Comparision of Lung Functions among Males and Females with Sickle Cell Anaemia

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ABSTRACT

Introduction: Sickle cell disorder has remained a neglected field of research in India and magnitude of problem has never been appreciated. Most of the reports spread a misconception that the sickle gene was confined to the tribal population. In India nearly 20 million people suffer from this disease. In it the red blood cells become deformed, rigid and obstruct the blood flow leading to tissue damage because of poor perfusion. The present study was undertaken to evaluate abnormalities in lung functions due to the disease.

Material and Methods: The study was carried out in department of Physiology in association with department of Medicine at Government Medical College. The study protocol was approved by the ethical committee. The study included 200 subjects, out of which 100 were sickle cell disease patients and 100controlsin the age group of 20-35 yrs. FVC, FEV1, FEV1/FVC%, FEF 25-75%, PEFR and MVV values were chosen. All the variables were compared among the cases and controls by performing unpaired't'test.p value <0.05 was considered as statistically significant and <0.001 as highly significant.

Results: All the PFT parameters were highly significantly reduced in cases,decline in the pulmonary function tests parameters in study group is suggestive of both restrictive and obstructive changes in sickle cell disease, restrictive pattern been more common.

Conclusion: Most common abnormal pattern found was restrictive type. Pulmonary function testing can be a used as routine test to predict respiratory dysfunction in these patients.

Keywords: Lung functions, restrictive pattern, obstructive pattern, sickle cell anemia

INTRODUCTION

Red blood cells of adult healthy human individual consist of respiratory protein known as haemoglobin. Its major function is to transport oxygen from atmosphere to lungs and finally pass on to all vital organs. The property of combining reversibly with oxygen is unique wonder and interesting.

The Sickle cell disease is the first molecular disease known to man.[1] It was first described in a 20 year old dental student from Grenada in 1910 after he was admitted for anaemia by James Herrick[2] and his intern Earnest Edward Irons who found peculiar elongated sickle shaped cells in the blood. Sickle cell anaemia (also known as sickle cell disease) is the second most common haematological disorder next only to thalassemia. Sickle haemoglobin was first discovered from a tribal population of Nilgiri hills of South India in 1952.[3]

It has remained a neglected field of research in India and magnitude of problem has never been appreciated because most of the subsequent reports spread a misconception that the sickle gene in India was confined to the tribal population and some scheduled castes only.

In this disease amino acid glutamic acid at position number 6 of β globin chain is replaced by valine. This happens due to change of nucleotide, adenine to thymine of codon 6 of β globin gene on chromosome 11.This changes the net charge of haemoglobin, oxygen affinity and three dimensional structure of haemoglobin which makes it an unstable one.

In India nearly 20 million people suffer from sickle cell anaemia. The belt extends from Assam, Orissa, Madhya Pradesh, Andhra Pradesh, Karnataka and Maharashtra. In Maharashtra, the reported prevalence of the disease varies from 1.9% to 33.5% in different communities.[4] The present study is undertaken to evaluate abnormalities in lung functions due to the disease.

MATERIAL AND METHODS

The present study was carried out in department of Physiology in association with department of Medicine in Government Medical College,Nagpur for two years between 2012 to 2013. The study protocol was approved by the ethical committee of the college.

The cases were selected from the patients attending Sickle cell outpatient department (OPD).Before enrollment in the study, informed written consent was obtained from each subject. Sample size was 200, based on inclusion and exclusion criteria. Out of these, 100 were sickle cell anaemia patients and 100 served as controls.

Inclusion criteria

1. Diagnosed cases of sickle cell disease (HbSS pattern) which was confirmed by cellulose acetate electrophoresis.
2. Patients attending OPD in a clinically steady state, in a symptom free interval, not in the crisis and not having acute chest syndrome.
3. Non smokers and non alcoholics.

Exclusion criteria

1. Patients in crisis or having acute chest syndrome when performing the test.
2. Smokers and alcoholics.
3. History of any respiratory disease, cardiovascular disease, diabetes mellitus.

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4. Patients engaged in occupation that can cause health hazard like dye industry, saw mill industry, etc.

Control group

1. Subjects with normal average height and weight for the same age and belonging to the same socio-economic status as that of the study group.
2. They had normal adult haemoglobin pattern (Hb AA) on electrophoresis.
3. They were non smokers and non alcoholics.
4. All subjects were free from cardiac and respiratory disease.

Method

The procedure was performed during morning OPD hours to avoid any diurnal variation. Before performing the pulmonary function tests, the following measurements were taken:-

1. Standing height
2. Weight
3. Body Mass Index (BMI)

Pulmonary Function Tests

The procedure of the pulmonary function tests was thoroughly explained. They were asked to sit comfortably and watch the demonstration.

The electronic computerized spirometer RMS Helios 401-version 1 was used.

In this procedure, each subject was asked to close the nostrils by the nose clip and execute fast forceful expiration as much as possible at the end of deep full inspiration into the mouthpiece. Three consecutive readings were obtained and best among the three was selected and noted.

After adequate rest, the test to obtain MVV was carried out. The subjects were asked to inhale and exhale as deep and as fast as possible for 12 seconds. The procedure was repeated for three consecutive times with adequate rest between each reading and best one was noted.

For each subject a sheet of predicted, pre i.e. observed and percentage predicted values of all the parameters was taken. The same procedure was followed for the control group. FVC, FEV1, FEV1/FVC%, FEF 25-75% and MVV values were chosen which are relevant to the study. The values obtained were in liters/min. Percent Predicted values were calculated by the instrument itself.

STATISTICAL ANALYSIS

All the variables were presented as mean ± standard deviation (SD).

Continuous variables (age, PFT parameters) were compared among the cases and controls by unpaired't test. p value <0.05 was considered as statistically significant and <0.001 as highly significant. All the tests were two sided. Statistical software STATA version 10.0 was used for data analysis

Observations

RESULT

All the parameters are highly significantly reduced in study group when compared with controls. Table-1 shows comparison of anthropometric parameters between cases and controls. Mean BMI was significantly reduced in cases when compared with controls. Table-2 shows comparison of mean values of PFT parameters in study group and controls. All PFT parameters are

significantly reduced in study group as compared to controls. Table-3 shows age wise distribution of abnormal pattern of PFT in study group. Most common abnormal pattern found is restrictive type followed by obstructive followed by mixed pattern. Most common age group affected is 25-29 years.

DISCUSSION

The statistical analysis of the observations in the present study reveals that the patients of sickle cell disease show significant decrease in their Body Mass Index as compared to controls.

Also there is statistically highly significant decrease in all the PFT parameters (% predicted) i.e. FVC, FEV1, FEF25-75%, PEFR and MVV in study group as compared to controls. These findings correlate with the findings of the previous studies. The finding that most of the SCD patients were below 30 years of age is in keeping with the notion that life expectancy of the SCD patients is reduced.[5] In the present study, Body Mass Index was highly significantly decreased in cases when compared with controls. This correlates with the findings of Modebe O et al.[6]

H. S. Nikhar et al has shown a significant decline in BMI in sickle cell disease children from rural areas as compared to urban areas.[7] In the present study, mean height was decreased though not significantly in cases as compared to controls, whereas weight was reduced significantly. It is stated that delayed skeletal maturation during adolescence may allow for a longer growth period in the long bones of the extremities, resulting in normal adult height among surviving adults with sickle cell disease.

Reduction in BMI might be reduced due to poor dietary intake because of appetite especially during vaso-occlusive crisis. It

Baseline characteristics	Cases (n=100)	Control (n=100)	p value
Age (year)	25.81± 3.20	25.56± 3.11	0.5766, NS
Height (cm)	156.95±5.13	157.11±4.14	0.808 NS
Weight (kg)	50.11±3.89	52.72±2.55	<0.001 HS
BMI (kg/m²)	20.36± 1.65	21.37± 1.20	<0.0001, HS

Table-1: Shows baseline characteristics in study group and controls

Parameters	Cases (n=100)	Controls (n=100)	p-value
FVC (% pred)	82.45±9.83	91.33±4.05	<0.0001,HS
FEV1 (% pred)	76.71±10.5	88.25±3.82	<0.0001,HS
FEV1/FV(%pred)	93.30±8.63	96.64±1.87	<0.0001,HS
FEF25-75(pred)	83.27±8.66	93.07±2.01	<0.0001,HS
PEFR (% pred)	84.38±7.90	91.2±2.97	<0.0001,HS
MVV (% pred)	86.62±8.50	92.51±2.20	<0.0001,HS

All values are expressed as mean± S.D.

Table-2: Shows pulmonary function test parameters in study group and controls

Age (years)	Total cases	Restrictive Pattern	Obstructive pattern	Mixed pattern
20-24	29	10	3	0
25-29	62	20	3	4
≥30	9	4	3	2
Total	100	34	9	6

Table-3: Shows age wise distribution of abnormal pattern of PFTs in study group

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is believed that anaemia plays a major role in pathophysiology of sickle cell disease but it is not clear whether anaemia affects overall cell metabolism sufficient to result in growth retardation.

Pulmonary Function Test Parameters

Forced Vital Capacity (FVC): In the present study FVC was highly significantly reduced in study group when compared to controls. The reason for decrease in FVC was anthropometric differences in these patients. The thorax is not only short relative to body stature in this disease, but the lateral chest diameter is also narrower than that of healthy individuals.[8]

FVC is usually decreased more than FEV1% in restrictive lung disease. The restrictive pathology may be due to the following reason -

In the sickle cell disease population, mechanism of restriction would be ineffective inspiration due to chest wall pain related to peripheral vasoocclusion, prior rib infarctions, or vertebral disease.[9]

Forced expiratory volume in one second (FEV1): In the present study FEV1 was highly significantly reduced in study group when compared with controls. FEV1 was also decreased in studies by Koumbourli et al, Hulke et al, Williams K et al.[10] FEV1 is usually considered as the marker of both central and peripheral airway obstruction. In some studiest the obstructive pattern was accompanied by an increase in diffusing capacity and suggested that it might have been related to an increase in lung blood volume.Obstructive lung disease possibly precedes the development of restrictive lung disease and airway reactivity may be part of the pathogenic mechanism.

FEF25-75%: The present study shows highly significant decrease in mean FEF25-75% in study group. Koumbourlis et al[11] suggested that chronic inflammation initially affects the smaller airways. Long-standing inflammation causes lower airway obstruction in early phases, which might lead to fibrosis in later phases.

Maximum Voluntary Ventilation (MVV): Study had revealed highly significant reduction in MVV in study group. It is comparable with the finding noted by Young et al, S Hulke et al.[10]

The decrease in MVV can be explained on the basis of pathological finding suggestive of restrictive changes as demonstrated by decreased FVC and MVV, obstructive changes by decreased FEF 25-75%, PEFR and FEV1. Thus it provides an overall assessment of pulmonary compliance, pulmonary obstruction and restriction.

CONCLUSION

Thus the study concludes that the decline in all the pulmonary function tests parameters in study group is suggestive of both restrictive and obstructive changes in sickle cell disease, restrictive pattern been more common. The highly significant decline in MVV is suggestive of increased airway resistance and lowered lung compliance. Cause of the restrictive lung disease may be vasculopathy, repeated episodes of acute chest syndrome, airway hypersensitivity, haemolysis and organ dysfunction associated with sickle cell disease.

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