Original Article

Acute chest syndrome in children with sickle cell disease in Basra, Southern Iraq

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ABSTRACT

Objectives: To look for the frequency of acute chest syndrome among children with sickle cell disease, and to evaluate the clinical, hematologic, and radiological features, and outcome of these children.

Methodology: A prospective study was carried out on 154 children with sickle cell disease, who presented with fever and respiratory symptoms. Clinical data were obtained, in addition to pulse oximetry, full blood count and chest x-ray.

Results: Twenty nine sickler children (18.83%) fulfilled the criteria of acute chest syndrome. Dyspnea and chest pain are found to be significant predictors of acute chest syndrome, P<0.05. In addition to asthma, history of splenectomy and surgery (P= 0.001, and <0.05 respectively). Hypoxia was present in a significantly higher percent of sickler children with acute chest syndrome (27.58%) compared to patients without acute chest syndrome (4%), P= 0.001. Acute chest syndrome was associated with longer mean duration of hospitalization (2.9±4.3) days compared to those without acute chest syndrome (1.6±1.8) days, P<0.05.

Conclusions: The frequency of acute chest syndrome is high among sickler children in Basra. Further studies are needed to look for the etiologic factors, recurrence rate and role of hydroxyurea and incentive spirometry in the prevention and treatment of acute chest syndrome.

KEY WORDS: Acute chest syndrome, Sickle cell disease, Basra.

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INTRODUCTION

Sickle cell disease (SCD) represents a major public health burden because of its significant morbidity and mortality.[1] SCD is common hematologic problem in Basra, around 6.48% of population are carriers for the sickle cell gene.[2]

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Acute Chest Syndrome (ACS) is an acute pulmonary illness that occurs in patients with sickle cell disease.[3] Incidence is inversely related to age; with children aged 2-4 years having the highest incidence.ACS is associated with all genotypes but occurs most frequently in patients with homozygous disease. Hematologic risk factors for the development of ACS include a high steady state leukocyte count, low steady-state hemoglobin F concentration, and a high steady-state hemoglobin level.[4] The risk for developing an ACS episode appears to be increased following surgery; an average of 3 days post-surgery.[5]

Infection appears to be the commonest cause in children, whereas fat embolism occurs more often in adults.[4,6] Prevention of ACS is possible and is essential to the long-term health of patients with SCD. Patients admitted to the hospital for painful crisis should be considered to be in the prodromal phase of ACS and should be monitored closely.[7]

This study was carried out to assess frequency of ACS among sickler patients, study the clinical and radiological features of children with ACS, evaluate the correlation of ACS with selected demographic and hematological findings, and study the outcome of patients with ACS.

METHODOLOGY

A prospective study has been carried out on children with SCD registered in the Center of Hereditary Blood disease in Basra, from the first of February 2009 till the end of January 2010, who presented with fever and/ or symptoms of ACS. ACS is defined as a new pulmonary infiltrate on chest x-ray associated with one or more new symptoms: fever, cough, sputum production, dyspnea, or hypoxia.[8]

History included: fever, pallor, cough, dyspnea, tachypnea, chest pain, and pain in other sites. Associated events (within 2 weeks of ACS): vaso-occlusive crises (VOC), fever, upper respiratory tract infection (URTI), surgery. Medical history included: asthma, chronic blood transfusion, history of splenectomy, cardiac problems, and passive smoking. A thorough physical examination was done, treatment given, duration of hospitalization and outcome were recorded.

An informed consent was obtained before recruitment in the study. The work was approved by the Department of Pediatrics of Basra Medical College and the Iraqi Counsel for Medical Specializations. A sample of blood was taken for estimation of hemoglobin, white blood cells (total and differential), and platelets counts by an Automated Hematology Analyzer CBC+3 parts diff. –Symex KX-21N. Genotype was evaluated according to the result of (HLPC-Bio-Rad). Chest x ray and Pulse oximetry to measure transcutaneous arterial oxygen saturation (Spo2) were done for all patients. Hypoxia was defined as Spo2 $\leq$ 95 %.[9]

Statistical analysis: Statistical analysis was done using SPSS program V.11. P-value of < 0.05 was considered as statistically significant. The t-test was used for quantitative comparisons of hematological variables of patients included in the study. Logistic regression analysis was done for the analysis of different variables, for each variable the odd ratio (OR) and 95% confidence interval (CI) were assessed.

Table-I: Selected characteristics of patients with SCD.

Variable	*Patients with ACS*		*Patients without ACS*		*Total*		*P value*
	No.	*%*	*No.*	*%*	*No.*	*%*	
Age (years)							
2-6	9	31.03%	41	32.8%	50	32.46%	
7-11	11	37.93%	58	46.4%	69	44.80%	
12-16	9	31.03%	26	20.8%	35	22.27%	
Total	29	100%	125	100%	154	100%	> 0.05
Sex							
Males	13	44.82%	70	56%	83	53.89%	
Females	16	55.17%	55	44%	71	46.10%	
Total	29	100%	125	100%	154	100%	> 0.05
Hb genotype							
Hb-SS	13	44.82%	61	48.8%	74	48.05%	
Hb-S/β thalassemia	16	55.17%	64	51.2%	80	51.94%	
Total	29	100%	125	100%	154	100%	>0.05
Medical history							
VOC	23	79.31%	94	75.2%	117	75.97%	>0.05
Asthma	13	44.82%	21	16.8%	34	22.07%	0.001
Passive smoking	17	58.62%	71	56.8%	88	57.14%	>0.05
Splenectomy	4	13.79%	5	4%	9	5.84%	< 0.05
Chronic blood transfusion	21	72.41%	80	64%	101	65.58%	>0.05
Cardiac problems	4	17.24%	13	10.4%	17	11.03%	>0.05
Associated events (occurred within 2 weeks of ACS)							
Pain	23	79.31%	94	75.2%	117	75.97%	> 0.05
URTI	17	58.62%	66	52.8%	83	53.89%	> 0.05
Fever	26	89.65%	87	69.6%	113	73.3%	> 0.05
Surgery	5	17.24%	2	1.6%	7	4.54%	< 0.05

RESULTS

A total of 154 febrile children with SCD were studied. Their age ranged from (2-16years); 83 (53.89%) were males, and 71(46.10%) were females. Seventy-four (48.05%) have sickle cell anemia (Hb-SS), and 80 (51.94%) have sickle cell / thalassemia.

Twenty-nine (18.83%) fulfilled the criteria of ACS. The mean age was 8.8±3.6 years for patients with ACS, and 8.4±2.6 years for those without ACS. Asthma, history of splenectomy and surgery were present in a significantly higher percent of patients with ACS compared to other group (P=0.001 and <0.05 respectively), Table-I.

Shortness of breath and chest pain were present in a significantly higher percent of patients with ACS (P<0.05), Table-II. Among physical findings; dyspnea and hypoxia were documented in a significantly higher percent of patients with ACS; P<0.05 and 0.001 respectively. The mean Spo2 for patients with ACS was 94 $\pm$ 3.5 compared to 98 $\pm$ 1.6 for those without ACS, P <0.05.

The hematological data were not significantly different between children with and without ACS, Table-III. The right lung was involved in 20 (68.96%); the right middle lobe was involved in 12(41.37%) patients. Left lung was involved in 3 (10.34%), and bilateral involvement in 6(20.68%) patients. Pleural effusion was reported in 2 cases.

No death was reported among patients included in this study. Duration of hospitalization ranged from (2-21days). The mean duration of hospitalization was (2.9±4.3) days in patients with ACS and (1.6±1.8) days for patients without ACS, P <0.05. Logistic regression analysis revealed that asthma, surgery, dyspnea, chest pain, splenectomy and hypoxia are significantly correlated with ACS, P <0.05, Table-IV.

DISCUSSION

Although the pathophysiology of SCD is essentially similar in different areas, the frequency and severity of complications may vary between different countries and probably different areas in the same country.

In this study, (18.83%) fulfilled the criteria of ACS. Jaiyesimi et al in Oman,[10] and Vichinsky et al in Oakland[7], reported ACS among (22%) and (25%) of patients respectively. These differences are probably related to the difference in the age groups of patients and pattern of SCD; homozygous SCD or other genotypes of SCD.

Age, sex, and Hb genotype were not significantly associated with ACS. Al-Trabolsi et al in Saudi Arabia have reported that the incidence of ACS was most common in younger children. The association of ACS with young children could be explained by that increased susceptibility to viral respiratory infection in young children.[11] ACS frequency was similar in both sexes; this is in agreement with results obtained by Jaiyesimi et al[10] and Boyd et al.[12]

Table-II: Presenting symptoms and signs.

Symptoms	*Patients with ACS*		*Patients without ACS*		*Total*		*P value*
	No.	*%*	*No.*	*%*	*No.*	*%*	
Shortness of breath	21	(72.4%)	32	(25.5%)	5	(34.4%)	<0.05
VOC Extremities	11		28		39		
Abdomen	3		8		11		
Back	5		24		29		
Multiple	6		31		37		
Total	25	(86.20%)	93	(74.40%)	118	(76.6%)	> 0.05
Chest pain	24	(82.75%)	63	(50.4%)	87	(56.49%)	<0.05
Cough	27	(93.10%)	106	(84.8%)	133	(86.36%)	> 0.05
Physical findings							
Dyspnea	21	(72.4%)	32	(25.5%)	53	(34.4%)	<0.05
Tachypnea	8	(27.58%)	22	(17.6%)	30	(19.48%)	> 0.05
Jaundice	8	(27.58%)	31	(24.8%)	39	(25.32%)	> 0.05
Hepatomegaly	8	(27.58%)	39	(31.2%)	47	(30.51%)	> 0.05
Splenomegaly	14	(48.27%)	57	(45.6%)	71	(46.10%)	> 0.05
Hypoxia(Spo2)	8	(27.58%)	3	(4%)	11	(7.14%)	0.001

Table-III: Hematological findings among patients with and without ACS.

Variable	*Patients with ACS*		*Patients without ACS*		*P value*
	Mean	*(±SD)*	*Mean*	*(±SD)*	
Hb (g/dl)	7.9	(±1.6)	8.1	(±1.5)	> 0.05
WBC (109/L)					
Total	11.7	(±4.7)	10.2	(±3.4)	> 0.05
Neutrophils	5.84	(±2.1)	5.44	(±1.34)	> 0.05
Lymphocytes	3.56	(±1.22)	3.36	(±1.42)	> 0.05
Platelets (109/L)	235	(±51.5)	221	(±47.2)	> 0.05

Asthma and history of splenectomy were significantly associated with ACS. Similar results were obtained by other studies.[12,13] Based on the pathogenesis of asthma the prevalence of airway obstruction and airway liability, ventilation/ perfusion mismatching may result in local tissue hypoxia, this promotes increased sickling of red cells, and initiates an ACS or VOC.[12]

The correlation between splenectomy (open surgery) and ACS is in agreement with the findings of Ghantous S et al in Saudi Arabia who reported that the incidence of ACS after splenectomy is 5.2% in laparoscopy group compared to 33.3% with open surgery.[14] Surgery within two weeks of ACS was significantly associated with ACS. This is probably related to changes in ventilatory functions after major surgery. Kokoska et al, reported that younger children with greater blood and heat loss during surgery appear more prone to ACS.[15]

Other events within two weeks of ACS did not significantly increase risk of ACS. Jaiyesimi et al have found that in 71% of cases of ACS a VOC preceded the episodes; other probable precipitating factors was URTI[10], while Vichinsky et al have found febrile events were more likely to present in the 2 weeks preceding ACS.[7]

The significant association of shortness of breath, chest pain, and hypoxia with ACS is in agreement to that reported by Jaiyesimi et al[10] and Al-Trabolsi et al.[11] The results reported by Vichinsky et al have found that wheezing, cough, and fever were most common among patients younger than 10 years of age, whereas extremities pain and dyspnea were more common among adults. This may be explained by etiology of ACS, in children usually due to infections whereas in adults, is due to fat embolism.[7]

Low oxygen saturation was significantly lower among sickler children with ACS and a significant predictor of ACS. Campbell et al found that lower hemoglobin oxygen saturation is independently associated with increasing degrees of anemia and hemolysis but not pulmonary function abnormalities among patients with SCD.[16]

Hematological findings were not significantly correlated with ACS. Al-Trabolsi et al have reported that higher steady state leukocyte counts is associated with ACS.[11] Vichinsky et al, reported a drop in Hb (~0.7 g/dl) and an increase in WBC count by 69% during ACS episode.[7]

Radiologically, the right lung especially middle lobe is mostly involved. Al-Trabolsi et al have reported bilateral lung involvement,[11] while Vichinsky et al reported a predominant involvement of the lower lobes. This is probably explained by different etiologic agents of ACS.[6] Crawford et al have reported that ACS complicating cholecystectomy or splenectomy shows a predilection for basal lung regions and for the lung on the side of surgery.[17]

No death was reported. However, Vichinsky et al reported a mortality rate of 1.1% among sickler children with ACS.[7] Mean duration of hospitalization ((2.9±4.3)) is lower than that reported by Vichinsky et al, in which children were hospitalized for less time than adults (mean, 5.4 *v* 9 days).[7]

From this study it can be concluded that the frequency of ACS is high among children with SCD in Basra and is associated with prolonged hospitalization. Children with concomitant asthma, history of splenectomy and recent surgery have increased risk of ACS. Further studies are needed to

Table-IV: Predictors of ACS.

Variable	*95% CI*		*OR*	*P value*
	Lower	*Upper*		
Asthma	0.01	0.37	0.07	<0.05
Surgery	0.03	0.28	0.06	<0.05
Dyspnea	0.06	0.81	0.23	<0.05
Chest pain	0.10	2.20	0.47	<0.05
Hypoxia(Spo2)	0.001	0.38	0.01	<0.05
Splenectomy	0.03	1.45	0.19	<0.05

look for the etiologic factors of ACS, recurrence rate and role of hydroxyurea and incentive spirometry in the prevention and treatment of ACS.

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