Levels of Uric Acid, Urea and Creatinine in Iraqi Children with Sickle Cell Disease

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Abstract

Objective: To determine the levels of serum uric acid, urea and creatinine in subjects with sickle cell disease and cotrtpare them to those reported in literature,
Setting: Department of Paediatrics, College of Medicine, University of Basrah.
Methods: Plasma uric acid, urea and creatinine was estimated by Varley's method, group of 65 sickle cell patients (35 H'h AS, 30 FIb 55) aged between 2-11 years. The results were compared with those obtained in a group of 45 age and sex-matched controls with normal haemoglobin (Hb AA).
Results: The uric acid level was elevated in sickle cell patients as compared with the normal control group. The 95% confidence intervals for differences in the mean of the two groups: HhAA vs HbAS was 4.22 (0.3), while for I-IbAA for HbSS was 3.4 (0.06), both being statistically highly signilicant Ip<0.0001]. Urea and creatinine levels were considerably lower in the sickk cell disease patients. The difference in the patient's mean for urea compared to the mean in the normal group (HbAA) was 9.64 (1.95) and 8.55 (1.76) for HbSS and HbAS, resectively. Like wise, the difference in the mean for creatinine in HbSS group was 0.71 (0.12) and in HbAS was 0.76 (0.1 2), which was statistically significant [p<0.0001].
Conclusion: Raised serum uric levels were found in lraqi children with sickle cell disease, creatinine cleaeance studies will be valuable to assess renal function (JPMA 50:98,2000).

Introduction

The main factors which influences serum urate concentration are the metabolic production of urate and the way iii which it is excreted by the Kidneys. Erthrocytes contairing mainly haemoglobin "S' have a short iife span: this is the basus of anaemia1. It would he expected that during enthropoiesis increased Synthesis of nucleic acid might occur, thus the destruction of red blood cells lead to increased nucleic acid degradation. which means that lysis of red cells in person with sicklc cell disedse does liherate the uric acid content in the cell2. Hyperuricemia was encoutered in several studies on sickle cell diseased patients[2-8]. It was suggested that there was an excessive level of uric acid pool due to an increased marrow activity[2], and tumover of nucleic acids[2]. These conditions were associated with many diseases including hemolytic anaemia and certain haemoglobinopathies. A decreased excretion of uric acid resulting l'rom impaired tubular function was also suggested[2,6,8].
Sickle cell gene is highly prevalent in southern Iraq arid particularly in Basrah, where its frequency is from 2.5-I 3%9, However studies have shown that the local disease runs a milder course and that there is greater chance for longer survival[10]. Several hematological changes c.g., anaemia (from normal to mild to severe) ad biochemical abnormalities accompany this disorder in Basrah[11].
This knowledge cvolved our concern to examine the uric acid, urea and creatinine levels in sickle cell diseased patients and to compare the results with those reported in the literature. With this aim in mind, we present in this paper our findings regarding the sickle cell diseased patients and normal controls in Basrah area and discuss our results with those reported previously From other countries and. population.

Material and Methods

Blood samples were collected from 65 male and female subjects. Thirty live were diagnosed, as heterozygote carrying Hb AS and 30 homozygote with Hb SS, by cellulose acetate electrophoresis[12]. The mean age of this group was 7 years with a range of 2-11 years. Forty five age and sex- matched non-anaemic controls with normal haemoglobin (HbAA) were selected from the same population. All subjects were from milliliters of blood was drawn in EDTA tubes by veinpuncture. The haem oglob in concen ti-at ion, phenotype and packed cell volume was measured by routine laboratory methods[12]. The plasma separated from the blood by centrifligation was used, in duplicates, for the estimation of uric acid, urea and creatinine as described by Varley[13]. All the results were calculated and presented as the mean±SD and the range with 95% confidence intervals. The statistical significance of the difference was obtained by student's "t" test and the difference between the mean with 95% confidence intervals for each parameter in the sickle ceLL diseased patients compared to the mean in normal individuals was estimated. A p-value of <0.05 was considered significant.

Results

The results expressed as mean valuesjSD and range with 95% confidence intervals of total haemoglobin, packed cell volume (PCV), uric acid, urea and creatinine in sickle cell anaemia (homozygote with Hb SS) patients and in sickle cell trait (heterozygote with Hb AS) compared with normal individuals with haemoglobin (Hb AA) are presented in Table 1 and 2 respectively.
The results showed that uric acid level in sickle cell diseased patients is higher than that in the control group and the difference is statistically significant (p<0.0001). The samples were subgrouped into males and females. The mean, SD and 95% confidence intervals for uric acid in each of the groups was calculated and (he result are presented in Table 3.
The overall levels of urea and ereatininc were signilleantly lower in the sickle cell patients compared with the normal controls (p<0.000l) Table I and 2.

Table 1. Levels of Uric Acid, Urea, Creatinine in Sickle Cell Anaemia Cases (HbSS) and Controls (HbAA).

Parameters	Haemoglobin Phenotypes		Statistical Analysis		
	HbAA	HbSS	t	p	95% C.I.
	n = 45	n = 30			diff. In mean
Hb	13.8±2.5	8.3±2.3	10	0.0001	4.5 - 6.5
Mg/dl	13.05 - 14.55	7.44 - 9.15			
PCV	46±7	24±3	17	0.0001	20 - 25
%	44 - 48	23 - 25			
Uric Acid	5.19±0.64	8.5±1.5	11	<0.0001	2.7 - 3.9
mg/dl	5.0 - 5.39	7.94 - 9.44			
Urea	32.37±4.94	23±3.1	10	<0.0001	7.51 - 11.24
mg/dl	30.63 - 35.1	21.82 - 24.18			
Creatinine	1.55±0.32	0.85±0.15	12	<0.0001	0.59 - 0.82
mg/dl	1.46 - 1.65	0.8 - 0.91			

Results are expressed as mean±SD
Values in parentheses are ranges with 95% confidence intervals.

Table 2. Levels of Uric Acid, Urea, Creatinine, in Sickle Cell Trait (HbAS), Cases and Controls (HbAA).

Parameters	Haemoglobin Phenotypes		Statistical Analysis		
	HbAA	HbAS			95% C.I.
	n = 45	n = 35	t	p	diff. in mean
Hb	13.8±2.5	11.2±2.8	4.43	0.001	1.4 - 3.8
mg/dl	13.05 - 14.55	10.26 - 12.13			
PCV	46±7	31±6	10	0.0001	12 - 18
%	44 - 48	29 - 33			
Uric Acid	5.19±0.64	9.4±0.76	26	<0.0001	3.9 - 4.5
mg/dl	5.0 - 5.39	9.13 - 9.64			
Urea	32.37±4.94	23.83±2.85	9.7	<0.0001	6.8 - 10.3
mg/dl	30.89 - 33.86	22.85 - 24.31			
Creatinine	1.55±0.32	0.79±0.1	14.8	<0.0001	0.59 - 0.81
mg/dl	1.46 - 1.65	0.76 - 0.83			

Results are expressed as mean±SD
Values in parentheses are range as 95% Confidence Intervals.

The levels in the different sex groups are presented in Table 3.

Table 3. Uric Acid, Urea and Creatinine Levels in Male and Female Sickle Cell Trait and Anaemic Cases and Normal Controls.

Paameter	Sex	Haemoglobin Phenotypes					
		AS		SS		AA	
		No.	mg/dl	No.	mg/dl	No.	mg/dl
Uric Acid	Male	16	9.27±0.83	20	8.56±0.16	21	6.0±0.68
			80.83 - 9.71		8.43 - 8.57		5.69 - 6.32
	Female	19	9.47±0.62	10	8.66±0.15	24	5.2±0.6
			9.11 - 9.69		8.47 - 8.7		4.9 5.5
	Total	35	9.4±0.76	30	8.50±1.51	45	5.19±0.64
			9.13 - 9.64		7.94 - 9.1		5.0 - 5.39
Urea	Male	16	23.84±2.4	20	23.05±3.66	21	31.85±4.59
			22.59 - 25.09		21.4 - 24.7		29.76 - 33.9
	Female	19	23.85±3.04	10	22.90±2.3	24	32.85±5.2
			22.41 - 25.25		21.28 - 24.5		30.63 - 35.1
	Total	35	23.83±2.85	30	23.00±3.15	45	32.37±4.94
			22.85 - 24.81		21.82 - 24.18		30.89 - 33.86
Creatinine	Male	16	0.77±0.17	20	0.82±0.13	21	1.56±0.35
			0.68 - 0.86		0.76 - 0.88		1.4 - 1.72
	Female	19	0.82±0.11	10	0.92±0.17	24	1.55±0.30
			0.77 - 0.87		0.8 - 1.0		1.42 - 1.68
	Total	35	0.79±0.11	30	0.85±0.15	45	1.55±0.32
			0.76 - 0.83		0.8 - 0.91		1.46 - 1.65

Results are expressed as mean±SD
Values in parentheses are range as 95% Confidence Intervals.

Discussion

The results showed that the uric acid levels were increased while urea and creatinine levels were significantly decreased in the sickle cell group patients as compared with their age and sex-matched controls.

Earlier studies on other populations have demonstrated a high prevalence of hyperuricemia in patients with sickle cell disease as shown in table 4. While, others didn't find such observation[14].

In the present study the prevalence of hyperuricaemia among the sickle cell group: 73% (22130), while Rb AS was 70% (23/36). No patient with gout was encountered. Our prevalence was similar to that reported by Reynolds[2] being 75% (9/12) in children with HhSS, It was concluded that this elevated level is due to a sustained high state of erythropoiesis in sickle cell anaemia patient which causes an increased turnover of purines and hence the generation of a greater than normal uric acid level[15]. The hyperuricaeniia was caused only if the excretion via kidneys Failed to keep pace with increased production, this often occurred as a result of impaired tubular function due to infarction and hypoxia resulting from sickling[7]. As a result of sustained hyperuricemia several sickle cell anaemia cases with gouty arthritis have been reported[2,3,8]. Hyperuricemia develops when urate clearance fall, probably as a result of renal parenchymal damage which has been reported in homozygous sickle cell disease patients[16,18].

The level of blood urea and creatinine were significantly lower in the overall sickle cell grouped patients compared with the values in controls ($p<0.0001$). Similar observations were reported by others[14]. The decrease in urea level may be a consequence of liver dysfunction while the decrease in serum creatinine may be due to reduced muscle mass in these patients. This conclusion is in line with a study investigating the effect of dietary nitrogen on urinary excretion of non-protein nitrogen in sickle cell patients. It was reported that creatinine excretion was lower and this was attributed to smaller physical statue of these patients[19]. In addition, diet_ influences the plasma urea and creatinine level. Since diet and muscle mass were not controlled during this study, further investigation are necessary to study the possihfc contribution of these variables on the level of biochemical parameters. Renal dysfunction in HbSS patients leading to disturbance in the normal ability of the kidney to concentrate urine is well known[18,20], which results in an increased concentration of serum creatinine and urea. Therefore it is important to assess the renal function in sickle cell diseased patients and that is by determination of renal clearance of uric acid, urea and creatinine in these patients. It will be of value to further investigate these patients with clearance studies to determine renal function[20,21].

In conclusion this study on Iraqi children has shown an increased level of uric acid and a slight decrease in the level of urea and creatinine in patients with sickle cell disease compared with the controls. No difference were found whether these patients were diagnosed as heterozygote (HbAS) or honiozygote (HbSS). Clearance test studies are important to be carried out on these patients as well as with other age groups for the evaluation of their renal function.

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