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Original Research Article

Pulmonary function profile of children with sickle cell disease

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ABSTRACT

Background: Lung disease is a major cause of morbidity and mortality in sickle cell disease (SCD). In view of severe anemia, decreased blood oxygen affinity, pulmonary arterial vaso-occlusion, microinfarction and microfibrosis being associated with sickle cell disease; an analysis of pulmonary function in them will be of great interest.
Methods: Seventy 6-12 years old children with SCD (SS pattern) were studied as cases along with age, sex and socioeconomic status matched 70 controls (AA pattern) and comparisons drawn between the two groups.
Results: All the static and dynamic pulmonary functions such as FVC, FEV_1, $MMEFR_{25-75\%}$, PEFR and MVV were found reduced in sickle cell disease, most of them significantly.
Conclusions: Any restrictive, obstructive or combined pattern may be produced in SCD depending upon frequency & severity of the acute chest syndrome and vaso-occlusive crises in past.

Keywords: Pulmonary function, sickle cell disease

INTRODUCTION

Sickle cell disease is the commonest heritable hematologic abnormality affecting humans.[1] The average incidence of sickle gene among Indians is approximately 4.3%.[2] The frequency is much higher (up to 45%) in many tribal population in India.[3] The prevalence of sickle cell disease is high in central India & certain localities of Maharashtra.[4]

Lung disease is a major cause of morbidity and mortality in sickle cell disease. Acute chest syndrome; which may be due to lung infection, infarction or fat embolism; affects nearly half of the patients.[5] Frequent exposure to hazardous environmental factors may facilitate repeated pulmonary infection and subsequent changes in anatomical characteristics of the lungs. In addition, previous episode of pulmonary embolism may lead to development of restrictive functional impairment. All of this will affect various respiratory functions of lungs.

In view of severe anemia, decreased blood oxygen affinity, pulmonary arterial vaso-occlusion, microinfarction and microfibrosis being associated with sickle cell disease; an analysis of pulmonary function in them will be of great interest.

METHODS

Study type: Hospital, out-patient based, prevalence study. Study setting: Sickle cell clinic and department of physiology, Indira Gandhi Government Medical College and Mayo Hospital, Nagpur, India. Study Duration: 2 years.

Selection criteria

Inclusion criteria

- Male children in the age group of 6-12 years, visiting the sickle cell clinics during study period,

- Those having Hb "SS" pattern (Cases) and "AA" pattern (Controls) on Hb electrophoresis.

Exclusion criteria

- Those with other causes of cardiac & pulmonary functional impairment which detoriates ventilation were excluded. E.g. CCF, Heart disease, valvular lesion, asthma etc,
- Obesity (BMI>25 kg/m2),
- The patients presenting in vaso-occlusive crisis,
- Refusal to give consent.

The study participants were divided into two groups: "Cases" and age, sex and socioeconomic status matched "Controls". Appropriate controls were recruited from a municipal corporation school in the vicinity of the study centre.

All the participants, after taking informed written consent, were subjected to detailed history taking, thorough physical examination and relevant investigations (Hemoglobin %, Sickling early/late, Hb electrophoresis and pulmonary function tests). This was supplemented by respiratory questionnaire designed by Fishman et al.[6] Pulmonary Function Tests (PFT) were performed using Medspirer- Recorder and Medicare System. FVC, FEV_1, FEV_1%, $MMEFR_{25-75}$%, PEFR and MVV were recorded.

Means and Standard Deviations were calculated while applying chi-square test using SPSS version 16 statistical software.

RESULTS

A total of 140 children (70 study group, 70 controls) were studied. The results have been analyzed in sub-groups of age 6, 7, 8, 9, 10, 11 and 12 years and comparisons drawn between study and control groups.

The children were distributed equally from 6 to 12 years of age (20 participants of each year; divided equally as 10 study and 10 controls). The cases had significantly less mean standing and sitting height than controls, except 12 years group, where the differences were insignificant. The study group children also had significantly lesser weight and body surface area than control group across age groups, except insignificant differences in 9 years age group. As for BMI, significantly low values were calculated for study age groups 7, 10, 12 years; while the differences, either way, were insignificant for other age groups.

As expected, the hemoglobin levels were significantly lesser among study groups across age groups. The resting chest circumference was significantly less in study group in the age groups of 7 and 9 years and insignificantly less in remaining age groups. The chest circumference in full inspiration also shows similar trend.

The observed pulmonary function test parameters are detailed in Table 1. The Forced Vital Capacity (FVC) was less in study group across ages than controls. The difference was statistically significant in 6, 10, 11 and 12 years age sub-groups and insignificant in 7, 8 and 9 years categories. The forced expiratory volume in one second (FEV1) was significantly lesser in study group across age categories, except 9 years sub-group, where the difference was not significant. The FEV_1% of the control group is within normal limit and is lower in study group than control group. The $MMEFR_{25-75}$% and PEFR of study group were consistently and significantly lower in study participants than controls across age categories. As for maximum voluntary ventilation, when compared with controls, the study group had significantly lower values in the age groups of 6, 8, 9, 10, 11 and 12 years and the difference was insignificant in 7 years age category.

DISCUSSION

With the present study we attempted to delineate pulmonary function parameters in patients with sickle cell disease vis-à-vis normal controls.

The standing and sitting height were lesser in sickle cell disease patients than controls. Weight was also lesser in study group. Study by Phebus et al showed the impairment in height and weight at all ages in both sexes.[7] Platt et al studied the influence of SS pattern on growth and development in 2115 patients in the age group 2-25 years.[8]

The patients were reported to be constitutionally smaller and sexually underdeveloped in both the sexes, with differences being more pronounced after 7 years of age. Both the studies postulated the chronic hypoxic state and poor nutrition. Body mass index (BMI) is a more valid indicator for obesity. Obesity is graded as I, II and III according to BMI.[9] (Normal <25 kg/m^2, Grade I Obesity- 25-29.9 kg/m^2, Grade II Obesity- 30-40 kg/m^2, Grade III Obesity >40 kg/m^2). Both study and control groups had BMI<20 kg/m^2. Obesity is known to affect pulmonary functions negatively.[10,11] Hence, we had excluded obesity during selection of participants. Chest circumference (resting as well as on full inspiration) was observed to be significantly lesser in sickle cell disease patients than controls. This may be due to small osteo-muscular stature of sickle cell individuals.

In the present study, FVC in children with sickle cell disease was observed to be significantly lesser than the normal subjects. This finding can be correlated with lower anthropomentric values and smaller thoraces in the study group. The findings of restrictive lung disease in adults with SCD are well described by Miller et al and Powars et al, but the reasons remained largely speculative.[12,13] Pianosi et al reported repated episodes of acute chest syndrome to be responsible for the development of restrictive lung disease.[14]

Table 1: Pulmonary function test (PFT) parameters in study and control group. (age wise sub-group analysis).

	Age						
Parameter	**6 years**	**7 years**	**8 years**	**9 years**	**10 years**	**11 years**	**12 years**
FVC							
Control	0.91± 0.11	0.88± 0.18	0.92± 0.20	1.23± 0.20	1.33± 0.12	1.41± 0.17	1.58± 0.16
Study	0.74± 0.10**	0.76± 0.17*	0.85± 0.08*	1.22± 0.31*	1.01± 0.14**	1.23± 0.17**	1.31± 0.22**
FEV_1							
Control	0.85± 0.22	0.82± 0.17	0.93± 0.22	1.13± 0.17	1.25± 0.13	1.37± 0.15	1.43± 0.14
Study	0.40± 0.09**	0.59± 0.11**	0.58± 0.18**	1.06± 0.29*	0.85± 0.09**	0.75± 0.19**	1.06± 0.21**
FEV_1%							
Control	82.36± 22.97	93.46± 7.84	98.23± 6.81	92.22±8. 40	94.07± 7.97	97.40± 3.35	91.50± 14.47
Study	53.89± 8.88**	80.51± 20.89*	68.40± 21.94**	80.66± 11.47**	82.79± 15.45*	61.78± 16.91**	83.71± 19.88*
$MMEFR_{25-75\%}$							
Control	1.57± 0.44	1.61± 0.42	1.80± 0.44	1.91± 0.52	1.94± 0.42	1.98± 0.21	2.16± 0.16
Study	0.77± 0.15**	0.93± 0.17**	0.99± 0.29**	1.11± 0.24**	1.33± 0.33**	0.97± 0.38**	1.60± 0.58**
PEFR							
Control	2.07± 0.24	2.18± 0.47	2.46± 0.63	2.63± 0.53	2.78± 0.37	3.17± 0.51	3.26± 0.48
Study	1.43± 0.17**	1.35± 0.25**	1.54± 0.45**	1.63± 0.21**	2.00± 0.32**	1.40± 0.30**	2.11± 0.51**
MVV							
Control	35.90±3.50	38.50± 5.72	45.80± 6.10	47.20± 8.70	49.10± 6.62	56.80± 5.26	57.80± 2.44
Study	27.60± 2.17**	34.30± 7.00*	32.50± 8.35**	37.60± 6.48**	36.10± 7.12**	38.10± 5.50**	43.80± 7.26**

Note: FVC- Forced Vital Capacity (Lit), FEV1- Forced Expiratory Volume in one second (Lit), FEV1%- Forced Expiratory Volume in one second expressed as percentage (%), MMEFR25-75%- Maximum Mid Expiratory Flow Rate (Lit/Sec), PEFR- Peak Expiratory Flow Rate (Lit/Sec), MVV- Maximum Voluntary Ventilation (Lit/Min) **- Significantly lower than control, *- Insignificantly lower than control.

The fact that the anthropometric abnormalities such as those observed in our study occurs early in life in children with SCD leads to believe that a small thorax and disparity between height and weight etc. are responsible for the reduced static and dynamic lung volumes.

FEV_1 is reported to be lower in SCD patients than normal children in our study; which is corroborative of the findings of Pianosi et al, Nair et al and Deshpande et al.[14-16] The FEV_1 % of the control group was within normal limit and is lower in study group. This finding of ours disagrees with most of the available literature.[14,17] It was further observed that FEV_1/FVC ratio, as an index of airway obstruction, was normal in all age groups. Thus, available literature appears to suggest that SCD does not affect the flow rates. In our study, those with decreased flow rates had repeated chest infections, which could the reason behind it. Thus, depending upon incidence of acute chest infections, there can be restrictive, obstructive or combined type of pathology in SCD.

The $MMEFR_{25-75\%}$ is considered to be representative of elastic recoil of the pulmonary parenchymal tissue and is considered to be effort dependent. The decreased $MMEFR_{25-75\%}$ observed in cases in our study means the amount of air expired per unit time is less than that of normal. It also reflects small airway obstruction. The plausible reason could be that, in sickle cell disease there is microfibrosis of the lung. If the elasticity as well as recoil of elastic tissue is decreased, then this will affect the pulmonary inflation and deflation and automatically the FVC, FEV_1 and $MMEFR_{25-75\%}$ will go down. Wall et al also observed lesser $MMEFR_{25-75\%}$ in SCD patients. Koumbourlis et al also showed, in the study of 20 infants, that there is significant difference in the $MMEFR_{25-75\%}$ in SCD patients and suggested existence of lower airway obstruction and hyperinflation, as discussed.[17]

We observed significantly lesser PEFR values in SCD patients as compared to controls. This is in agreement with findings of Bowen et al.[18] The theory being propagated is that, the repeated episodes of acute chest syndrome ultimately result in pulmonary fibrosis, which decreases lung compliance, which in turn decreases PEFR.[18]

Maximum voluntary ventilation (MVV), which is a combined indicator of compliance and airway resistance, was found to be lower in SCD.[19] MVV by definition is the volume of a gas that a subject can ventilate by voluntary effort per unit time breathing as quickly and as deeply as possible.[20] It provides overall assessment of efforts, co-ordination and elastic flow resistive properties of the respiratory system. Unfortunately, MVV has not been studied elaborately by researchers till now, as per available literature.

CONCLUSION

In conclusion, it may be noted that static and dynamic pulmonary functions such as FVC, FEV_1, $MMEFR_{25-75\%}$, PEFR and MVV are reduced in sickle cell disease. The FEV_1 may or may not reduce, depending upon the underlying pattern of pulmonary parenchymal disorder. Any restrictive, obstructive or combined pattern may be produced depending upon frequency and severity of the acute chest syndrome and vaso-occlusive crises in past. We recommend complete profile of pulmonary function test at definite time interval in sickle cell disease patients.

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