

Pulmonary Function in Nigerian Children and Young Adults with Sickle Cell Anaemia

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SUMMARY

Olanrewaju DM, Adekile AD and Ariwodola JO. Pulmonary Function in Nigerian Children and Young Adults with Sickle Cell Anaemia. *Nigerian Journal of Paediatrics* 1988;15:7. Pulmonary function on (FEV, FVC, PEFR) was evaluated in 105 HbSS patients aged 5-20 years and the same number of age and sex-matched haematologically-normal controls. The influence of age, sex, anthropometry, previous episodes of pneumonia and presence of digital clubbing on the pulmonary function was examined. The results showed that pulmonary function was significantly compromised among the patients when matched for sex and height with controls. The younger patients had better pulmonary function. Pulmonary function correlated well with anthropometric measurements, especially height, in both groups. The observed mean FVC value in patients who had had more than 3 previous episodes of pneumonia was 78.8% of the predicted value, while it was 83.5% in those without previous pneumonia. There is a need to prevent pneumonia as much as possible in SS in patients, if pulmonary function is not to be severely compromised.

Introduction

SEVERAL workers have reported ventilatory impairment in sickle cell anaemia (SCA) patients¹

. Bromberg and Jensen² documented reduced vital capacity and concluded that, in view of the tendency for pulmonary vascular obstruction to develop in SCA patients, it is conceivable that subtle parenchymal changes peculiar to the disease are responsible for the reduction in lung volumes, rather than the anaemia per se. Femi-Pearse, Gazioglu and Yu³ also came to a similar conclusion.

Miller and Serjeant found that the lung function and anthropometry (height, sitting height

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and chest circumference) of SCA patients differ from those of healthy subjects of African origin. They attributed the reduced total lung capacity and vital capacity found in these patients to the reduction in their thoracic size.

Most of the studies assessing pulmonary function in SCA were in adult patients. However, Wall, Platt and Strieder⁵ investigated pulmonary function in 12 children aged 7 to 13 years. They found lung volumes and expiratory flow to be comparable with those of a normal (HbAA) control group, except in a child who had had 3 episodes of pneumonia.

However, the abnormal carbon monoxide diffusing capacity and mild hypoxaemia described in adult patients were also documented in the children. They suggested that the defects seen in older patients appear to follow recurrent pulmonary thrombo-embolism and pneumonia and develop progressively with age.

The present study was designed to investigate pulmonary function, using vitalography (FEV^{*}, FVC) and peak expiratory flow rate (PEFR) in Nigerian children and young adults with SCA, and compare this with that in age and sex-matched haematologically normal controls. The second objective was to correlate pulmonary function with the clinical course of the disease.

Materials and Methods

Study Population

One hundred and five consecutive homozygous SCA patients (53 males and 52 females) attending the sickle cell clinic of the Obafemi Awolowo University Teaching Hospital, Ile-Ife, were studied. Their ages ranged from 5 to 20 years. The diagnosis of SCA was based on solubility studies, haemoglobin electrophoresis and screening.

Only patients in "steady state" i.e not in crisis or acutely ill for at least four weeks prior recruitment, were included in the study.

One hundred and five age and sex-matched

controls were selected from apparently healthy school children and young adults in the same community. They did not possess the HbS gene, as shown by a solubility screening test (*Sickledex*).

In both groups (patients and controls), any individual with a past or family history suggestive of chronic pulmonary disease such as asthma, were excluded from the study. Informed consent was obtained from their parents or guardians.

Anthropometric Measurements and Pulmonary Function Tests.

Weight (kg), height and sitting height (cm) and chest circumference (cm) were obtained, using standard techniques. The body surface area was computed from a standard nomogram from the values of the heights and weight.

The following pulmonary function tests were done: forced expiratory volume in one second (FEV₁) forced vital capacity (FVC) and peak expiratory flow rate (PEFR), using vitalography (*Vitalograph Ltd, Burkingham, England*) and a Wright Peak Flow Meter (*AIRMED, England*).

Indices of Clinical Course

The major index used to subgroup the patient population, with regard to their clinical course, was the number of previous episodes of pneumonia. This was determined by a review of the patients' records. A clinical or radiologic diagnosis was taken as evidence of pneumonia.

The other subgrouping index was the presence or absence of digital clubbing, which was graded clinically by at least two of the authors.

The data obtained were analyzed statistically with an IBM 5081 Computer, at the Computer Centre, Obafemi Awolowo University. Student's 't' test was used to determine statistical significance of the difference between the mean values within the different subgroups. Pearson's correlation coefficients were computed between each

parameter of pulmonary function and each of the variables and its subgroups where applicable. Predicted FEV₁, FVC and PEF_R values, using formulae obtained for normal Nigerian children⁶⁻⁷, were compared to the observed values for the purpose of assessing pulmonary function according to the number of previous episodes of pneumonia. Also, the mean FEV, FVC and PEF_R values of SCA patients with digital clubbing were compared to those of the patients without clubbing.

Results

Age and Sex Distribution

Table I shows the age and sex distribution of the patients and controls. Almost half of the total population were between the ages of 5 and 10 years, while about 90% were 15 years or below. There was no significant difference in the age and sex distribution of the patients and controls (p > 0.05).

Anthropometric Measurements

The mean values for weight, ratio of sitting height to height, chest circumference and body surface area were statistically higher (p < 0.01) in the control group.

Although higher among the controls, the difference between the mean values of height and sitting height in the two groups, were not statistically significant (p > 0.05).

Further analysis, according to sex, showed no significant difference between males and females in the patients population. However, weight and height mean values were significantly higher (p < 0.05) in the males than the females in the control group. It was also observed that the controls were significantly heavier at all age groups (p < 0.001).

Furthermore, the controls had significantly higher mean height values than the patients in the 16-20 years age group (p < 0.001), but there was no significant difference between the mean height values up to the age of 15 years. A similar pattern was observed in the mean values of the sitting in the patients and controls up to the age of 10 years, but after this age, the ratio became significantly lower i < n the patient (p < 0.001).

TABLE I

Age and Sex Distribution of Patients and Controls

Age (yrs)	Males				Females				Total			
	Patients		Controls		Patients		Controls		Patients		Controls	
	n	%	n	%	n	%	n	%	n	%	n	%
5-10	26	49	25	47	23	44	22	42	49	47	47	45
11-15	22	42	22	42	23	44	23	44	45	53	45	43
16-20	5	9	6	11	6	12	7	14	11	10	13	12
Total	53	100	53	100	52	100	52	100	52	100	105	100

Pulmonary Function Test Values

The mean FEV₁, FVC and PEFR values were significantly higher ($p < 0.001$) in the controls than in the patients (Table II). However, the mean FEV₁/FVC% in the two groups were comparable. There was no significant difference in pulmonary function test values between males and female patients, while control had significantly higher ($P < 0.01$) mean values of FEV₁ and FVC than their female counterparts.

Table III shows the mean values of FEV₁, FVC and PEFR subanalysed according to age groups. The values were significantly greater ($p < 0.01$) in the control at all age groups. This difference became progressively pronounced with age.

Further subclassification according to weight and sex showed no significant difference in the means values of FEV₁ and FVC in the patients and controls at similar weight in both sexes. However, the patients were matched for sex and height with the controls, the latter had significantly higher ($p < 0.05$) PEFR values than the patients at similar heights.

Correlation Coefficients

There was significant linear correlation between all the anthropometric measurements and the parameters of pulmonary function in the total study population (Table IV). The only exception was chest circumference which showed a poor correlation with FEV₁, among the patients. Height correlated best with pulmonary function indices in both groups. When subgrouped according to sex, the same trend was found as for the total population.

Influence of Pneumonia on Pulmonary Function

Table V shows a comparison of predicted and observed pulmonary function test values in patients without previous pneumonia and those with varying numbers of previous episodes (60 patients had no history of pneumonia, while 36 had one or two

episodes and nine had three or more). The former had significantly higher ($p < 0.05$) percentages of predicted FEV₁, FVC and PEFR values than those with three or more documented episodes. However, there was no significant difference in the percentages of predicted pulmonary function indices between those that have not had any episode and those that have had only one or two episodes of pneumonia, with the exception that those in the former group had significantly higher percentages of predicted PEFR.

Digital Clubbing and Pulmonary Function

All the 11 patients with digital clubbing in this study were below the age of 10 years. Their pulmonary function mean values were compared to those of the 38 patients within the same age group who did not have clubbing. The percentages of predicted FEV₁, FVC and PEFR were lower in those with clubbing, although the differences were not significant ($p < 0.05$).

Discussion

This study has confirmed previous reports of physical growth retardation in SCA patients^{8,9}. The mean weight values of the controls were significantly greater than the patients values at all age groups, but the mean height of the former was only greater than those of the patients in the 16-20 years group. The latter observation might be related to the late onset of puberty which has been described in SCA patients¹⁰.

The ratio of sitting height to height was higher in the controls especially in the age group 16-20 years. This is in keeping with the typical habitus in SCA, which is characterised by relatively long limbs; thus, the thorax is short, relative to body stature. This, combined with reduced chest diameter, may partly explain the reduction of lung volumes in SCA patients⁴.

The positive correlation between age and the parameters of pulmonary function observed in this study was not unexpected because the older the

TABLE II
FEV₁, FVC and PEFR values (total population and sex groups)

Parameter	Total	Patients		Total	Controls	
		Male	Female		Male	Female
FEV ₁ (litres)	1.35 ± 0.5	1.37 ± 2	1.33 ± 0.5	1.70 ± 0.7	1.77 ± 0.4	1.62 ± 0.3
FEC (litres)	1.50 ± 0.5	1.50 ± 0.2	1.49 ± 0.7	1.94 ± 0.7	2.00 ± 0.6	1.77 ± 0.5
FEV ₁ /FVC(%)	89.53 ± 5.4	90.20 ± 5.5	88.69 ± 5.3	88.69 ± 5.8	89.81 ± 5.5	88.54 ± 5.8
PEFR (liters/min)	256.69 ± 55.1	238.17 ± 50.5	232.98 ± 51.2	283.45 ± 81.3	283.29 ± 84.8	271.54 ± 76.9

Values are means ± SD

TABLE III
FEV₁, FVC and PEFR values according to Age Groups

Parameter	5-10 years		11-15 years		16-20 years	
	Patients	Controls	Patients	Control	Patients	Controls
FEV ₁ (litres)	1.04 ± 0.2	1.21 ± 0.2	1.58 ± 0.2	2.29 ± 0.7	2.29 ± 0.2	3.09 ± 0.6
FVC (litres)	1.26 ± 0.2	1.38 ± 0.2	1.74 ± 0.2	2.13 ± 0.2	2.47 ± 0.3	3.35 ± 0.7
PEFR (liters/min)	189.37 ± 17.9	212.40 ± 14.8	261.75 ± 17.2	301.20 ± 34.9	323.18 ± 28.3	439.38 ± 36.6

TABLE IV
 Person's correlation coefficients ('r' values) for the Total Population

Parameter	FEV ₁	Patients		Controls		
		FVC	PEFR	FEV ₁	FVC	PEFR
Age	0.59	0.98	0.98	0.94	0.95	0.93
Weight	0.60	0.79	0.88	0.88	0.85	0.94
Height	0.81	0.99	0.99	0.98	0.97	0.95
SH	0.61	0.98	0.98	0.95	0.96	0.95
CC	0.32*	0.70	0.70	0.96	0.97	0.95
BSA	0.80	0.89	0.90	0.96	0.95	0.95

* p < 0.001 except for this value

SH = Sitting Height CC = Chest Circumference BSA = Body Surface Area

TABLE V
 Observed: Predicted FEV₁, FVC and PEFR in Patients according to Frequency of Pneumonia

	Group I	Group II (0)* n = 60	Group III (1-2)* n = 36	(> 3)* n = 9
<u>FEV₁</u>				
Predicted		1.54	1.72	1.97
Observed		1.26	1.40	1.55
Observed/Predicted(%)		81.98	81.75	78.34
<u>FVC</u>				
Predicted		1.75	2.02	2.41
Observed		1.56	1.65	1.84
Observed/Predicted(%)		83.50	81.3	78.75
<u>PEFR</u>				
Predicted		304.33	282.25	342.35
Observed		260.38	231.95	272.34
Observed/Predicted(%)		85.56	82.98	79.55

* No. of episodes of pneumonia

subject, the greater the height and weight and the more the co-operation in the performance of the tests. There was also good correlation between the other anthropometric measurements and the parameters of pulmonary function. The observation that height correlated best with all the indices of pulmonary function (in patients and controls) is in keeping with that of previous workers^{6 10 11}

There was no significant difference in pulmonary function between male and female patients, while male controls performed better than their female counterparts. This probably indicates that sex is not a very important determinant of pulmonary function in SCA. The better performance of the male controls over their female counterparts is in keeping with the observation from other studies^{6 11 12}. Femi-Pearse, Gazioglu and Yu³ pointed out that anthropometric measurements alone cannot explain the difference in the lung volumes of normal male and female subjects. They stressed further that factors such as muscle strength, and the size and shape of the thoracic cage could play important roles in determining the values.

The observation that the younger SCA patients in this study had relatively better pulmonary function than the older patients suggests that the abnormalities in pulmonary function become more pronounced with age. They are likely to result from recurrent pulmonary insults, the commonest of which is pneumonia. Pneumonia was, therefore, used as the index of clinical course in the present study. Our result shows that pulmonary function of SCA patients is related to the frequency of pneumonia. Thus, the means of observed FEV₁, FVC and PEFR values were closer to the predicted values in the patients with few or no episodes of pneumonia. In patients with three or more episodes, the observed FVC value was only 78.8% of the predicted value, while it was 83.5% in those without previous pneumonia in those without previous pneumonia. Similarly, there was a significant difference between FVC values in those

who have had three or more episodes of pneumonia and those who have had only one or two. However, there was no significant difference between those that have had one or two episodes and those that have not had any.

Pneumonia in SCA patients, is more severe than in normal children and resolution is slow, the average duration of fever being 10 to 12 days, in spite of appropriate antibiotic therapy.¹ This slow resolution might be due to the regional hypoxia in the inflamed and consolidated lung, which might promote local sickling and vaso-occlusion, thus delaying resolution of the inflammation. Secondly, the access of antibiotics to the areas of inflammation might be compromised by the presence of subclinical pulmonary thrombi and infarcts. It therefore, follows that repeated pneumonias, in these patients, would lead to scarring, giving rise to a restricted defect of pulmonary function.

This may partly, explain the relatively better pulmonary function observed in the younger patients. This premise is supported by the findings of Platt and Strieder⁵

It is therefore, important to prevent pneumonia in SCA patients, as much as possible. One way of doing this is by routine pneumococcal vaccination, since this organism is responsible for most cases of pneumonia in SCA⁴. A polyvalent vaccine is now available against 14 of the more common serotypes of the organism and Amman, Addiego and Wara¹³ have shown that SCA patients respond to immunization with the vaccine, much like healthy controls.

Digital clubbing is an occasional finding in SCA, the significance of which is still unknown. Konotey-Ahulu⁸ reported a prevalence of 13% among his SCA patients in Ghana, while Adekile, Isangedighi and Ariwodola¹⁴ reported a figure of 12.4 among their patients in Nigeria. In the present study, 10.5% of the patients presented with clubbing. Preliminary studies²¹ have shown that the mean arterial oxygen saturation among SCA

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patients with clubbing is significantly lower than in those without¹⁴. This is why the pulmonary function of the patients with clubbing in the present study was compared to that of their counterparts without. This latter had higher mean FEV₁, FVC and PEFR values than the former, although the difference were not stastically significant. This issue deserves further investigation.

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