Int J Biol Med Res. 2011; 2(3): 723-726

BioMedSciDirect Publications

Contents lists available at BioMedSciDirect Publications

International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com

Original Article

Pulmonary function in adults with sickle cell disease.

Sandip Meghnad Hulke*, Avinash Eknath Thakare

** Assistant Professor, Dept. Of Physiology, LN Medical College, Bhopal .*
[a]Assistant Professor, Dept. Of Physiology, LN Medical College, Bhopal .

ARTICLE INFO

Keywords:
Sickle cell disease
FVC
PEFR

ABSTRACT

Background: Pulmonary involvement is a major cause of morbidity and mortality in patients with sickle cell disease (SCD). Our aim was to determine the pattern of pulmonary dysfunction. METHODS: pulmonary function test was performed in sickle cell disease patient and these findings were compared with the normal subjects. Results: Forced vital capacity (FVC), forced expiratory volume in one second, forced expiratory flow rate at 25% to 75% of FVC (FEF(25%-75%)), and expiratory flow rate values were significantly lower in the patient group than in the controls. There was higher incidence of restrictive lung disease amongst person with abnormal lung function. Conclusions: Abnormal pulmonary functions were found in 42% of the patients. PFT parameters are significantly decreased as compared to the control. Common abnormality seen is the restrictive lung disease.

1. Introduction

Sickle cell anemia (Hb-SS) results from homozygosity for a point mutation in the globin gene (HBB;Glu6Val) causing the resultant sickle hemoglobin (Hb S) to be less soluble when deoxygenated than normal hemoglobin [1]. Pulmonary complications, including acute chest syndrome (ACS), pulmonary hypertension (PH), and pulmonary fibrosis, account for 20–30% of deaths sickle cell disease patients[2, 3].

Studies of lung function to date in this population have been of modest size, often involving fewer than 50 patients [4,5,6] and largely inconclusive. Their results have yielded a spectrum of abnormalities, including restrictive lung disease, obstructive disease, and hypoxemia [4,6,7]. No definitive profile for pulmonary function in sickle cell disease has emerged. As a result, clinicians find pulmonary function tests (PFTs) difficult to interpret in this population and their clinical utility for directing further investigation. Larger scale studies are necessary to elucidate more clearly. Also in this part of the world i.e. Nagpur where sickle cell disease is highly prevalent, studies are needed to be performed to evaluate the characteristics of lung function in the sickle cell disease (SCD) population. Hence we undertook this study to know rhe pattern of lung function in sickle cell disease patients.

2.Material and Method

The present study was done the patients attending sickle cell OPD in Government Medical College and Hospital, Nagpur. One hundred and thirty-three patient had undergone pulmonary function testing. Pulmonary function tests (PFTs) were performed during the symptom-free interval while the patient was not in crisis or having acute chest syndrome.

2.1.Inclusion criteria

- Diagnosed case of sickle cell disease
- Age: 20 to 40 years
- Patient must be symptom free, in clinically in the steady state attending OPD for routine follow up.
- Nonsmoker

2.2.Exclusion criteria

- patients in crisis or having acute chest syndrome.
- Smokers
- H/o cardiac disease
- H/O Dibetes mellitus
- Extremes of weight and height

* Corresponding Author : Dr Sandip Meghnad Hulke
Assistant Professor,
Dept. Of Physiology,
LN Medical College, Bhopal
Mobile: 9039769805
E.mail: smh555@rediffmail.com

PFTs of sickle cell disease patients were compared with eighty-five healthy subjects from the staff of medical college. Inclusion and exclusion criteria were as follows.

2.3.Inclusion criteria

- Age: 20to 40 years
- Healthy, nonsmoker

2.4.Exclusion criteria

- Smokers
- H/o chronic respiratory disease
- H/o cardiac disease
- Examination finding suggestive of respiratory or cardiac disease
- H/O Dibetes mellitus
- Extremes of weight and height

For pulmonary function test:- MIR Spirolab II(Via Del Maggiolino, 125, 00153, Rome, Italy) was used. Pulmonary function test was recorded at the OPD.

All the subjects were made familiar with the instrument and the procedure for performing the test. The data of the subject as regards to name, age, height, weight, sex, date of performing the test, atmospheric temperature was fed to the computerized MIR Spirolab.

The tests were performed in sitting position. The subject was asked to take full inspiration which was followed by as much rapid and forceful expiration as possible in the mouthpiece of MIR Spirolab. Three consecutive readings were taken and the best reading amongst the three was selected. We have followed the standard guidelines [8].

Lung function parameters studied were forced vital capacity (FVC), Forced expiratory volume in 1 sec (FEV1), FEV1 as percentage of FVC in % (FEV1 (%)), Peak expiratory flow rate in liters / sec (PEFR), Forced expiratory flow rate in liters / sec in 25% of FVC (FEF25%), Forced expiratory flow rate in liters / sec in 50% of FVC (FEF50%), Forced expiratory flow rate in liters / sec in 75% of FVC (FEF75%), Forced expiratory flow rate during 25 to 75% of expiration (FEF25-75%), maximum voluntary ventilation (MVV).

2.5.Classification of Pulmonary Function

The pulmonary function of each subject was classified into four categories based on American Thoracic Society criteria [9].

- Normal: FEV1, FVC within the normal range (at least 80% predicted) with FEV1/FVC at least 70%
- Obstructive: An FEV1/FVC ratio less than 70%, associated with decreased FEV1 and FVC (less than 80% predicted).
- Restrictive: Reduction in the FVC with a normal or elevated FEV1 -to-FVC ratio
- Mixed obstructive and restrictive: FEV1/FVC ratio reduced, suggestive of obstructive disease. Reduction in the FVC with a normal or elevated FEV1 to-FVC ratio.

Then the data of the observation for all parameters were statistically analyzed by calculating mean and standard deviation. The data was analyzed using Graph pad prism5 software. Unpaired t test was applied and p value <0.05 was considered as statistically significant.

3.Result

3.1.Patient characteristics

In the present study, pulmonary function test of one hundred and thirty-three patients (80 male and 53 females) were compared with eighty five controls (49 males and 36 females). Patients characteristics are shown in table 1 and there was no significant difference in the patient and control characteristics.

Table 1: patients characteristics

PARAMETERS	Cases (n=133)	Control (n=85)
Age (yrs)	28.12±3.42	27.41±4.11
Height (cms)	178.41±12.14	176.98±11.15
Weight (kg)	66.14±11.14	65.15±12.56
BMI(kg/m2)	20.95± 1.88	21.14±2.11

No significant difference

3.2.Pulmonary function test

Lung function parameter of cases and control is compared in the table 2. All the parameters except FEF50% and FEF75% were significantly decreased in sickle cell disease patients. (table2) Pulmonary function tests were within normal limits in all controls. In sickle cell disease patients, Most common findings were the normal (58%) during the asymptomatic period. Abnormal pulmonary functions were found in 42% of the patients. Restrictive findings were seen in 24.06% of the patient which was followed mixed findings (10.52 %). Obstructive findings were observed in 6.7 % of the patients.

Table 2: lung function parameters in cases and control

PARAMETERS	Cases (n=133)	Control (n=85)
FVC(%predicted)	81.67±4.58	93.25±5.13**
FEV1(%predicted)	82.23±4.33	94.33±4.22**
FEV1 (%)	86.67±5.11	92.25±5.38**
PEFR (%predicted)	84.25±4.68	88.59±4.97*
FEF25-75% (%predicted)	82.56±4.89	99.11±7.13***
FEF25% (%predicted)	85.59±4.45	89.47±4.98*
FEF50% (%predicted)	92.23±6.14	94.33±7.11
FEF75% (%predicted)	93.67±7.01	92.25±7.58
MVV (%predicted)	94.58±7.28	102.36±10.25**

Values are MEAN±S.D.
***:= p<0.05 significant change, **:= p<0.01 very significant change**

Table3: Sub classification based on the pulmonary function test in sickle cell disease patients

PARAMETERS	N(%)
Normal PFT	78 (58.64)
Obstructive PFT	9 (6.7)
Restrictive PFT	32 (24.06)
mixed PFT	14 (10.52)

4.Discussion

In the present study, we found significant pulmonary function impairment. Restrictive pattern of PFT was comparatively more common in sickle cell disease patients.

Prior studies have suggested that abnormal pulmonary function tests are the first objective sign of chronic sickle cell lung disease and that they could be helpful in patient management [10]. Previously, multiple small studies have demonstrated a spectrum of PFT abnormalities in adult sickle cell disease including restrictive physiology, decreased DlCO, hypoxemia, and obstructive disease[6,7,11,12]. The most common PFT abnormality observed was restrictive Disease as in our study as well as in others[11,12,13,14].

In a study in Saudi patients, pulmonary function tests were abnormal in 51%, out of which 36% of patients had a restrictive pattern, and 5% had a mixed restrictive-obstructive pattern[11]. Sen N et al also found decreased forced vital capacity (FVC), forced expiratory volume in one second, forced expiratory flow rate at 25% to 75% of FVC (FEF(25%-75%)), and peak expiratory flow rate as compared to control[13]. Previously, in a largescale study of a healthy white population, only 2.4% of subjects with a normal FVC had restrictive disease and it was recommended that spirometry alone was sufficient to exclude the presence of restriction unless a high degree of clinical suspicion was present [15].

Why in sickle cell patients abnormal pulmonary function is found even in asymptomatic period? In the sickle cell disease, mechanism of restriction would be ineffective inspiration due to chest wall pain related to peripheral vasoocclusion, prior rib infarctions, or vertebral disease[16]. Although the PFTs obtained in this study were done while the subjects were clinically at their baseline, even when clinically well, patients with Hb-SS may have subacute vasoocclusion [17]. All these factor may have contributed to chest wall discomfort during testing. As result of vasoocclusion, repeated bony infarction would have occurred during the growth and development, because of which there may be different chest wall structure[18].

Other cause for derangement in pulmonary function may be air way hyperresponsiveness. The prevalence of airway hyperresponsiveness was high in adult patients with sickle cell disease [13,14]. A significant correlation was found between airway hyperresponsiveness and recurrent acute chest syndrome episodes. Anti-inflammatory controller agents can be used routinely to decrease pulmonary morbidity associated with SCD, even in the absence of asthmatic symptoms[13,14]. Younger age, serum IgE concentration, and LDH level, a marker of hemolysis, are associated with airway hyperresponsiveness [19]. Hemolysis and leukocytosis were independent risk factors for an early decline in lung volumes in this pediatric SCD cohort [20].

Other cause may be repeated episodes of acute chest syndrome and it may be a risk factor for mortality, pulmonary infarction and pneumonia are the most frequent concomitant conditions associated with acute chest syndrome [2]. Development of pulmonary hypertension which occurs as result of chronic pulmonary crisis, may also cause restrictive lung disease. Association of pulmonary hypertension with a history of renal dysfunction was shown [21]. In addition, platelets appear to have an important role in the development of pulmonary hypertension, both as mediators of serotonin metabolism and in their role in thrombosis [7,21]. In CT scan study in sickle disease patient, 41%had significant multifocal interstitial disease[22].

To conclude, Abnormal pulmonary function were found in 42% of the patients. PFT parameters are significantly decreased as compared to the control. Common abnormality seen is the restrictive lung disease. Cause of the restrictive lung disease may be vasulopathy, repeated episodes of acute chest syndrome, airway hypersensitivity, hamolysis and other organ dysfunction asoociated with sickle cell disease.

5.Limitation of the study.

We should have measured total lung capacity and diffusing capacity, as it was not possible for us as our sample size was large. In the future similar studies should be encouraged to assess all the parameters.

In addition,testing for airway hyperreactivity, such as response to inhaled bronchodilators or methacholine challenge testing, was not done. It is possible that subjects with coexistent asthma may not have been detected in the current study as airflow typically normalizes in these patients between acute exacerbations.

We should have correlated pulmonary function abnormality with the haematological investigation which was not done in the present study, as our main aim was to assess the pulmonary function abnormality. In the future we would recommend further study where pulmonary function should be supplemented with radiological as well as haematological investigation.

6. References

[1] Ganong WF. Circulating body fluids. In Ganong WF ed. Review Of Medical Physiology, 22nd edition, New Delhi, McGraw Hill,2005;515-546.

[2] Platt OS, Brambilla DJ, Rosse WF, Milner PF, Castro O, Steinberg MH, et al. Klug PP. Mortality in sickle cell disease: life expectancy and risk factors for early death. N Engl J Med. 1994;330:1639–1644.

[3] Steinberg MH, Barton F, Castro O, Pegelow CH, Ballas SK, Kutlar A, et al. Effect of hydroxyurea on mortality and morbidity in adult sickle cell anemia: risks and benefits up to 9 years of treatment. JAMA. 2003;289:1645–1651.

[4] Delclaux C, Zerah-Lancner F, Bachir D, Habibi A, Monin JL, Godeau B, et al. Factors associated with dyspnea in adult patients with sickle cell disease. Chest. 2005;128:3336–3344.

[5] Miller GJ, Serjeant GR. An assessment of lung volumes and gas transfer in sickle-cell anaemia. Thorax .1971;26:309–315.

[6] Santoli F, Zerah F, Vasile N, Bachir D, Galacteros F, Atlan G. Pulmonary function in sickle cell disease with or without acute chest syndrome. Eur Respir J. 1998;12:1124–1129.

[7] Elizabeth S. Klings, Diego F. Wyszynski, Vikki G. Nolan, Martin H et al. Abnormal Pulmonary Function in Adults with Sickle Cell Anemia. Am J Respir Crit Care Med. 2006 ;173:1264–1269.

[8] Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A Standardisation of spirometry.Eur Respir J. 2005; 26: 319–338.

[9] American Thoracic Society. Lung function testing: selection of reference values and interpretative strategies.Am Rev Respir Dis. 1991;144:1202–1218.

[10] Powars D, Weidman JA, Odom-Maryon T, Niland JC, Johnson C. Sickle cell chronic lung disease: prior morbidity and the risk of pulmonary failure. Medicine (Baltimore). 1988;67:66–76.

[11] Alameri HF, Aleem A, Kardas W, Jehangir A, Owais M, Al-Momen A. Dyspnea, pulmonary function and exercise capacity in adult Saudi patients with sickle cell disease. Saudi Med J. 2008;29:707-713.

[12] Klings ES, Wyszynski DF, Nolan VG, Steinberg MH. Abnormal pulmonary function in adults with sickle cell anemia. Am J Respir Crit Care Med. 2006 1;173:1264-1269.

[13] Sen N, Kozanoglu I, Karatasli M, Ermis H, Boga C, Eyuboglu FO. Lung. Pulmonary function and airway hyperresponsiveness in adults with sickle cell disease.2009;187:195-200.

[14] Vendramini EC, Vianna EO, De Lucena Angulo I, De Castro FB, Martinez JA, Terra-Filho J. Lung function and airway hyperresponsiveness in adult patients with sickle cell disease. Am J Med Sci. 2006;332:68-72.

[15] Aaron SD, Dales RE, Cardinal P. How accurate is spirometry at predicting restrictive pulmonary impairment? Chest. 1999;115:869–873.

[16] Leong CS, Stark P. Thoracic manifestations of sickle cell disease. J Thorac Imaging. 1998;13:128–134.

[16] Leong CS, Stark P. Thoracic manifestations of sickle cell disease. J Thorac Imaging. 1998;13:128–134.

[17] Akinola NO, Stevens SM, Franklin IM, Nash GB, Stuart J. Subclinical ischaemic episodes during the steady state of sickle cell anaemia. J Clin Pathol. 1992;45:902–906.

[18] Silva CM, Viana MB. Growth deficits in children with sickle cell disease.Arch Med Res. 2002;33:308–312.

[19] Field JJ, Stocks J, Kirkham FJ, Rosen CL, Dietzen DJ, Semon T et al. Chest. Airway hyperresponsiveness in children with sickle cell anemia.2011;139:563-568.

[20] Tassel C, Arnaud C, Kulpa M, Fleurence E, Kandem A, Madhi F. Leukocytosis is a risk factor for lung function deterioration in children with sickle cell disease.Respir Med. 2011;105:788-795.

[21] Kato GJ, McGowan VR, Machado RF, Little JA, Taylor VJ, Morris CR, et al. Lactate dehydrogenase as a biomarker of hemolysis-associated nitric oxide resistance, priapism, leg ulceration, pulmonary hypertension and death in patients with sickle cell disease. Blood. 2006;107:2279–2285.

[22] Aquino SL, Gamsu G, Fahy JV, Claster S, Embury SH, Mentzer WC, Vichinsky EP.Chronic pulmonary disorders in sickle cell disease: findings at thin-section CT. Radiology. 1994 ;193:807-811.