance of comprehensive and sensitive renal evaluation in pediatric β thalassemia to enable early diagnosis and management of renal tubular dysfunction [4]. The purpose of this research was to compare the efficacy of urine sodium versus serum creatinine for prediction of renal tubular dysfunction in the β thalassemia major and intermedia patients.

Patient and Methods

Study Design and Patient Setting

Fifty children of Beta thalassemia (major and intermedia) disease participated in the present study. Their age ranged from 3 to 20 years with mean age of 10.27±4.24 years. Patients were selected from pediatric outpatient clinic of Shebein Elkom Teaching Hospital.

Ethical Consideration

The study complied with the World Medical Association's Declaration of Helsinki, according to the authors. The local committee of the Shebein Elkom Teaching Hospital approved all study methods. The advantages, possible hazards, and every stage of the procedure were explained to all participants. Before taking part in the research, each participant signed an informed consent form.

Subjects of the Study were Categorized into two Main Groups

Group I (thalassemia patients) was subdivided into Group Ia, which included 35 patients with thalassemia major (12 males and 23 females) aged 3–20 years, with a mean age of 11.24 ± 4.87 years, and Group Ib, which comprised 15 patients with thalassemia intermedia (7 males and 8 females) aged 4.5–20 years, with a mean age of 12.23 ± 5.17 years. Group II (control group) consisted of 20 apparently healthy children matched for age (3–19 years, mean 11.0 ± 4.67 years), sex (10 males and 10 females), and socioeconomic status.

Patients' Selection Criteria

In this study we included subjects that had a diagnosis of B thalassemia major, or intermedia documented by hemoglobin electrophoresis, they were regularly transfused with packed RBCs, and Subjects were receiving ongoing chelation therapy with deferoxamines or deferiprone mostly in an irregular manner. However, the following criteria were excluded from this study, previous renal pathology and previous treatment for thyroid dysfunction.

All Patients were Subjected to the Following

A detailed personal and family history, documenting each patient's name, age, sex, residence, family pedigree, and any family member requiring frequent blood transfusions. The history of present illness focused on clinical features such as pallor and jaundice, history of blood transfusions, drug intake particularly iron chelators and whether these were taken regularly. Additional details included the age at first blood transfusion and the frequency of transfusions. General examination assessed the presence of pallor and jaundice, anthropometric measurements including weight and height plotted on standard growth charts, and abdominal examination for hepatosplenomegaly. Routine laboratory investigations included complete blood count (CBC) using the ADVIA 2120 Siemens Automounter to evaluate hemoglobin levels and red cell indices (MCV, MCH, MCHC, and RDW), kidney function tests such as serum creatinine (modified Jaffe method), and serum ferritin measured by ELISA. Special laboratory investigations comprised urinary electrolytes (sodium, potassium, calcium, and phosphorus), creatinine clearance from 24-hour urine collection, and estimation of urinary

β2-microglobulin. Urinary phosphorus, calcium, sodium, and potassium were measured using the Synchron CX9 analyzer (USA) according to standard manufacturer instructions and established methodologies [5] 1925; Goodwin, 1970; Bauer, 1981; Kratochvil and Xi-Wen-He, 1990; Jansen and Helbing, 1991).

Estimation of creatinine in serum and urine examinations

Serum creatinine was measured based on the principle that creatinine reacts with picric acid under alkaline conditions to form a yellow-red complex, the absorbance of which is measured at 492 nm and is directly proportional to the creatinine concentration in the sample. A standard creatinine solution (2 mg/dL, 177 µmol/L) was used, with reagents consisting of picric acid (38 µmol/L) as R1 and sodium hydroxide (0.4 mol/L) as R2. The working solution was prepared by mixing equal volumes of R1 and R2, and all reagents were stable until the expiration date when stored at 15–25 °C. Serum creatinine concentration was calculated using the ratio of the absorbance of the specimen to that of the standard. Creatinine clearance was estimated using the endogenous creatinine clearance formula by (Schwartz et al., 1987).

Statistical Analysis Methods

The collected data were tabulated and statistically analyzed using an IBM personal computer with SPSS software version 11. Both descriptive and analytic statistics were performed. Descriptive statistics included percentages, means, and standard deviations. Analytic statistics included the Chi-square test to examine associations between qualitative variables, Student's t-test for comparing two groups with normally distributed quantitative variables, and the Mann–Whitney test for comparing two groups with non-normally distributed quantitative variables. For comparisons among three or more groups, ANOVA was used for normally distributed data, while the Kruskal–Wallis test was applied for non-normally distributed data. Pearson correlation was used to assess associations between two quantitative variables. Receiver Operating Characteristic (ROC) curves were constructed to evaluate the diagnostic performance of variables with two categories, determining cutoff values with the highest accuracy. Sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy were calculated using standard formulas, where aaa = true positive, bbb = false positive, ccc = false negative, and ddd = true negative cases. A P-value of < 0.05 was considered statistically significant

Results

According to a workflow diagram that describes the cohort of 56 children with Beta thalassemia who enrolled at Shebein Elkom Teaching Hospital, 6 individuals weren't included in the study (2 denied consent and 4 did not match the inclusion criteria). This led to the inclusion of 50 patients in the research. Group Ia included 35 patients with β-thalassemia major (12 males and 23 females) aged 3–20 years, with a mean age of 11.24 ± 4.87 years. Group Ib comprised 15 patients with β-thalassemia intermedia (7 males and 8 females), aged 4.5–20 years, with a mean age of 12.23 ± 5.17 years. Group II consisted of 20 healthy children (10 males and 10 females) aged 3–19 years, with a mean age of 11.0 ± 4.67 years, matched for age, sex, and socioeconomic status, serving as the control group (Figure 1). The current study found non-significant difference between the studied groups regarding to age, sex (P>0.05). (Table 1).

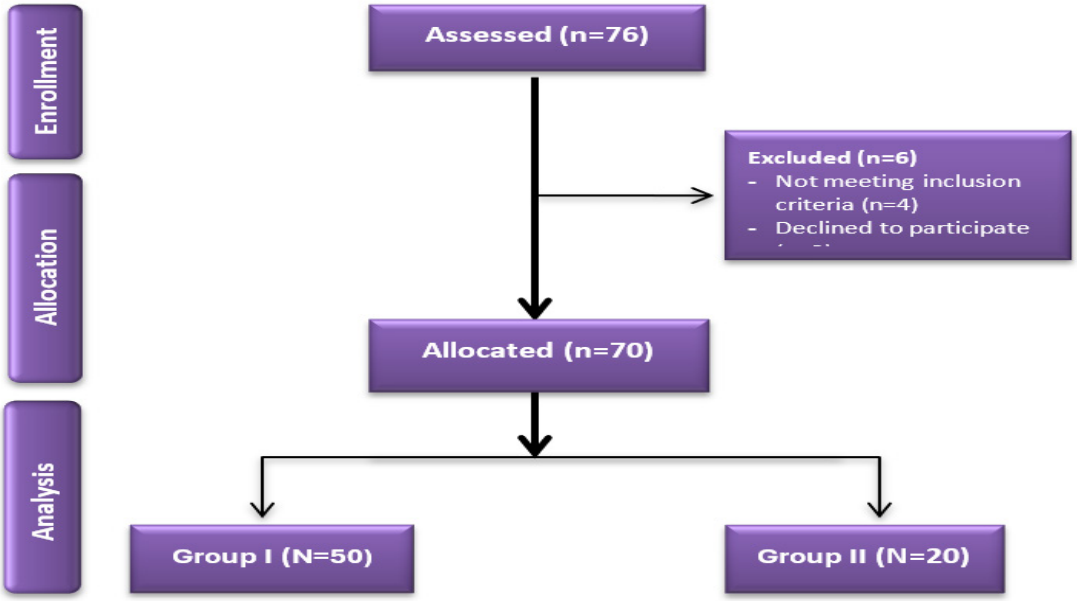

Figure 1. Flowchart of the patients studied.

Demographic data	Thalassemia major (n=35)		Thalassemia intermediate (n=15)		Control (n=20)		X2	P value
	No	%	No	%	No	%		
Sex Male Female	 12 23	 34.3 65.7	 7 8	 46.7 53.3	 10 10	 50 50	1.51	>0.05
Age in years (mean ±SD)	11.24 ± 4.87		12.23 ± 5.17		11.0 ± 4.67		F=0.42*	>0.05
Range	3-12		4.5-20		3-19			

Chi-square test (X2), ANOVA F-test (F), *Significant

Table 1. Comparison between studied groups regarding demographic data.

The present study shows highly significant difference between thalassemia major and thalassemia intermediate as regarding duration of chelation (P<0.001) and non-significant difference between both types of thalassemia regarding to frequency of transfusion Per month. and non-significant difference between both types of thalassemia regarding to splenomegaly & splenectomy (P>0.05), (Table 2).

Parameter	Thalassemia major (n=35)		Thalassemia intermediate (n=15)		X2	P value
	No	%	No	%		
Transfusion in months						
2m	0	0	0	0	0	>0.05
6m	28	80	0	0	25. 60	<0.001**
6m -1 year	6	17.1	0	0	2.92	>0.05
>2years	1	2.9	15	100	45.54	<0.001**
Frequency of blood transfusion per month						
Once	34	97.1	15	100	0.44	>0.05
Twice	1	2.9	0	0		
Duration of chelation						
Mean ±SD	7.57 ± 4.83	3.2±1.46	F=3.47	<0.001**		
Splenomegaly	11	31.4	7	46.7	1.06	>0.05
Splenectomy	24	68.6	8	53.3	3.97	>0.05*

Chi-square test (X2), ANOVA F-test (F), *Significant

Table 2. Comparison between two types of thalassemia regarding age at start of blood transfusion, frequency of blood transfusion, duration of chelation and splenomegaly and splenectomy.

The present study shows highly positive significant decrease regarding the Hb level and increase regarding to serum ferritin among thalassemia group and control (P<0.001). While it shows a non-significant difference between both types of thalassemia regarding to Hb and ferritin level (P>0.05) and non-significant difference between the studied groups regarding to kidney function test (S urea, serum Creatinine and Creatinine clearance) (P>0.05), (Table 3).

parameter	Thalassemia major (n=35)	Thalassemia intermediate (n=15)	Control (n=20)	F	P value
Hb(g/dl)					P1>0.05 P2<0.001 P3<0.001
Mean +SD	6.03 ± 0.79	6.47 ± 0.89	13.15 ± 1.41	335.26*	
Range	4-7	5-8	11-16		
Ferritin (ng/ml)					P1>0.05 P2<0.001 P3<0.001
Mean +SD	3738.83 ± 3717.56	2762.13 ± 1524.75	102.25 ±24. 09	42.31**	
Range	400-15900	1050-7000	50-140		

Blood urea (mg/dl)					p>0.05 P2>0.05 P3>0.05
Mean +SD	26.17 ± 4.54	27.27 ± 7.23	25.25 ± 5.27	0.59	
Range	18-35	18.45	18.35		
Serum creatinine (mg/dl)					P1>0.05 P2>0.05 P3>0.05
Mean +SD	0.48 ± 0.1	0.58 ± 0.2	0.45 ± 0.17	4.54*	
Range	0.34-0.70	0.4-1.2	0.4-0.7		
Creatinine clearance 24h urine (ml/min/1.73m2)					P1>0.05 P2>0.05 P3>0.05
Mean +SD	122.67±12.19	120.84±12.06	120.25±7.91	0.34	
Range	106.2-145	108-143	110-135		

ANOVA F-test (F), *Significant

Table 3. Comparison between studied groups regarding hemoglobin & ferritin level and kidney function test.

The current results show non-significant difference between both types of thalassemia (P>0.05) highly positive, significant difference between both types of thalassemia and control (P>0.001) regarding urine electrolytes (Na, K, Ca, Ph). (Table 4).

Electrolytes	**Thalassemia major (n=35)**	**Thalassemia intermediate (n=15)**	**Control (n=20)**	**F**	**P value**
Urine sodium (Na)					P1>0.05 P2<0.001 P3<0.001
Mean +SD	206.91 ± 97.35	220.07 ± 100.89	68.35 ± 28.08	26.7	
Range	30-340	50-350	30-125		
Urine potassium (K) (mEq/L)					P1>0.05 P2<0.001 P3<0.001
Mean +SD	67.39 ± 29.73	72.69 ± 29.61	27.1 ± 11.67	25.24	
Range	14.7-121	20-110	15-50		
Urine calcium (Ca) (mg/24h)					P1>0.05 P2<0.05 P3<0.05
Mean +SD	211.66 ± 99.27	227.9 ± 7.65	127.2 ± 30.82	8.19	
Range	30-360	95-340	100-225		
Urine Phosphorus (Ph) (g/24h)					P1>0.05 P2<0.001 P3<0.001
Mean +SD	5.02 ± 5.45	5.88 ± 4.75	0.54±0.19	36.84	
Range	05-20.6	0.6-17	0.3-0.9		

ANOVA F-test (F), *Significant

Table 4. Comparison between studied groups regarding urine electrolytes.

Additionally, highly positive significant correlation was found between Serum creatinine, age, S urea, B2M, Na, Ca and Ph(P<0.001), positive significant difference with K (P<0.05), and highly negative significant correlation with Cr 24 urine collection (Table 5).

Parameters	**Thalassemia major (n=35)**		**Thalassemia intermediate (n=15)**		**Control (n=20)**	
	r	**P value**	**r**	**P value**	**r**	**P value**
Age (in years)	0.52	<0.001	0.51	<0.001	0.6	<0.05
Age at start of transfusion (in months)	- 0.12	>0.05	- 0.13	>0.05	-0.09	>0.05
Frequency of transfusion (per month)	0.08	>0.05	0.09	>0.05	0.08	>0.05
Duration of chelation (in years)	0.01	>0.05	-0.15	>0.05	0.19	>0.05
Hb (g/dl)	- 0.02	>0.05	- 0.22	>0.05	-0.36	>0.05

Serum Ferritin (ng/ml)	0.003	>0.05	0.11	>0.05	-0.05	>0.05
S. urea (mg/dl)	0.71	<0.001	0.73	<0.001	0.73	<0.001
Creatinine clearance24hour urine collection (ml/min/1.73m2)	-0.46	<0.001	-0.53	<0.001	-0.46	>0.05
B2 M (µg/l)	0.57	<0.001	0.68	<0.001	0.41	>0.05
Na (mEq/L)	0.49	<0.001	0.42	<0.05	0.65	<0.05
K (mEq/L)	0.36	<0.05	0.49	<0.001	0.25	>0.05
Ca (mg/24hour)	0.52	<0.001	0.54	<0.001	0.58	<0.05
Ph (g/24hour)	0.45	<0.001	0.69	<0.001	0.23	>0.05

Chi-square test (X2), ANOVA F-test (F), *Significant

Table 5. Pearson correlation between serum creatinine and other parameters.

Also, there is highly positive significant correlation between Na in urine& age, ferritin, S urea, S Cr, B2 M, K, Ca & Ph (P<0.001), and highly negative significant correlation with Hb and C Cr by 24hour urine (P<0.001), (Table 6).

Parameters	**Thalassemia major (n=35)**		**Thalassemia intermediate (n=15)**		**Control (n=20)**	
	r	**P value**	**r**	**P value**	**r**	**P value**
Age (in years)	0.68	<0.001	0.66	<0.001	0.71	<0.001
Age at start of transfusion (in months)	- 0.12	>0.05	-0.13	>0.05	-0.09	>0.05
Frequency of transfusion (per month)	0.08	>0.05	0.09	>0.05	0.08	>0.05
Duration of chelation (in years)	0.10	>0.05	0.01	>0.05	0.34	>0.05
Hb (g/dl)	-0.604	<0.001	-0.6	<0.001	-0.5	<0.001
Serum ferritin (ng/ml)	0.458	<0.001	0.42	<0.05	0.4	<0.05
S urea (mg/dl)	0.56	<0.001	0.49	<0.001	0.69	<0.001
S Creatinine (mg/dl)	0.49	<0.001	0.42	<0.05	0.65	<0.05
Creatinine clearance 24hour urine (ml/min/1.73m2)	-0.7	<0.001	-0.66	<0.001	-0.79	<0.001
B2 M(µg/l)	0.60	<0.001	0.61	<0.001	0.66	<0.05
K(mEq/L)	0.60	<0.001	0.60	<0.001	0.59	<0.05
Ca (mg/24hour)	0.65	<0.001	0.61	<0.001	0.44	>0.05
Ph (g/24 hour)	0.48	<0.001	0.49	<0.001	0.44	>0.05

Table 6. Pearson correlation between sodium in urine& other parameters.

In our study urine sodium has the best diagnosis efficiency value "regarding sensitivity, specificity and positive predictive value" when compared with serum S Cr (Table 7).

Validity	**Area under curve**	**Cut off value**	**Sensitivity %**	**Specificity %**	**Accuracy**	**PPV**	**NPV**
Serum creatinine	0.55	0.37	69%	10%	71%	73%	50%
Urine sodium	0.89	300	92%	81.3%	83%	85%	75%

Table 7. Validity of serum creatinine and urine sodium in detecting cases of renal impairment.

Discussion

Thalassemia is a hereditary anemia resulting from genetic disorders of hemoglobin synthesis. It is not a single disease but a group of disorders, each resulting from an inherited abnormality of globin production, and inherited defects in the

rate of synthesis of one or more of the globin chains (α or β). The result is unbalanced globin chain production. Multiple studies have documented evidence of both glomerular and tubular dysfunction in children with β thalassemia major and intermedia, including abnormalities such as proteinuria, increased urinary excretion of low molecular weight proteins, and elevated urinary electrolyte ratios, despite normal serum creatinine and estimated glomerular filtration rate (eGFR) values. The aim of our work is to compare the efficacy of urine sodium versus serum creatinine for prediction of renal tubular dysfunction in the β thalassemia major and intermedia patients. The study was carried out on 50 thalassemic patients, they were divided into 35 TM &15 TI. They were diagnosed as β thalassemia by CBC&HB electrophresis. 20 apparently healthy children were served as controls. they were matched in age, sex and socio-economic standard.

Results of this study showed no significant differences between the studied groups and the controls as regards to age and sex (P > 0.05). However, in our patients there was a highly significant decrease in heights in TM (128.49 + 21.32), TI (135.6 + 19.19) when compared with controls (137.8 + 21.1) (p<0.001). It is explained by [6] who reported that the major cause of growth retardation is hypogonadism, hypothyroidism, and probably, impairment of the GH- IGF-1 axis secondary to hemosiderosis of the pituitary gland and liver. Our results agreed with [7] Desanctis, (2002), [8] and Lanskowsky, (2011) who demonstrated significant decrease in the height of thalassemic children due to growth retardation.

Regarding to the results of the age of the start of blood transfusion in our patients, patients with TM were put on regular blood transfusion earlier because of their severe anemia (5.92± 3.89 months) that becomes apparent after 6 months of age [9], whereas patients with TI received blood transfusion somewhat later because of their milder symptoms (54.20 ± 27.22 months) [10]. Comparing the number of patients who had splenectomy, no significant difference was detected between the TM (68.6%) and TI (53.3%). This come in agreement with [11] as both types of B-TM (TM and TI) was exposed to same factors that leads to increase transfusion requirement and the need for splenectomy.

Regarding the results of HB, there was a highly significant decrease in the studied groups when compared to the controls (P<0.001) as the anemia was the first presentation in the diagnosis of thalassemia [9,12] documented that anemia is usually profound when first documented. Before transfusion, Hb concentration was 2.5 to 6.5 g/dl.

On comparing the results of HB level between TM (6.37 ± 0.84 g/dl) and TI (6.26 ± 1.03 g/dl) they showed no significant differences (P>0.05) and significant decrease in Hb level in thalassemic group when compared to controls (13.15±1.41), (P>0.001) and this is in agreement with Vladislav et al., (2008). On comparing the level of serum ferritin between TM (3738.83±3717.56 ng/ml), TI (2762.13±1524.75 ng/ml)and in controls (102.25±24.09), they showed highly significant increase in thalassemia group when compared to controls (P<0.001) As The patients were maintained on regular blood transfusion and one unit of blood deliver about 200 mg iron to tissue [13,14], and no significant difference between TM and TI (P>0.05)This come in agreement with [15 ,16]

Iron overload coming from multiple life-long transfusions and enhanced iron absorption results in secondary hemosiderosis and ineffective erythropoiesis with resultant increase in serum ferritin and this come in agreement with [17-19,12,14] Sumboonnanonde et al., (2008) reported that chronic anaemia, chronic hypoxia, iron overload and DFO toxicity are the key factors for damage of renal tissue cells. Early identification of patients at high risk of developing renal failure is of great importance as it may allow specific measures to delay the progression of renal damage and thus reduce the incidence of end- stage renal failure and mortality. The measurement of endogenous blood substances to estimate GFR is a common practice. Properties of an ideal endogenous blood substance to estimate GFR should include release into the blood stream at a constant rate, free filtration by the glomerulus, no reabsorption or secretion by the renal tubules and exclusive elimination via the kidney [20,21]

The ideal endogenous marker would be characterized by stable production rate, stable circulating levels (unaffected by pathological changes), lack of protein binding, free glomerular filtration, and lack of reabsorption or secretion; to date, no such marker has yet been identified [22].

There was no significant difference between the studied groups and the controls in TM (0.48± 0.1 mg/dl) and TI (0.58± 0.2 mg/dl) and in controls (0.45+0.17) regarding to the level of serum creatinine (S Cr). Voskaridou et al., (2006), as well as [14] reported that S Cr did not rise until about 50% of renal functions had been lost as S Cr is insensitive for detection of small decrease in GFR because of the nonlinear relationship between its plasma concentration and GFR (Filser et al., 2001). On comparing the level of blood urea between studied groups and controls in TM (26.17+4.54), TI (27.27+7.23) and in controls (25.25+5.27). There was no significant difference between them (P>0.05). On comparing the level of creatinine clearance 24 hours urine collection between studied groups and controls in TM (122.67+12.19), TI (120.84+12.06) and in controls (120.25+7.91). There was no significant difference between them (P>0.05) this come in agreement with [23-25,16]

In the current study, the diagnostic efficiency values for the studied biochemical markers were assessed by estimating creatinine clearance using 24 hours urine collection not by Shwartz formula because, Shwartz formula in not used in persons whom heights is affected as it may not reflect the muscle mass, so this method cannot be applied in the thalassemic patients as their heights is retarded [26].

Regarding the results of serum creatinine in the present study, the best cut off level was 0.37 mg/dL, 48 patients were above this cut off and 2 below it and none of the control was

below this cut off. At this level, the diagnostic sensitivity was 69%, the diagnostic specificity was 10%, the diagnostic accuracy was 71%, and the positive predictive value was 73%. [27] reported that, for serum creatinine, the best cut off level was 0.55 mg/dL. At this level, the diagnostic sensitivity was 75%, the diagnostic specificity was 75%, the diagnostic accuracy was 75%, and the positive predictive value was 75%. This may be attributed to the difference in patients' numbers and the methodology used. while [28] reported that the best cut-off level was 0.8 mg/dL. At this level, the diagnostic sensitivity was 70%, the diagnostic specificity was 95%, the diagnostic accuracy was 60%, and the positive predictive value was 60%. As regards to urine sodium (Na), the best cut off level was 300 mEq/L 11 patient were above this level and 39 were below it and none of the control group was above this level. At this level the diagnostic sensitivity was 92%, diagnostic specificity was 81.3%, the diagnostic accuracy was 83% and the positive predictive value was 85%. So; the diagnostic accuracy of urine level and urine electrolytes especially sodium was better than that of S Cr.

Strength and limitations of the study

this study has several strengths, including the inclusion of both β-thalassemia major and intermedia pediatric patients, the use of age-, sex-, and socioeconomically matched healthy controls, and comprehensive assessment of clinical, hematological, and renal parameters. The use of 24-hour urine collection for creatinine clearance and evaluation of urine sodium as a sensitive marker of early renal tubular dysfunction are notable advantages. However, the study has some limitations, including a relatively small sample size, particularly in the intermedia group, its cross-sectional design, potential variability in patients' transfusion and chelation histories, lack of assessment of additional urinary biomarkers, and being a single-center study, which may limit the generalizability of the findings

Conclusion

Urine sodium is a significant important marker of renal tubular dysfunction especially in young thalassemic patients as compared to serum creatinine, Urine sodium had more sensitivity (92%), specificity 81.3% at area under curve 0.89 with the best predictive cutoff value 300 as compared to serum creatinine which recorded lowest sensitivity 69% and specificity 10%, with area under curve 0.55. Finally, urine sodium has the best diagnosis efficiency value "regarding sensitivity, specificity and positive predictive value" when compared with serum S Cr.

Declaration

Consent for publication: All authors have read and revised the manuscript and agreed to its publication.

Availability of data and material: All data supporting the study are presented in the manuscript or available upon request.

Acknowledgments: Not applicable

Authors' information (optional): Not applicable

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