EVALUTION OF SERUM BETA-2-MICROGLOBULIN AS A MARKER OF RENAL DYSFINCTION IN PEDIATRIC PATIENTS WITH SICKLE CELL DISEASE

By

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ABSTRACT

Background*: Sickle-cell disease is a multisystem disease, associated with episodes of acute illness and progressive organ damage, and is one of the most common severe monogenic disorders worldwide.*

Renal dysfunction is a frequent complication in sickle cell disease as a result of long-standing anemia and disturbed circulation through the medullar capillaries, so early detection of it is important to guard against chronic kidney disease.

Beta-2-Microglobulin, a low molecular weight protein, is freely filtered in the glomerulus wherefrom it is totally reabsorbed and degraded in the renal tubules. Thus, it is a sensitive marker of the glomerular filtration capacity of the kidney.

Objective*s: To identify the role of serum Beta-2-Microglobulin as early predictor of renal dysfunction in patients with sickle cell disease.*

Patients & Methods: *We measured serum B-2-Microglobulin in 67 children previously diagnosed as Sickle Cell Disease and attending to Bab Elsharia (Sayed Galal) University Hospital and Misr Children Hospital in period from November 2016 to September 2017.*

This group of patient was matched with control group (20 children) with the same ages who do not have Sickle Cell Disease and recruited from the same study site.

Results: *Although, serum B2M was within the reference range, cases had significantly lower serum B2M to the control group. Serum level of B2M was not affected by gender and our data clearly demonstrate age independency for serum concentrations of B2M.*

Comparing serum B2M to serum creatinine by ROC curve, showed that area under the curve of serum B2M (0.48) versus (0.05) was insignificantly higher and both were below 0.7; indicating that overall predictability of SCD of serum B2M as well as serum creatinine were not statistically significant.

Conclusion:

● *Renal dysfunction in SCD children may occur before the occurrence of any symptoms or complication.*

● *Serum B2M is not a good marker in detection of early stages of SCD nephropathy in children.*

● *A/C ratio and GFR are considerable methods of preliminary detection of glomerular affection in SCD children.*

Recommendations:

● *Routine screening of SCD children with A/C ratio and GFR is mandatory for early detection of renal affection.*

● *Further studies of establishment of best marker used for early assessment of tubular and glomerular dysfunction in SCD children is recommended.*

INTRODUCTION

Sickle-cell disease (SCD), also known as sickle-cell anemia (SCA), is a group of genetically passed down blood disorders. It results in an abnormality in the oxygen-carrying protein hemoglobin found in red blood cells. This leads to a rigid, sickle-like shape under certain circumstances. Problems in sickle cell disease typically begin around 5 to 6 months of age. A number of health problems may develop, such as attacks of pain ("sickle-cell crisis"), anemia, bacterial infections, and stroke. Long term pain may develop as people get older **(National Heart, 2015).**

Children with sickle cell disease (SCD) are remarkably more prone than others to renal dysfunction. The kidneys, as one of the systemic long term hazards in SCD, may be affected by both the haemodynamic changes of chronic anemia as well as by the consequences of vaso-occlusion **(Badr et al., 2013)**.

A wide spectrum of renal abnormalities is associated with SCD, including glomerular hyper filtration and proteinuria, micro albuminuria, defect in urine concentrating ability, defect in proximal renal tubular reabsorption and defect in hydrogen ion and potassium excretion **(Nath K.A, Katusic Z.S, 2012).**

Serum beta2 microglobulin has now been identified as an important prognostic marker in a large number of hematologic and non-hematologic disorders. Urine beta-2-microglobulin levels are high in renal tubular disorders despite normal plasma levels, reflecting a dysfunction in reabsorption by the proximal tubules **(Orgentec, 2012).**

PATIENT AND METHODS

(A) PATIENTS:

This study was done on 68 Egyptian children previously diagnosed as SCD and regularly attending Bab Elsharia University Hospital and Misr Children Hospital. Their ages ranged between 1 and 18 years with mean age 9.44+3.79 years over a period November 2016 to September 2017.

This patient group was matched with control group (20 children) with the same age and sex who do not have SCD and recruited from the same study sites.

Inclusion criteria:

- Patients with diagnosis of SCD, based on conventional clinical and hematological criteria.
- Patients aged 1 year or more.
- Both males and females.
- Patients in a steady state (defined as being crisis-free for at least 2 weeks before enrollment).

Exclusion criteria:

- Patients with documented renal failure.
- Patients with clinical or laboratory evidence of renal failure.
- Patients with evidence of urinary tract infections.

(B) METHODS:

The authors declared that is no conflict of the interest with respect to the research, authorship or publication.

All the data of the patient and results of the study are confidential and the patient has the right to keep it.

The patient has the right to withdraw from the study at any time.

Ethical committee approval of Faculty of Medicine, Alazhar University was obtained before starting the study.

After obtaining required consents, all patients were subjected to the following:

Medical history assessment:

- Full history taking and thorough review of medical records were performed focusing on age at diagnosis, frequency and severity of vaso-occlusive crises, disease related complications (for example, acute chest syndrome, pulmonary hypertension, sequestration crisis, priapism, leg ulcers, stroke.etc), and treatments (emergency department visits, hospital admissions, and drugs), transfusion and "chelation

history. History suggestive of renal dysfunction (e.g. polyuria, nocturia, hematuria...etc) were also obtained.

Physical examination and laboratory investigations:

A complete physical examination was performed for all patients.

The following investigations were done for all the subjects:

- Complete blood picture by Coulter Counter.
- Reticulocytic count.
- Steady state serum ferritin and lactate dehydrogenase (LDH).
- Urine analysis, urinary albumin and creatinine.
- Serum creatinine, electrolytes by conventional methods.
- GFR was estimated by the Schwartz formula (Schwartz et al., 1976) for patients 17 years of age or younger and by the Cockcroft-Gault formula for those 18 years or older (Cockcroft and Gault 1976) as well as by creatinine clearance.
- Serum beta-2-microglobulin was measured using commercially available kit.
- The percentages of HbA, HbS, HbA2, and HbF were determined using hemoglobin electrophoresis system.
- Liver function tests: alanine transaminase (ALT), aspartate transaminase (AST) and serum bilirubin (total and direct).

For the control group the following were done after obtaining the required consent:

- Hemoglobin electrophoresis.
- Serum creatinine and serum beta-2-microglobulin.
- Urine samples were taken from the patients for microscopic examination and chemical measurements of urinary protein, creatinine, protein/creatinine ratio and GFR (estimated by the Schwartz formula for patients 17 years of age or younger and by the Cockcroft-Gault formula for those 18 years or older) as well as by creatinine clearance.

Beta-2-Microglobulin Determination

Principle:

Highly purified anti-human-beta-2-microglobulin antibodies are bound to microwells. The reaction is based on indirect enzyme immuno assay (ELISA) method.

Measuring range:

The calculation range of this EL1SA assay is 0 - 12 μg/ml.

Expected values:

In a normal range study with samples from healthy blood donors the following ranges have been established with this ELISA assay: Cut-off 0-3 μg/ml Serum.

Interpretation of results:

- Normal < 3 μg/ml Serum.
- Elevated > 3 μg/ml Serum **(Evrin et al., 2002).**

Statistical analysis of data:

Analysis of data was done by IBM computer using SPSS (statistical program for social science version 15) as follows:

- Description of quantitative variables as mean, SD and range.
- Description of qualitative variables as number and percentage.
- Unpaired t-test was used to compare two groups as regard quantitative variable in parametric data (SD<25% mean).
- Mann Whitney Willcoxon test was used to compare two groups as regard non parametric data (SD>50% Mean).

P value > 0.05 insignificant.

P value < 0.05 significant.

P value < 0.01 highly significant.

RESULTS

Table (1): Demographic and Clinical characteristics of the studied cases (n=68):

	The studied cases (n=68)
	Number (%)
Gender: Male Female	33 (48.5%) 35 (51.5%)
Positive consanguinity	37 (54.4%)
Splenectomized Splenomegaly	11 (16.2%) 7 (10.3%)
Indication of Splenectomy: Frequent blood transfusion	10 (14.7%)

	Minimum	**Maximum**	**Mean**	**SD**
Age (years)	1	18	9.441	3.791
Age at diagnosis (months)	1	72	21.397	14.540
DOF (years)	0.5	16	6.919	3.707
Weight (kg)	10	80	31.5	13.6
Height (cm)	80	165	130.7	18.3
BMI	11.1	29.385	17.47	3.383
Transfusion rate (unit/year)	0	12	4.221	3.701
Splenectomy duration (years)	2	14	8.364	3.042
Admission/year	0	7	1.967	1.488
VOC (times/year)	1	7	3.279	1.256

DOF: Duration of follow up.

BMI: Body mass index.

VOC: Vaso-occlusive crisis.

Sixty-eight patients were included in this study; 33 (48.5 %) males and 35 (51.5%) females with; m/f ratio 0.94, their mean age was 9.4 ± 3.8 years (range 1-18 years).

Referring to their medical records, their age at diagnosis ranged from 1 to 72 months with a mean of 21.4 ± 14.5 months and the duration of follow-up which reflect duration of disease ranged from 0.5 to 16 years with a mean of 6.9 ± 3.7 years.

Hemoglobin electrophoresis revealed that 28 cases had hemoglobin SS disease, 39 S/beta thalassemia and 1 hemoglobin SC disease with none of our cases had hemoglobin AS (sickle cell trait). Thirty-seven patients (54.4%) had history of positive consanguinity. Eleven patients (16%) had

been splenectomized because of huge spleen and/or frequent transfusions. Table (1) illustrates the baseline data of the studied cases.

Table (2): Markers of renal integrity and functions:

	The studied cases (n=68)				Reference
	Minimum	Maximum	Mean	SD	Range
Serum creatinine (mg/dl)	0.1	0.7	0.4	0.1	0.4-1.4
BUN (mg/dl)	2	18	7.8	2.9	5.0-20.0
Serum B2M (µg/ml)	0.720	3.86	1.9	0.8	0.3-3 Charlize Theron.5
Protein/creatinine ratio	0.05	0.5	0.1	0.1	< 0.2
Urinary creatinine(mg/dl)	5	6	5.3	0.5	40-300
Estimated creatinine clearance (ml/min/1.73m2)	120	336	235.3	45.5	90-100
GFR(ml/min/1.73m2)	106.43	745	194.79	90.33	90-100
Specific gravity	1010	1030	1018.0	5.5	1005-1025

BUN: Blood urea nitrogen.

B2M: Beta-2-microglobulin.

GFR: Glomerular filtration rate.

This table (table 2) shows that mean values of all measured parameters lie within the reference range except urinary creatinine, Creatinine clearance and GFR.

Table (3): Incidence of impaired renal function in the studied patients:

	The studied cases (n=68)
	Number (%)
A/C ratio >0.2	10 (14.7%)
GFR>165(ml/min/1.73m2)	37 (54.4%)
Creatinine clearance >120 (ml/min/ 1.73m2)	67 (94.1%)
Serum B2M > 3 µg/ml	0

A/C: Albumin to creatinine ratio.

GFR: Glomerular filtration rate.

B2M: Beta-2-microglobulin.

This table shows that none of our cases had elevated serum creatinine, while 32 (47%) cases had levels below the reference range. None of our cases had GFR below 89 ml/min/1.73 m2 and no cases had creatinine clearance below 80 ml/min/1.73m2

Table (3): Comparison between cases and controls as regard clinical and laboratory data:

	Cases (n=68)		**Control (n=20)**		**p-value**
	Mean	**SD**	**Mean**	**SD**	
Age (years)	9.4	3.8	9.6	4.1	0.3
Weight (kg)	31.5	13.6	41.5	12.9	0.002*
Height (cm)	130.7	18.3	140.8	15.3	O.001*
BMI (kg/m2)	17.6	3.4	21.0	4.3	<0.001*
Serum creatinine (mg/dl)	0.371	0.108	0.455	0.128	0.004*
BUN (mg/dl)	7.835	2.852	12.5	3.426	<0.001*
Serum B2M (µg/ml)	1.926	0.757	4.298	0.872	<0.001*

* Statistically significant.

BMI: Body mass index.

BUN: Blood urea nitrogen.

B2M: Beta-2-microglobulin.

This table shows that the studied cases had significantly lower weight, height and BMI when compared to control group (p=0.002, <0.001, <0.001 respectively). On comparing the studied cases and controls; cases had significantly lower serum creatinine, BUN and serum B2M (p=0.004, <0.001, O.001 respectively).

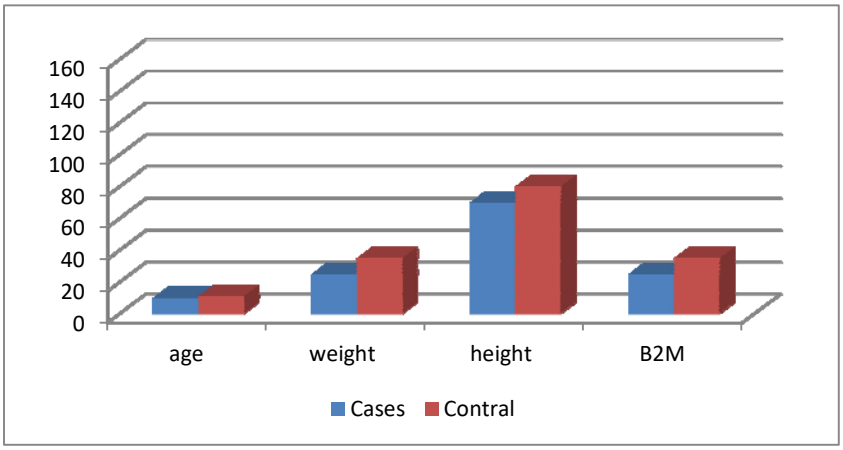

Figure (1): Demographic data of patients and control groups.

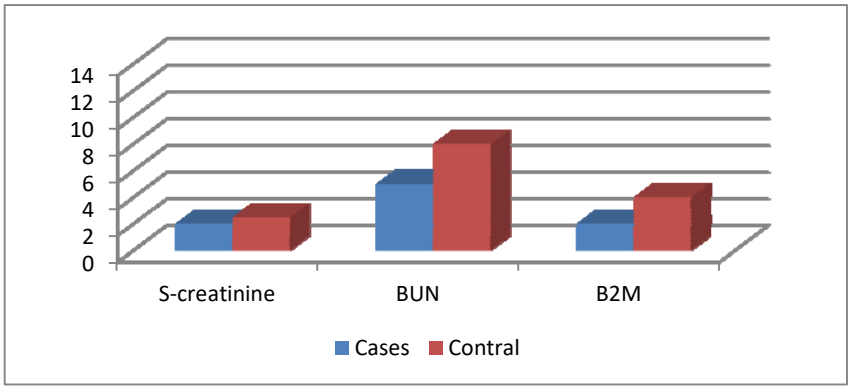

Figure (2): Markers of renal function among patients and control groups.

Table (5): Correlations of GFR and creatinine clearance with other variables:

Variables	GFR		Estimated Cr clearance	
	R	R value	R	P value
Age (years)	0.381	0.001*	-0.52	0.673
Follow up duration	0.273	0.024*	0.29	0.817
Transfusion rate	0.309	0.010*	-0.131	0.285
Splenectomy	0.282	0.020*	0.035	0.776
Weight (kg)	0.314	0.009*	-0.067	0.589
Height (cm)	0.395	0.001*	-0.078	0.529
Hct %	-0.252	0.038*	0.117	0.343
Platelets count 10^3/ul	0.250	0.040*	0.187	0.127
Serum ferritin (ng/ml)	0.452	O.001*	-0.036	0.769
Serum creatinine (mg/dl)	-0.756	<0.001*	0.181	0.139
BUN (mg/dl)	-0.251	0.039*	0.018	0.886

* Statistically significant p value.

HCT: Hematocrit.

BUN: Blood urea nitrogen.

In table (5) We found no significant correlations of creatinine clearance and any of the studied clinical or laboratory variables. There were no significant correlations between GFR and indicators of hemolysis or disease severity.

Table (6): Clinical and Laboratory data for patients according to gender:

	Males (n=33)	Females (n=35)	P value
	Mean ± SD	Mean ± SD	
Age (years)	9.12(3.59)	9.7 (4)	0.5
Hemoglobin (g/dl)	7.73(1.08)	7.38(1.15)	0.2
Total bilirubin (mg/dl)	1.9(0.8)	2.48(1.01)	0.02*
HbS%	65.7(23.53)	65.2(23.37)	0.9
Serum creatinine (mg/dl)	0.36(0.11)	0.37(0.1)	0.9
BUN (mg/dl)	7.7(3.04)	*7.95(2.69)	0.7
Serum B2M (ug/ml)	1.97(0.8	1.88(0.69)	0.6
Protein/creatinine ratio	0.15(0.098)	0.127(0.04)	0.2
Creatinine clearance (ml/min/1.73m2)	234.9(49.27)	235.7(42.3)	0.9
GFR (ml/min/1.73m2)	496.59(111.48)	193.08(66.13)	0.8
Urinary proteins	0.03(0.17)	0.0(0)	0.3
Specific gravity	1018.5(5.3)	1017(5.6)	0.5
	Median (IQR)	**Median (IQR)**	**P value**
Reticulocytes%	8.86 (8.9) 7(5.8)	10.7(8.07) 9.4 (7.4)	0.3
LDH (U/L)	465.14(267) 481(322)	447(408) 360(431)	0.8
HbF%	10.4(12.18) 2.1(19)	10.49(11.56) 9.1(18)	0.9
Serum ferritin	1033.6(2058) 342(512)	598(606.5) 404(546)	0.23

BUN: Blood urea nitrogen.

B2M: Beta-2-microglobulin.

GFR: Glomerular filtration rate.

LDH: Lactate dehydrogenase.

This table shows no significant difference was found between male and female patients regarding age, hemoglobin, reticulocytes, LDH, serum ferritin, Hb F, Hb S, serum creatinine, BUN, urinary proteins, protein/creatinine ratio, creatinine clearance, GFR, specific gravity, serum B2M ($P > 0.05$ for all).

Table (7): Area under the ROC curve for Serum B2M and creatinine in predicting abnormal filtration:

Variables	Area	St. error	95% CI
S creatinine	0.05	0.026	0.003 0.1
Serum B2M	0.484	0.07	0.345 0.6

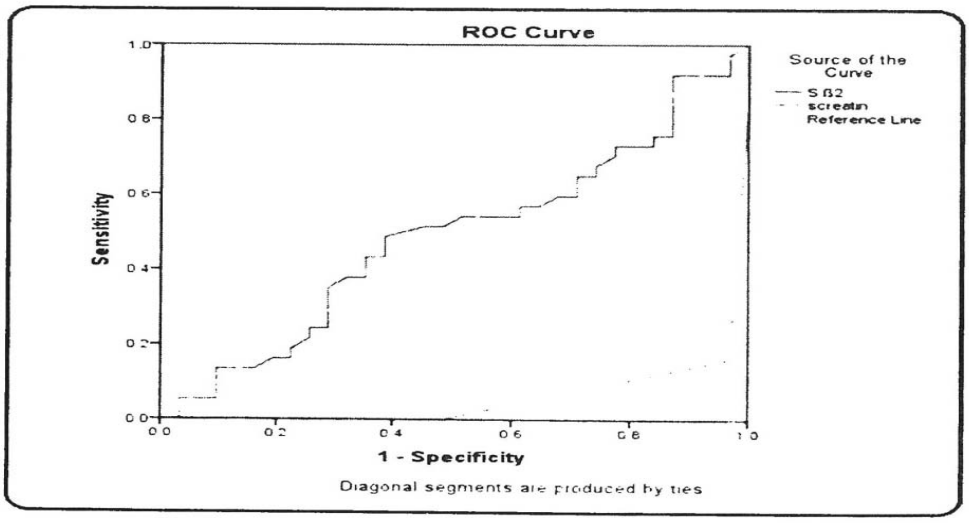

Figure (3): ROC curve of serum creatinine and B2M and for prediction of SCO nephropathy.

We compared overall predictability of SCT nephropathy by serum creatinine and serum B2M by ROC curve, it was found that areas under the curve of serum B2M (0.48) was higher when compared to that of serum creatinine but it didn't reach significance (p >0.5) indicating that overall predictability of both B2M is not significantly higher when compared to serum creatinine; making adoption of any as a good predictor of SCD nephropathy unlikely (Figure3).

DISCUSSION

The goal of the current study was to explore whether serum level of B2M may serve as early indicators of renal dysfunction in a large cohort study of SCD children, as compared to serum creatinine and creatinine clearance.

Sixty-eight patients 33 (48.5 %) males and 35 (51.5%) females were included in this study. All children were aged 1-18 years with established diagnosis of SCA in a steady state disease (28 Hb-SS disease, 39 Hb-S/beta thalassemia and 1 Hb-SC disease). Further 20 apparently healthy subjects with matching age & sex were included and served as a control group. Both cases and controls were comparable regarding gender and age (p 0.05). However, the studied cases had significantly lower weight, height and BMI when compared to control group (p=0.002, 0.001, 0.001 respectively) which is explainable by nature of underlying disease.

The demographics and genotypic characteristics of our cases were quite different from **Aygun et al., (2011)** as their cohort was mainly of Hb-SS disease with male sex predominance and from **Economou et al., (2011)** who studied 17 Hb SB subjects.

In the current work 37 patients had positive consanguinity this can be explained that the high rate of consanguineous marriage in Egypt **(El-Hazmi et al, 2011; Hamamy 2012).** The age at diagnosis ranged from 1 to 72 months with a mean of 21.4±14.5 months and the duration of follow-up which reflect duration of disease ranged from 0.5 to 16 years with a mean of 6.9±3.7 years. Eleven patients (16%) had been splenectomized because of

huge spleen and/or frequent transfusions.

Analysis of urinary symptoms and results of complete urine analysis revealed that more than 50% had polyuria and 4.5% had hematuria **(Chukwu et al., 2011)**. Despite the well-known increased secretion of creatinine in renal proximal tubules **(Ataga et al., 2000)**, we found that mean urinary creatinine in our patients was much lower than the reference range and all cases had low urinary creatinine, however, this agree with previous reports in SCD patients **(Rodby et al, 1995, Lima et al., 2002)**. This may be explained by the expected dilution of the urinary creatinine by the high urinary volume that results from the impaired urinary concentrating ability seen in patients with sickle cell disease **(Ataga et al., 2000)**.

The mean value of urinary albumin/creatinine ratio (A/C) ratio in our patients was within the normal range but 10 (14.7%) cases had elevated A/C ratio and this was consistent with the 15-28% prevalence previously reported for children with SCA **(Aygun et al., 2011; McKie et al, 2007; Alvarez et al., 2008; Dharnidharka et al., 1998; Becton et al., 2010; Alvarez et al., 2006)**.

Abnormal proximal tubular function, partly related to chronic use of analgesics, results in increased clearance of creatinine and possibly other markers of GFR **(Saborio and Scheinman, 1999; Pham et al. 2000)**. This fact may explain why our patients with elevated GFR had lower serum creatinine and BUN ($p = 0.001$, 0.001 and 0.03 respectively) when compared to those with normal GFR, but their Serum b2 microglobin was comparable.

An elevated GFR is considered one of the earliest manifestations of sickle nephropathy and has been observed in children with SCA as young as 12 months of age with an age-dependent increase until the second decade of life **(Wigfall et al, 2000; Ware et al. 2010, Aygun et al., 2011)**. Our data documented this finding as mean GFR of our patients was within the reference range with none of our cases had below average GFR and more than half of SCA children have elevated GFR (165 ml/min/1.73m); similarly, mean value of creatinine clearance was within the reference range, but up to 98% subjects had elevated creatinine clearance (120 ml/min/ 1.73m2) **(Aygun et al, 2011; Economou et al., 2011)** and this finding showed age-dependant

increases as our patients with high GFR were significantly older.

Although it is a crude marker, serum creatinine is the most widely used to predict glomerular filtration rate (GFR).Creatinine concentrations are insensitive to mild to moderate reductions in GFR.In childhood, the age and muscle mass dependency of serum creatinine complicates GFR assessment even when body length/creatinine ratios are used **(Guido Filler et al,2002)**.

Among our patients, mean value of serum creatinine was within the reference range and none of our cases had elevated serum creatinine. However, 32 (47%) cases had levels below the reference range and the studied cases had significantly lower serum creatinine compared to controls this was in agreement with previous reports **(Aygun et al., 2011, Junior et al., 2012)**. Creatinine correlated negatively with GFR, patients with increased GFR had significantly lower creatinine compared to those with normal GFR and creatinine was not affected by gender or age and this contradicts previous reports that proved significantly lower creatinine in adult females compared to males **(Marouf et al., 2006)**.

Serum B2M was normal in all subjects and mean value was within the reference range. However, cases had significantly lower serum beta 2 compared to the control group (0.001). Serum level of B2M was not affected by gender and our data clearly demonstrate age independency for serum concentrations of B2M, this finding agree with previous reports **(Filler et al., 1997)**. We found no significant correlations of serum B2M with any of the studied clinical or laboratory variables including serum creatinine, GFR, creatinine clearance this was in line with **Marouf et al., (2006)** that reported similar results in their cohort.

In conclusion, we found that polyuria, albuminuria and glomerular hyperfiltration are the main renal findings in children with SCD, serum creatinine and serum B2M are poor predictors of SCD nephropathy in children.

In addition, we compared overall predictability of SCD nephropathy by serum creatinine versus serum B2M by ROC curve, it was found that area under the curve of serum B2M (0.48) was insignificantly higher when compared to that of serum creatinine (0.05) and both were below 0.7; indicating that overall predictability of serum B2M as

well as serum creatinine were not statistically significant; making adoption of any of them as a good predictor of SCD nephropathy in children unlikely. Our data regarding the sensitivity of serum creatinine as a predictor of early renal insult is in line with the previous reports **(Perrone et al, 1992; Bentley et al, 1993; Sheridan et al., 1994)**. Nevertheless, our conclusion on B2M contradicts all previous studies proved that single estimates of serum B2M can be used for estimation of GFR and may be more sensitive in detecting minor reductions in GFR **(Voskaridou et al, 2006)**. This may be explained by the possible variations in B2 M production in SCA subjects, which can be affected by the increased bone marrow activity or chronic inflammation in addition all these studies were carried on adults.

CONCLUSION

- Renal dysfunction in SCD children may occur before the occurrence of any symptoms or complications.
- Polyuria is the main clinical finding in SCD children.
- Albuminuria and glomerular hyperfiltration are the main laboratory renal finding in children with SCD.
- Serum B2-MG is not a good marker in detection of early stages of SCD nephropathy in children.
- A/C ratio and GFR are considerable methods of preliminary detection of glomerular affection in SCD children.
- Renal affection in SCD children can occur regardless age of patients.

RECOMMENDATIONS

- Routine screening of SCD children with A/C ratio and GFR is mandatory for early detection of renal affection.
- Further studies of establishment of best marker used for early assessment of tubular and glomerular dysfunction in SCD children is recommended.

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تقييم مصل بيتا-2-ميكروجلوبيولين كمؤشر علي اعتلال وظائف الكلى فى الأطفال المصابين بمرض فقر الدم المنجلي

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يعتبر اعتلال الكلي الناتج عن مرض خلايا الدم المنجلية من الحالات الغير قابلة للشفاء. لذلك من الأهمية بمكان تحديد تأثر الكلي المتوقع حدوثة مبكرا لتفادي حدوث هذا المرض وذلك عن طريق قياس بعض الدلالات التي تتنبأ بحدوث ذلك.

من هذه الدلالات قلة كثافة البول و زيادة افراز البروتين و زيادة مستوي الكرياتينين مع قلة استخلاصه بالبول.

ويعتبر الكرياتينين من أسهل و أكثر الدلالات شيوعا والذي كثيرا ما يستخدم للتنبؤ بمعدل فلترة الكلي . وقد وجد ارتباط وثيق بين البيتا 2 ميكروجلوبيولين و معدل فلترة الكلي خاصة لدى الأطفال.

لذلك كان الهدف من الرسالة الحالية هو قياس مستوي البيتا2 ميكروجلوبيولين في الأطفال المصابين بمرض خلايا الدم المنجلية و مقارنة قيمته في تشخيص اعتلال الكلي بالدلالات الأخري مثل الكرياتينين و معدل فلترة الكلي و زيادة افراز البروتين.

وقد أجريت هذة الدراسة علي سبعة و ستين طفلا مصريا مصابا بمرض خلايا الدم المنجلية والذين تتراوح أعمارهم بين 1 - 18سنه من المترددين علي مستشفى باب الشعرية الجامعى و مستشفى أطفال مصر خلال عام 2017.

وتم اختيار عشرون طفلا من الأصحاء في نفس عمر و نوع المرضي لتكون هي المجموعه الضابطة لمجموعة المرضي.

تـم قيـاس نسـبة مخـزون الحديـد و انـزيم LDH والكريـاتينين و الصـوديوم و البوتاسـيوم و انزيمـات الكبـد و مسـتوي الصـفراء والبيتـا 2 ميكروجلوبيـولين و فصـائل الهيموجلوبيلين بالدم. وتحليل بول و قياس مستوي الزلال و استخلاص الكرياتينين ومعدل فلترة الكلي بالبول.

وقد أوضحت الدراسة الأتي:

- انخفاض في مستوى استخلاص الكرياتينين في البول في الأطفال المصابين.
- ارتفاع معدل فلترة الكلـي مـع انخفـاض مسـتوي الكريـاتينين و البولينـا والبيتـا 2 ميكروجلوبيولين بالدم.
- وجود توافق ارتباطي سلبي بين مستوي الكرياتينين بالـدم و ومعـدل فلتـر ومعـدل فلترة الكلى.
- عدم وجود توافق احصائي بين مستوي الكرياتينين و البيتا 2 ميكروجلوبيولين.

ولذا توصي الدراسة بإجراء ابحاث أخري علي نطاق أوسع حيث أنها لا تزال جديدة. بالدراسةالعين بصفة دورية لاكتشاف أى تغيرات مبكراً.