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ORIGINAL STUDY

Assessment of Serum Copeptin Levels in Pediatric Patients with Sickle Cell Anemia

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Abstract

Objectives: **To assess the serum copeptin levels in children with Sickle cell anemia.**

Background: **Sickle cell anemia (SCA) is one of the most common hereditary diseases in the world. Copeptin is the C-terminal part of the prohormone for provasopressin and seems clinically relevant in various clinical conditions.**

Methods: **This is a case control study conducted on 62 subjects, 31 pediatric patients with Sickle cell anemia and 31 healthy children, all aged 1 year to 18 to assess the serum copeptin levels in children with Sickle cell anemia. Who attended pediatric hematology clinics of the Menoufia university hospitals, during a period time from April 2021 to September 2022. All cases were subjected to detailed history, clinical examination, anthropometric measurement, radiological and laboratory investigations including serum copeptin levels.**

Results: **Serum copeptin level was significantly increased among case group (5.02 ± 4.30 ng/ml) than control group (2.79 ± 1.21 ng/ml) with *P* value 0.007. Also, serum copeptin level was increased in direct relation with prevalence of complications among case groups, ($P < 0.05$).**

Conclusion: **pediatric patients with sickle cell anemia have significantly higher serum copeptin levels than healthy children, also this study found that the more incidence of complications the higher serum copeptin levels in children with sickle cell anemia.**

Keywords: Copeptin level, Hemoglobin genotype, Pediatric, Sickle cell anemia, Vaso-occlusive crisis

1. Introduction

Sickle cell anemia (SCA) is one of the most common hereditary diseases in the world. The substitution of amino acid valine for glutamic acid at the sixth position of beta chain of hemoglobin is the cause of the genetic abnormality. Hemoglobin S (HbS) polymerizes due to deoxygenation and causes sickling in erythrocytes, leading to clinical manifestations of Sickle cell anemia including recurrent vaso-occlusive crisis (VOC) which leads to microvascular obstruction, anemia, and decreased red cell survival [1].

The pathophysiology of vaso-occlusive crisis includes the activation of endothelial and coagulation factors, acute aggravation of ongoing inflammation with neutrophils and other inflammatory cells and increased oxidative stress. The activation of inflammatory cells and their signaling pathways leads to the production and secretion of numerous molecules that propagate the inflammatory state in sickle cell disease [2].

Even in sickle cell patients without vaso-occlusive crisis, a chronic inflammatory state is present as reflected by increased levels of circulating C-reactive protein, inflammatory cytokines, increased levels of von Willebrand factor antigen, and activated neutrophils, indicating chronic endothelial activation [3].

The hypothalamic pituitary adrenal axis is activated in response to stress. Arginine vasopressin (AVP) is a key stress hormone involved in hemodynamics and osmoregulation. Copeptin is a 39-aminoacid glycopeptide that comprises the C-terminal segment

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of arginine vasopressin that is co-released with arginine vasopressin from hypothalamus in stress [4]. Copeptin is a biomarker of non-specific stress response but due to the positive association of copeptin with the severity of illness and outcome has been proposed as a prognostic marker in sepsis, pneumonia, heart failure, acute coronary syndromes, stroke, subarachnoid hemorrhage, and other acute illnesses [5]. The need for faster diagnosis, more accurate prognostic assessment, and treatment decisions in various diseases has led to the investigations of new biomarkers. Arginine vasopressin (AVP) is a multifunctional nano peptide with endocrine, hemodynamic, and osmoregulatory effects, also known as antidiuretic hormone. AVP is a primary hypothalamic stress hormone stimulated by stress factors such as hypotensive, hypoxic, hyperosmolar, hypovolemic, and acidic stimuli. Due to its short half-life and instability in circulation, the measurement of AVP as a biomarker in daily clinical practice is limited. Copeptin, a peptide consisting of 39 amino acids, is a fragment of preprovasopressin that is synthesized and secreted in equimolar amounts to vasopressin. Unlike AVP, copeptin is stable for a long time in plasma and can be measured easily. It is secreted in a pulsatile manner and is removed from circulation by binding to platelets [3]. Perhaps there is less response to severe stress in the hypothalamus than in the pituitary and adrenal gland or a more exaggerated response distally in the HPA axis than centrally. This indicates that cortisol and copeptin as well as their ratio could be used in assessing the degree of SCA severity [6]. Thus, this study aimed to assess the serum copeptin levels in pediatric patients with Sickle cell anemia.

2. Methods

This is a case control study conducted on 62 pediatric subjects, 31 pediatric patients with Sickle cell anemia as diagnosed according to **Darbari** et al. [7], and 31 healthy subjects, all aged from 1 year to 18 to assess the serum copeptin levels in pediatric patients with Sickle cell anemia who attended pediatric hematology clinics of the Menoufia university hospitals, during a period time from April 2021 to September 2022.

2.1. Ethical consideration

Written informed consent from their parents and care givers after explaining the aim of study. Approval of the study protocol was obtained by Ethical Scientific Committee of Menoufia faculty of medicine (IRB number 2/2022 PEDI44).

All children in this study were divided into 2 groups as group I included 31 pediatric patients with sickle cell anemia. Group II included 31 subjects who are apparently healthy with haemoglobin genotype (HbAA) matched for age and gender as control group. Subjects with bone and joint pain or pain in multiple sites, requirement for analgesics, and patients considering the episode as typical of crisis which necessitates hospital admission was clinically considered as being in vaso-occlusive crisis [7]. Both sexes' children aged 1–18 years, sickle cell anemic children with vaso-occlusive crisis, sickle cell anemic children with steady state were included. While Subjects with Hb variants different from HbSS (such as HbSC and HbAS), acute major stresses other than vaso-occlusive crisis, end-stage renal failure (GFR<15 ml/min/1.73 m^2 or renal replacement treatment), diabetes mellitus, hypertension, hepatitis, cancer children, established endocrine dysfunctions and children with previously corrected congenital heart diseases were excluded. **Exclusion criteria for controls** whose parents refused to give consent or children who refused assent to participate in the study.

All cases were subjected to the following, detailed history included age, sex, duration of illness, frequency of blood transfusion, type of chelation therapy, history of splenectomy. Clinical examination included general examination including vital signs, central nervous system examination, cardiovascular system examination, abdominal examination. Anthropometric measurements included weight, height with centiles and calculation of body mass index. Laboratory evaluation in the form of complete blood count, serum ferritin, Hb electrophoresis, liver function tests (AST, ALT), renal function tests (urea, creatinine) and serum copeptin level. Radiological investigations echocardiographic examination was performed.

Analytical procedures: Venous blood samples were withdrawn by sterile venipuncture. For all patients and controls, the following laboratory tests were performed: Complete blood count was analyzed by automated Sysmex XN-10 hematology analyzer (Sysmex, Kobe, Japan), serum ferritin levels were measured using Cobas e411 immunoassay analyzer (Roche Diagnostics, Mannheim, Germany) and serum copeptin levels. For sickle anemia patients, Hb electrophoresis was performed using Capillarys 3 OCTA automated capillary electrophoresis system (Sebia, Lisses, France). Serum samples for the estimation of copeptin levels were measured using a specific enzyme-linked immunosorbent assay kit according to the manufacturer's instructions (Human copeptin ELISA Kit: Sunred Biological Technology

Co. Ltd. Shanghai, China. Catalog No. 201-12-5463). The inter-assay and intra-assay calculation values were <12% and <10%, respectively. Furthermore, the detection range of copeptin was 0.07–20 ng/ml, with sensitivity 0.076 ng/ml.

2.2. Statistical analysis

Statistical analysis was done by statistical package for the social sciences (version 20.0; IBM Corp., Armonk, New York, NY, USA). Data were expressed in the form of mean and standard deviation for continuous quantitative variables while number and percent were used for description of qualitative variables. Chi-square test ($\chi 2$) was used to study the association between categorical variables. In two groups' comparison of normally and abnormally distributed quantitative variables, Student's t test and Mann–Whitney U test were utilized, respectively. P value of less than 0.05 was considered statistically significant.

3. Results

A CONSORT flowchart of the study population shows in Fig. 1. Of the 75 children who attended to pediatric hematology clinics of Menoufia University Hospitals. 13 children were excluded from the study (5 children declined consent and 8 children did not meet the inclusion criteria, 62 children were willing to participate in the study and consented for participation. Thus, 31 children in steady state of sickle cell anemia are those with hemoglobin SS and 31 children who apparently healthy with hemoglobin genotype (HbAA) as control group.

There was not a significant difference among the studied group regarding age, sex, history of splenectomy and age of onset ($P > 0.05$). The mean of age among case group was (12.45 ± 3.18 year) while among control group was (10.61 ± 2.85 year). Additionally, most of cases were females (64.51%) and males were (35.48%). Also, among control group, females were the most common (54.83%) while males were less common (45.16%). Additionally, a significantly decrease among case than control group regarding weight, height, and body mass index ($P < 0.05$) (Table 1).

Furthermore, heart rate was significantly increased among case group than control group ($P < 0.001$). While, respiration rate was significantly increased among case group than control group ($P < 0.001$). Normal cardiovascular system and mild splenomegaly were the most common among case group (58.06%, 64.51%), respectively, ($P < 0.001$). On the other hand, no significant differences found among the studied groups systolic blood pressure, diastolic blood pressure and central nervous system ($P > 0.05$) (Table 2).

Also, hemoglobin, hemoglobin A and hematocrit test were significantly decreased among case group than control group ($P < 0.001$). While, fetal hemoglobin, white blood cells, serum ferritin and serum copeptin level were significantly increased among case group than control group ($P < 0.05$). However, there were no significant differences among the studied groups regarding hemoglobin A2 and platelets ($P > 0.05$). Additionally, urea and creatinine were significantly increased among case than controls ($P < 0.05$). While, no significant differences found among the studied groups regarding aspartate transaminase and alanine transaminase ($P > 0.05$) (Table 3).

This study showed that, urinary tract infection, bossing of the forehead, hepatomegaly, painful crisis, and hand foot syndrome were the most common complications among case group (90%, 90%, 77%, 74%,74%), respectively ($P < 0.001$). Also, L-carnitine, folic acid, hydroxyurea, deferasirox iron chelator and long-acting penicillin were the most common treatment among case group (100.00%, 100.00%, 100.00%, 61.29%, 100.00%) respectively (Table 4). Furthermore, copeptin level was significantly increased among patients had infections, painful crisis, acute chest syndrome, neurological complications, cardiac complications, renal complications, hepatobiliary complications, priapism, bone complications and dermatological complications than others that did not have these complications ($P < 0.05$) (Table 5).

4. Discussion

The present study showed that, there were not a significant difference among the studied group regarding age, sex, history of splenectomy and age of onset. The mean of age among case group was while among controls. Additionally, most of cases were females and males. Also, among control group, females were the most common while males were less common. Our result in agreement with the result obtained by **Fadhil** et al. [8] who reported that, there were no significant difference among SCA group and control group according to age and sex. Also, **Deveci** et al. [3] found that, no significant difference was found in terms of age in the studied groups. Additionally, **Talha** et al. [9], noted that, their study included 207 patients, with a mean age of 7.5 ± 3.1 years. More than half of patients were females. Two-thirds of patients had no family history of sickle cell disease.

Our study showed that, there were significant decrease among case than control group regarding weight, height, and body mass index. In agreement

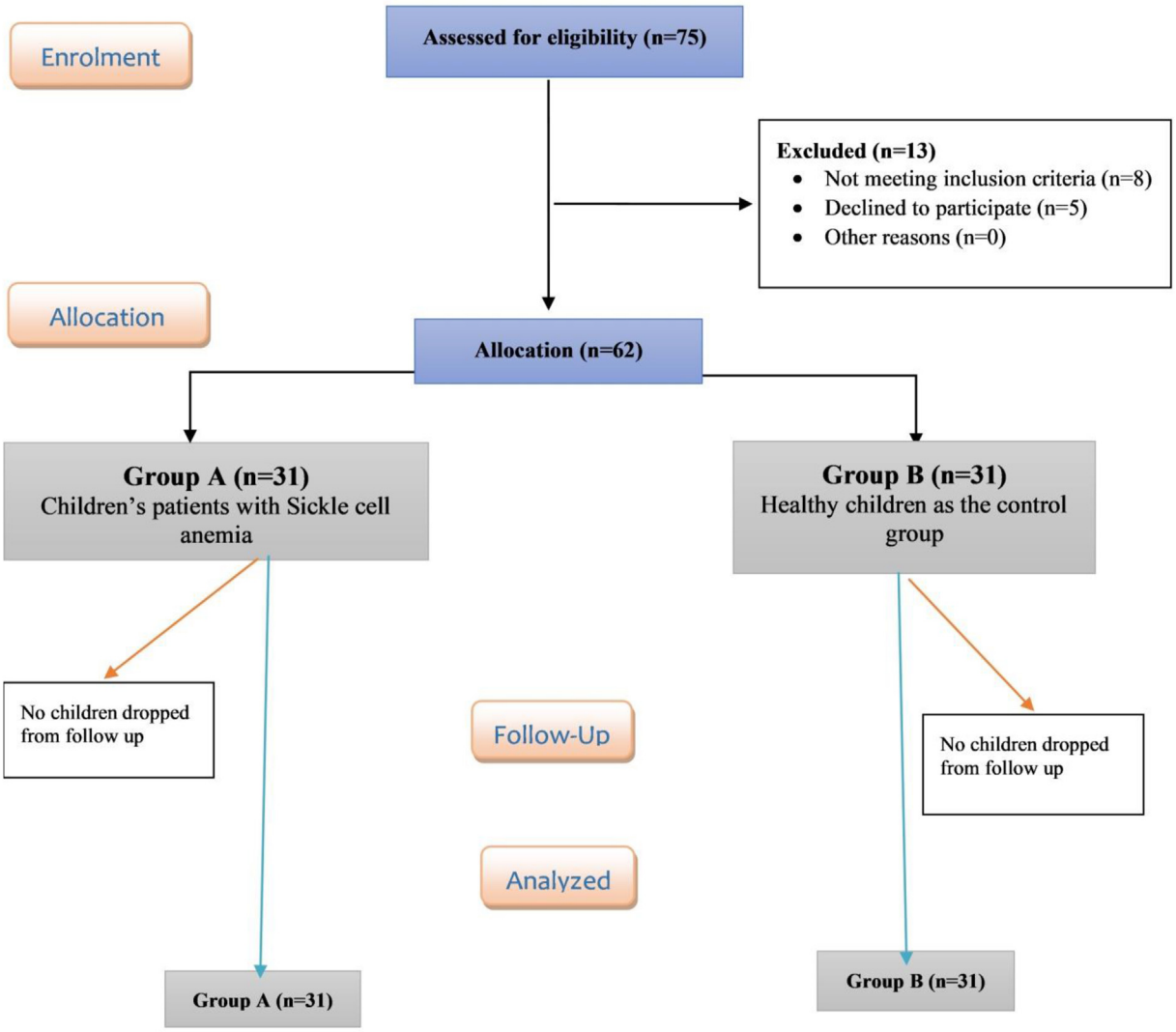

Fig. 1. Flowchart of the studied children.

with our study **Odetunde** et al. [10]. found that, almost half of the children with sickle cell anemia were underweight, other authors have also reported deficits in nutritional status among subjects with Sickle Cell Disease (SCD). For instance, **Singhal** et al. [11] reported significantly lower weight, and BMI in 20 Jamaican children with sickle cell anemia. Also, **Fadhil** et al. [8] reported that, significantly higher frequencies of underweight, stunting, and wasting conditions among patients with SCA than in the healthy control group, Moreover, the growth of patients in early age groups was comparable to the control group. Many factors affect the nutritional status and growth of patients with SCA. Importantly, the socioeconomic status of patients and their families may affect the patient's growth.

The current study showed that, hemoglobin, hemoglobin A and hematocrit test were significantly decreased among case group than control group. While, fetal hemoglobin, white blood cells, serum ferritin and copeptin level were significantly increased among case group than control group. On The other hand, there were no significant differences among the studied groups regarding hemoglobin A2 and platelets. In the same line, **Akinlade** et al. [6] observed that, higher proportion of elevated WBC in the severe SCA group indicates a significant association between severe SCA and elevated WBC. Their observation indicates that SCA subjects with elevated WBC are likely to suffer from severe SCA thus, suggesting that monitoring of WBC are important tools in the classification and management of severe SCA. Also, **Akinlade** et al. [6] found that, copeptin levels of moderate and severe SCA patients were higher than copeptin levels of mild SCA patients. Additionally, **Deveci** et al. [3] reported that,

Table 1. Socio demographic data among case and control studied groups (N = 62).

Variables	Cases (n = 31)	Control (n = 31)	t	P value
Age/year				
Mean ± SD	12.45 ± 3.18	10.61 ± 2.85	1.309	0.816
Range	6.00–17.00	3.00–13.00		
Sex	**Number (%)**	**Number (%)**	**X^2**=0.603	0.437
Female	20 (64.51)	17 (54.83)		
Male	11 (35.48)	14 (45.16)		
History of splenectomy				
No	31 (100.00)	31 (100.00)	—	—
Age of onset/months				
Mean ± SD	19.23 ± 3.05	–	—	—
Range	12.00–24.00			
Weight/kg				
Mean ± SD	33.45 ± 8.48	39.89 ± 11.50	3.637	**0.028**[a]
Range	13.00–45.00	17.60–55.00		
Height/Cm				
Mean ± SD	140.32 ± 15.58	148.29 ± 16.51	3.402	**0.035**[a]
Range	90.00–150.00	110.00–165.00		
BMI (kg/m^2)				
Mean ± SD	15.94 ± 2.29	18.36 ± 2.37	2.78	**0.041**[a]
Range	13.61–22.50	14.55–23.14		

BMI, Body mass index; **CI**, Confidence interval for Mean; **t**: independent *t*-test; **X^2**, Chi-square test.
[a] Significant.

Table 2. Clinical examination among case and control studied groups (N = 62).

Variables	Cases (n = 31)	Control (n = 31)	t	P value	95%CI	
					Lower	Upper
HR (beat/minute)						
Mean ± SD	106.90 ± 14.41	94.97 ± 8.73	3.944	<0.001[a]	5.88	17.99
Range	79.00–130.00	79.00–104.00				
RR (breath/minute)						
Mean ± SD	25.29 ± 2.73	21.42 ± 2.72	5.590	<0.001[a]	−5.26	−2.49
Range	20.00–30.00	17.00–27.00				
SBP (mmHg)						
Mean ± SD	112.00 ± 8.08	114.68 ± 8.26	1.290	0.202	−6.83	1.48
Range	100.00–125.00	100.00–124.00				
DBP (mmHg)						
Mean ± SD	64.84 ± 6.55	63.32 ± 6.58	0.909	0.367	−1.82	4.85
Range	52.00–80.00	52.00–72.00				
	Number (%)	**Number (%)**	**X^2**	***P* value**		
General condition (average)	31 (100)	31 (100)	–	–		
Jaundice	**Number (%)**	**Number (%)**	**X^2**	***P* value**		
	31 (0)	31 (0)	–	–		
Pallor (present) (not present)	**Number (%)**	**Number (%)**	**X^2**	***P* value**		
	15 (48.38)	0 (0)	–	–		
	16 (51.61)	31 (100)				
CNS (normal)	**Number (%)**	**Number (%)**	**X^2**	***P* value**		
CVS						
Normal	31 (100.00)	31 (100.00)	–	–	–	–
Abnormal	18 (58.06)	31 (100.00)	16.449	<0.001[a]	–	–
Tachycardia	8 (25.80)	0 (00.00)				
Hemic murmer	5 (16.12)	0 (00.00)				
Abdominal						
Normal	11 (35.48)	31 (100.00)	29.524	<0.001[a]	–	–
mild Splenomegaly	20 (64.51)	0 (00.00)				

CI, Confidence interval for Mean; **CNS**, Central nervous system; **CVS**, Cardiovascular system; **DBP**, Diastolic blood pressure; **HR**, Heart rate; **RR**, Respiration rate; **SBP**, Systolic blood pressure; **t**, independent *t*-test; **X^2**, Chi-square test.
[a] Significant.

Table 3. Lab investigations among case and control studied groups (N = 62).

Variables	Cases ($n = 31$)	Control ($n = 31$)	t	*P* value	95%CI	
					lower	Upper
Hb(gram/deciliter)						
Mean ± SD	9.35 ± 1.82	12.73 ± 0.75	9.537	<0.001[a]	−4.08	−2.66
Range	6.601−2.60	11.40−14.00				
HCT (%)						
Mean ± SD	27.31 ± 4.64	36.87 ± 3.55	U = 9.106	<0.001[a]	−11.67	−7.46
Range	21.70−37.70	32.00−42.70				
WBCs (billion cells/l)						
Mean ± SD	10.85 ± 4.93	8.04 ± 1.88	2.966	0.004[a]	0.91	4.70
Range	2.90−22.80	5.30−10.50				
Platelets (billion/L)						
Mean ± SD	302.63 ± 139.25	267.85 ± 57.62	U;=1.285	0.204	−19.37	88.92
Range	152.00−644.00	192.50−334.10				
HbA (%)						
Mean ± SD	23.54 ± 24.29	96.31 ± 0.96	U = 16.666	<0.001[a]	−81.50	−64.04
Range	0.00−62.20	95.00−98.00				
HbF (%)						
Mean ± SD	12.48 ± 12.10	1.19 ± 0.55	U = 5.194	<0.001[a]	6.95	15.64
Range	0.00−40.90	0.00−2.50				
HbS (%)						
Mean ± SD	61.54 ± 18.47	0	NA	—	–	–
Range	28.65−98.00					
HbA2 (%)						
Mean ± SD	2.51 ± 1.22	2.50 ± 0.73	U =0.045	0.964	−0.50	0.52
Range	0.00−6.80	1.20−4.00				
Serum ferritin (ng/ml)						
Mean ± SD	625.60 ± 90.94	66.40 ± 17.71	3.421	0.001[a]	232.23	886.17
Range	15.60−3756.00	34.00−83.20				
Urea (mg/dl)						
Mean ± SD	19.98 ± 8.47	24.02 ± 3.85	2.419	0.019[a]	−7.38	−0.70
Range	4.00−39.00	18.10−30.20				
Creatinine (mg/dl)						
Mean ± SD	0.71 ± 0.35	0.45 ± 0.06	4.053	<0.001[a]	0.13	0.38
Range	0.30−1.60	0.30−0.50				
AST (u/l)						
Mean ± SD	29.75 ± 13.34	25.12 ± 4.61	1.827	0.073	−0.44	9.70
Range	7.00−53.00	18.70−31.90				
ALT (u/l)						
Mean ± SD	21.31 ± 8.85	20.96 ± 5.58	0.182	0.856	−3.42	4.10
Range	4.00−42.00	13.50−30.60				
Copeptin level (ng/ml)						
Mean ± SD	5.02 ± 4.30	2.79 ± 1.21	u2.780	0.007[a]	0.63	3.84
Range	2.27−18.70	1.32−4.95				

ALT, Alanine transaminase; **AST**, Aspartate transaminase; **CI**, Confidence interval for Mean; **CI**, Confidence interval for Mean; **Hb**, Hemoglobin; **HbA**, hemoglobin A; **HbA2**, Hemoglobin A2; **HbF**, Fetal hemoglobin; **HbS**, Hemoglobin S; **HCT**, Hematocrit test; **t**, independent *t*-test; **t**, independent *t*-test. *: Significant; **U**, Mann−Whitney test; **WBCs**, White blood cells.

[a] Significant.

the mean hematocrit level was significantly higher in controls compared with SCA subjects in steady state in the other hand, **Akinlade** et al. [6] found that, copeptin levels of SCA patients were lower than those in the control group. Additionally, **Deveci** et al. [3] found that, copeptin levels of SCA patients were lower than those in the control group. In a previous study by **Qadah** et al. [12] showed that, 75% of the enrolled patients had an increase in the HbF level with an average 6.01% ± 3.5. The influence of HbF level on SCA is well known to ameliorate disease morbidity and mortality in adulthood based on clinical observation. Therefore, the higher expression of HbF reduces disease severity in term of disease crisis and complications. Also, **Odunlade** et al. [13] shows that, the mean serum ferritin levels of patients with sickle cell anaemia were higher than in control children of the same age group, confirming the results of two earlier studies. **Siimes** et al. [14] found raised serum ferritin levels in 14 children in San Francisco with sickle cell anaemia of similar age to those in their study.

Table 4. Complications and treatment among cases and control studied groups (N = 62).

Variables	Cases (n = 31) Number (%)
Complications	
Infections	
Pneumonia	16 (51)
UTI	28 (90)
Painful crisis	23 (74)
Acute chest syndrome	15 (48)
Neurological complications (transient ischemic attacks)	8 (25)
Cardiac complication (diastolic dysfunction)	2 (6)
Renal complication (glomerulopathy)	3 (9)
Hepatobiliary complication (hepatomegaly)	24 (77)
Priapism	3 (9)
Bone complications	28 (90)
bossing of the forehead	
hand foot syndrome	23 (74)
Dermatological complication (leg ulcers)	8 (25)
Treatment	
L-carnitine	31 (100.00)
Folic acid	31 (100.00)
Hydroxyurea	31 (100.00)
Iron chelator	0 (00.00)
No	19 (61.29)
Deferasirox	12 (38.70)
Deferpxamine mesylate	
Long-Acting Penicillin	100.00

X^2: Chi-square test.
*Significant.

Table 5. Relation between complication and copeptin level among cases and control studied groups (N = 62).

Variables	Copeptin level (ng/ml) Mean ± SD	t	P value
Infections			
Yes	5.28 ± 4.64	2.544	0.017*
No	2.91 ± 1.22		
Painful crisis			
Yes	5.40 ± 4.72	2.612	0.015*
No	2.89 ± 1.15		
Acute chest syndrome			
Yes	5.36 ± 4.72	2.529	0.018*
No	2.92 ± 1.21		
Neurological complications			
Yes	5.42 ± 4.59	2.833	0.009*
No	2.81 ± 1.14		
Cardiac complications			
Yes	5.37 ± 4.72	2.061	0.050*
No	3.15 ± 2.02		
Renal complications			
Yes	5.44 ± 4.70	2.693	0.012*
No	2.86 ± 1.14		
Hepatobiliary complications			
Yes	5.44 ± 4.80	2.519	0.019*
No	2.93 ± 1.20		
Priapism			
Yes	5.35 ± 4.72	2.521	0.018*
No	2.92 ± 1.21		
Bone complications			
Yes	6.06 ± 5.08	2.769	0.012*
No	2.88 ± 1.08		
Dermatological complications			
Yes	5.34 ± 4.63	2.676	0.012*
No	2.86 ± 1.15		

Our study showed that, urea and creatinine were significantly increased among case group than control group. In the same line **Garg** et al. [15], reported that, levels of uric acid and creatinine in SCD subjects than control. Creatinine is the product of creatine metabolism. Creatine found in muscle, in free form as well as in the form of creatinine phosphate [16]. Increase in serum creatinine is seen in any renal impairment when its clearance is significantly reduced. This may be due to intrinsic renal lesion, decreased perfusion of kidney or by obstruction of the lower urinary tract. On the other hand, **Ajite** et al. [17] found that, serum creatinine levels were majorly less than 1 mg/dl in the children with Sickle Cell Anaemia. Reduced muscle mass as compared with normal healthy individuals may be one of the contributing factors. Similar finding was reported in a study among adults with sickle cell disease [18].

This study showed that, Urinary tract infection, bossing of the forehead, hepatomegaly, painful crisis, and hand foot syndrome were the most common complications among case group (90%, 90%, 77%, 74%,74%) respectively. Also, copeptin level was significantly increased among patients had infections, painful crisis, acute chest syndrome, neurological complications, cardiac complications, renal complications, hepatobiliary complications, priapism, bone complications and dermatological complications. Our findings coincide with previous studies conducted by **Fouda** et al. [19], who reported higher levels of copeptin (medians of 79 vs. 37 pmol/L); in children with complicated pneumonia compared to children with uncomplicated pneumonia. **Du** et al. [20], **Mohamed** et al. [21], who reported that higher levels of serum copeptin were also in association with CAP-related complications compared to uncomplicated children. On the same hand, another study conducted by **Sheb** et al. [22], reported higher levels of serum copeptin in severe complicated children with medians of 5.6 compared to uncomplicated children with medians of 0.97. On the contrary, **Alcoba** et al. [23], found that serum copeptin did not differ between children with complicated and uncomplicated pneumonia. The possible explanations of that indifference were the sample size which might limit such conclusions. This could also be due to the low prevalence of severe CAP in their population compared to that

observed in other studies, and the absence of mortality, even in cases with bacteremia and empyema.

4.1. Conclusion

In conclusion, pediatric patients with sickle cell anemia have significantly higher serum copeptin levels than healthy children, also this study found that the more incidence of complications the higher serum copeptin levels in children with sickle cell anemia.

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Nil.

Conflict of interest

There are no conflicts of interest.

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