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Prevalence of Specific Respiratory Symptoms, in Children with Sickle Cell Disease in UMTH, Maiduguri.

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Abstract

Respiratory related problems are among the known leading causes of death in patients with sickle cell disease. This study was conducted to identify prevalence of specific respiratory symptoms in children with sickle cell disease (SCD) in the university of Maiduguri teaching hospital (UMTH), Maiduguri, Nigeria. A retrospective sample of eighty children was studied. This comprised of boys and girls aged 2 to 12 years with presenting respiratory symptoms and physical signs who were admitted to the paediatric ward over a period of 3 years. The prevalence of specific respiratory symptoms between the males and females in the different age groups were analyzed. Clinical, laboratory, and radiological features of the chest were equally evaluated and analyzed. Oxygen therapy, antibiotics, analgesic such as simple paracetamol, narcotics, blood transfusion and mechanical ventilation were used as required. Participants [N = 80; 52(65%) males, 28(35%) females, with male: female ratio of 1.8:1.] The age ranged from 2 to 12years. The results revealed that the prevalence of specific respiratory symptoms is age dependent. The symptoms were more prevalent in the younger children than the older ones. Fever and cough seemed more pronounced in the age 2-8years, whereas chest pain, productive cough and shortness of breath were more prevalent amongst the 10-12 years category. Though, these symptoms were age dependent, their overall presence as symptoms and signs were all significant [$p < 0.01$]. This study supported the importance of respiratory pathology as a cause of morbidity and mortality in children with sickle cell disease in our environment. Hence, high prevalence of respiratory symptoms among patients with sickle cell disease may trigger other associated acute complications of the disease, such as painful episodes that may ensue due to associated hypoxia. Early screening and recognition, ongoing monitoring, and proactive management of respiratory symptoms may minimize the degree of morbidity and other unexpected complications.

Keywords: prevalence, specific respiratory symptoms, sickle cell children in UMTH.

Introduction

Sickle cell anemia is the most severe form of haemoglobin diseases [1]. Africa is the most affected region, with sickle cell prevalence ranging from 2 to 30% depending on the

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geographical areas [1-4]. The natural history of sickle cell disease is characterized by chronic anemia, which appears early in life and is accompanied by simple or complicated Vaso-Occlusive Crises (VOCs), which may sometimes Involve the patient's vital prognosis as well as chronic life-threatening And functional complications [5]. Under certain conditions, Sickle haemoglobin (HbS) gelation is the cause of these VOCs [6].The African population is growing and more children with sickle cell anemia are surviving into adulthood and developing pulmonary complications of their disease.[6,7]Nigeria, the most populous country in Africa has the largest number of sickle cell anemia patients in the world[8]. In addition to asthma, thromboembolism, acute chest syndrome, and chronic pulmonary fibrosis, pulmonary hypertension are common complication that may occur in those that survived to adulthood [9, 10].SCD is an inherited disorder of hemoglobin that follows an autosomal recessive inheritance pattern and refers to a family of genetic mutations that affect the beta globin gene. The most common mutation in SCD involves substitution of glutamine for valine at codon six of the beta globin gene. Instead of wild type hemoglobin (referred to as hemoglobin A), this mutation produces hemoglobin S which forms rigid polymers under deoxygenated conditions (thus giving red cells their characteristic sickled shape [9-11]. Individuals who are homozygous for this mutation have hemoglobin SS (widely referred to as sickle cell anemia) however a number of other mutations of beta globin have been described [9-11]. The umbrella term "sickle cell disease" refers to genotypes in which both hemoglobin genes carry a mutation at least one of which is hemoglobin S. For individuals living with the disease, the process of red cell sickling under deoxygenated conditions contributes to a complex state of altered blood rheology[11]. The lung is the only organ capable of reversing the polymerization of hemoglobin and decreasing the proportion of red blood cells that are sickled, the cells that initiate vascular injury and the cascade of systemic complications. Thus, any pulmonary disease occurring in SCD would be expected to significantly compromise individuals with SCD because of attenuated ability to reverse red blood cell polymerization[11, 12]. Clinical and pre-clinical data strongly suggest that lung disease increases SCD related morbidity and mortality. More specifically children and adults with asthma have an increased rate of vaso-occlusive pain episodes, acute chest syndrome (ACS) episodes, and premature mortality when compared to those without asthma [13]. However, the diagnosis of asthma is challenging, particularly among children with a pre-existing chronic disease that has many asthma like symptoms (wheezing, coughing, and shortness of breath)[14] Pain and respiratory symptoms are two of the most common causes of hospitalization in children with sickle cell anaemia [14, 15].In this study, we analyzed in retrospect, children with sickle cell disease to examine the prevalence of respiratory symptoms, such as wheeze, cough, and shortness of breath and determined whether respiratory symptoms were associated with age of the patients and also to note whether there are gender disparity in their occurrences. The aim of the study was to evaluate in retrospect, the prevalence the specific symptoms in SCD patients admitted to the paediatric unit of the university of Maiduguri teaching hospital in north-eastern, Nigeria.

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Methodology

It is retrospective study of all children aged 2 to 12 years with sickle cell disease admitted to the paediatric ward from January 2004 to December 2007. All patients admitted on account symptoms of cough, chest pain, breathing difficulties, high fever, bone pains, pyrexia of unknown or a combination of two or more symptoms. A total of 80 patients' case files were analyzed. Files of 52 males and 28 females were reviewed. The following information wasevaluated: Sex, age, presenting symptoms, presenting signs, laboratory values, radiological findings as well those that had other associated complications. All the Patients were then categorized into gender group of males and females. Each gender group was divided on the basis of age 2-4 years, 5-7 years, 8-10 years, and 11-12 years. The data on symptoms, physical signs, laboratory and radiological findings was studied. Almost all the patients were treated with intravenous fluid, simple analgesia paracetamol, antibiotics and narcotic analgesics where necessary. Oxygen therapy was given for hypoxia (partial pressure of oxygen (PO2) <60 mm hg, or oxygen (O2) saturation <90%). As a routine most of the patients were given third-generation cephalosporin because of the seeming conventional antibiotic abuse and resistance in the community. Simple blood transfusion was given to patients with severe disease, very low pack cell volume and evidence of consolidation involving one or more lobes.

Data analysis

Data analysis was done using the Statistical Package for Social Sciences Software (SPSS version 16). The measures of central tendency and dispersion were computed for all quantitative variables. Frequency distribution was used for variables such as numbers of males and females in the different age groups and the degree of occurrences of the presenting symptoms and the physical examination findings. The unpaired Student's' test was employed to assess the difference between the means of the two extreme age groups. A p value of 0.01 was used as the criteria for a statistically significant difference.

Results

The study consisted of 52(65%) males and 28(35%) females, with male: female ratio of 1.8:1. The age ranged from 2 to 12years. A greater number of the patients in both sexes fell within the 2-4 age groups, with the numbers diminishing to lower number in the age group 11-12years. This result is shown (fig.1).

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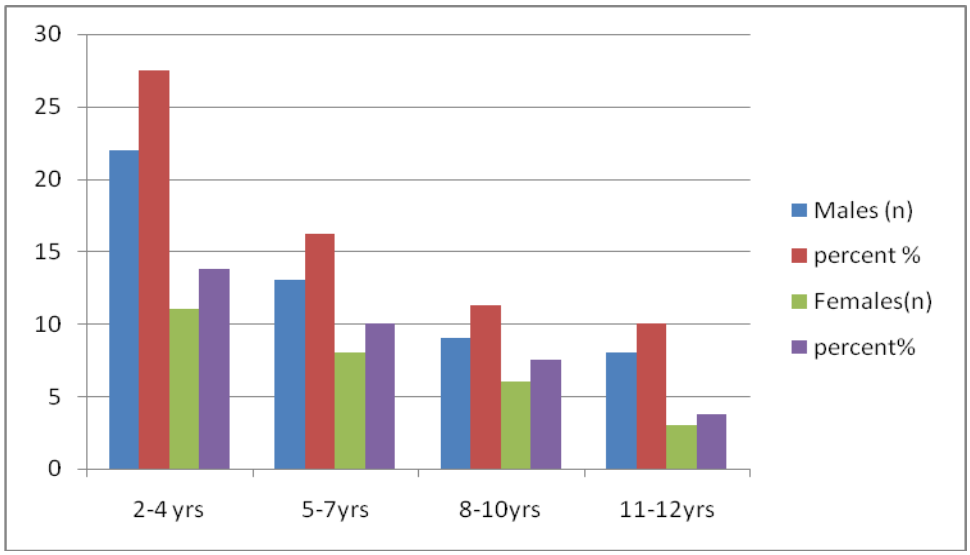
Fig.1Distribution of the patients in the age groups



Age Group

Prevalence of symptoms is shown in table 1. Symptoms prevalence was similar in both males and females. Symptoms of fever, cough, and chest pain were more prevalent in the patients. However, greater number of the females had symptoms of productive cough [93%]; and shortness of breath [96%], in relation to their male counterpart [87% cough; and 67% shortness of breath].

Table1.Prevalence of specific respiratory symptoms

Presenting Symptoms	Males n)	Percent%	Females (n)	Percent %
Fever	49	94	26	93
cough	45		22	78
Chest pain	42	81	26	
Productive cough	29	56	18	64
Shortness of breath	35	67	27	96

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wheezing	20	38	11	39

Prevalence of respiratory: Symptoms were more prevalent in the younger children than the older ones. Fever and cough seemed more pronounced in the ages 2-8, whereas chest pain, productive cough and shortness of breath were more prevalent amongst the 10-12 years category. This is shown in (Table2a). The most common presenting symptoms were fever, cough, and chest pain, while less common, were shortness of breath and productive cough. Fever was the most common presentation across all the age groups followed by chest pain and cough. The prevalence of these symptoms were significant ($p<0.01$).

Table2a. Prevalence of specific respiratory symptoms in Age groups

Presenting symptoms	Total	Age group (YR) % of patients 2-4yrs	5-7yrs	8-10yrs	11-12yrs	P value
Fever	80	94	88	78	92	<0.01
cough	68	79	92	84	68	<0.01
Chest pain	60	24	45	84	92	<0.01
Productive cough	45	20	38	86	81	<0.01
Shortness of breath	24	33	44	68	78	<0.01
wheezing	16	23	12	16	20	0.15

* P value for the difference between age groups 2 to 4 years and age 11-12 years.

Physical findings: physical findings at the time of hospitalization are shown in (Table 2b). Examination findings of the patients with regards to recording of Vital signs and bedside examination findings seemed to vary across the age groups. The distribution of the signs were

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similar in both males and females, however greater number of males presented with wheezing (62%) compared to the females (21%). whereas normal chest examination was observed in only (n =7) 13% of the males and (n=9) 32% of the females.

Table2b. Presentation of respiratory physical signs in the study population.

Signs	Males(n)	Percent%	Females(n)	Percent%
Temperature				
> 39o C	46	88	18	64
< 39o C	6	11	10	36
Tachypnea	44	85	22	78
Retraction	25	48	16	57
Tachycardia	48	92	28	100
Dullness to percussion	16	31	13	46
Decreased breath sound	36	69	15	54
Crepitation	19	36	9	32
Wheezing	32	62	6	21
Bronchial breathing	28	54	19	68
Normal exam	7	13	9	32

Prevalence of associated problems is shown in (Table 3). Painful vaso-occlusive crisis was the most common in both males (83%) and females (82%). The majority of patients reported having acute painful episodes, and most reported having chest pain. It has been considered the most common associated event with the respiratory symptoms, followed by underlying infectious processes in the form of urinary tract infection, upper respiratory tract infection, and acute cholecystitis. Bronchopneumonia was the single common clinical diagnosis made on the basis of physical examination with (62%) males and (65%) females respectively. The most dominant infection in females was urinary tract infection whereas males had acute cholecystytis as the most common.

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Table 3. Prevalence of associated features and complications

Associated complications	males	Percent%	females	Percent %
Painful Crisis	43/52	83	23/28	82
Infection				
- Bacteria	24/52	46	17/28	61
- URTS	16/52	31	9/28	32
- UTI	12/52	23	22/28	78
- Acute Cholecystitis	32/52	62	15/28	53
Sequestration crisis	10/52	19	6/28	21
Bronchopneumonia	34/52	65	19/28	68

Laboratory findings: These are shown in (Table 4). Full blood count and erythrocyte sedimentation rate documented was compared with previous steady state value. Hemoglobin and white blood counts showed significant changes as result of the respiratory problems, including a drop in the total platelets count. The acute phase protein ESR was raised indicating presence of acute phenomena. All the changes were statistically significant ($p<0.01$) except for reticulocyte count ($P=0.07$).

Radiographic findings: radiographic findings vary by age and the gender. The predominant radiological findings were bilateral lungs involvement in form of bronchopneumonia in both males and females (24 vs. 12; n=34) 45 %. In the unilateral, involvement of more than one zone was (21%), there was more right side involvement (14%) than left side (11%). Even in the bronchopneumonia radiographs, the right side involvement appeared more florid and extensive. It was often found in the younger age group. This Indicate that, presentation may be age dependent. Pleural effusion was found in a total of five patients (0.1%). Two females had normal chest radiograph (0.02%).

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Table 4.(a) Hematological indices or both males and females

Test	Baseine(mean)	Symptomatic (mean)	P. value
Haemoglbin g/dl	7.4	5.2	<0.01
ESR	20mm/hr	45mm/hr	<0.01
White blood cells($x10^9$)	8.4	17.5	<0.01
Platelets count($x10^9$)	280.5	203.8	<0.01
Reticulocyte count (%)	6.8	7.3	0.07

P value <0.01 is significant

b)Radiological findings

Test	Males	Females	Percent
Right lung involvement	9	2	14
Left lung involvement	6	3	11
More than one zone in one side	10	7	21

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Bronchopneumonia	24	12	45
Pleural effusion	3	2	0.1
Normal findings	0	2	0.02

The finding of significant serological titer for mycoplasma infections was seen only in two female patients. None of the patient had any growth in the blood culture. If many patients have had significant serological titer for mycoplasma,, it would and may support the current practice of giving erythromycin (or new macro ides) to all sickle cell patients with respiratory infection. This is also supported by recent study which showed *Chlamydia pneumoniae* and *Mycoplasmapneumoniae* were the most frequent isolated pathogens in sickle cell patients with productive cough, in several previous studies[6,7,21].

(c) Microbiology Test males females

Mycoplasma pneumonie titre	0	2
Blood culture	ALL NEGATIVE	ALL NEGATIVE

Discussion

As observed in this study, we examined the prevalence of respiratory symptoms among a retrospective sample of 80 children with sickle cell disease. It could be deduced that such a sample may be a representative sample of many patients with associated respiratory symptoms in a descriptive way. Respiratory symptoms were more common in the younger children when compared to the much older ones which was in agreement with previous studies [14-16].Many prospective studies in sickle cell children with painful crisis have found that respiratory symptoms were more common in patients with low levels of foetal haemoglobin and high levels of total sickle haemoglobin. [16, 17]. Pulmonary complications and disease were one the leading causes of death in patients with sickle cell disease, It affects both boys and girls; there may be a predominance of males [18]. In this study we found similar trend with male: female ratio of 1.8:1. A greater number of the patients in both sexes fell within the 2-4 age groups, with the numbers diminishing to lower number in the age group 11-12years. The most common

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presenting symptoms were fever, cough, and chest pain, while less common, were shortness of breath and productive cough. Fever was the most common presentation across all the age groups followed by chest pain and cough. The prevalence of these symptoms were significant ($p<0.01$). This finding is similar to other studies [16, 17, 18], and this study also revealed that the prevalence of specific respiratory symptoms was strongly influenced by patient age, being most common in younger children and least frequent in older children. Higher prevalence in young children could also be explained by reasoning that the children, as usual must have increased susceptibility to viral respiratory infection. As observed in similar studies, one of the factors associated with an increased prevalence of respiratory symptoms is a high steady-state leukocyte count [19].We equally observed leucocytosis, high ESR, and low platelets in these patients. The reason for the association between high leukocyte counts and the increased incidence of respiratory symptoms is not well substantiated. However, others believed that, it couldbe explained by the increasing susceptibility to viral respiratory infection in young children.[6,7,19].Because of the increased prevalence of respiratory symptoms in children with sickle cell disease, approximately 50% of patients ultimately have a higher chance of dying at an early age, and the overall mortality rate following repeated respiratory pathology can be as high as 10-12% [11,14, 20]. Hence, as such, it is pertinent to recognise and diagnose these symptoms right from the outset, with a view to treat the ailment aggressively, as has been underscored by the observation that they were among the leading causes of death among sickle cell patients [14, 17, 20]. In many previous studies, radiological findings were more of disease affecting the lower lobes of the lungs [11, 18, 20], however, in variance, our study showed predominance of diffuse lung involvement, in form of bronchopneumonia. This was followed by involvement of more zones on the same side. This variance could be attributed probably to the geographical location of the study environment, to lower age of the children studied, and the expected low immunity in the very young children. As such, the possibility of other associated infectious process could also be expected to be high. Serological test for mycoplasma was not significant in this study, only two females tested positive. If the finding of mycoplasma infections is more than 40% in the study population, then, it would and may support the current practice of giving erythromycin (or new macrol ides) to all patients with presenting with all the specific respiratory symptoms. [7, 15, 20, 21]

Conclusion

This retrospective study demonstrates the importance of specific respiratory symptoms as a cause of morbidity and mortality in children with sickle cell disease in our environment. The results were similar to previously published data among similar age group. This result is believed to serve as a baseline for subsequent studies in a more elaborate manner. Future studies need to examine the benefits of early screening and aggressive treatment of respiratory problems in sickle cell disease. Respiratory screening should be a regular component of comprehensive care in sickle cell disease to minimize interference of recurrent respiratory symptoms with sleep, exercise, and predisposition to chronic lung disease and its attendant complication with age progression,

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Competing interest: Authors declare no competing interest

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