

Ventilatory function in young adult Nigerians with sickle cell anaemia

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Abstract

Sickle cell disease is an important genetic disorder among Africans, and results in abnormalities of the haemoglobin molecules. The inflammation that occurs in the disease is now believed to be responsible for chronic complications in affected patients. Abnormal lung function is one such complication that can occur in all age groups. The observational case-control study objective was to determine the pattern of ventilatory function among adult Nigerians with sickle cell anaemia. The anthropometric data and ventilatory function indices of 57 consenting sickle cell anaemia patients were compared with those of 60 age- and sex-matched healthy control patients as well as values obtained from predicted equations for healthy adult Nigerians. It was observed that although the age and sex in the sickle cell anaemia patients and controls were similar, the sickle cell anaemia patients were of smaller stature; also the observed forced vital capacity and expiratory volume in 1 s, and peak expiratory flow rate were significantly smaller in these patients than in the healthy controls. The mean forced expiratory volume percentage was, however, similar in both sickle cell anaemia patients and controls. Ten (17.5%) of the patients had obstructive ventilatory defects. The results showed that the sickle cell anaemia patients had reduced ventilatory function (mostly due to restrictive defects) compared to the controls that this may be related to their smaller stature.

Introduction

Sickle cell disease (SCD) is one of the commonest genetic disorders of haemoglobin molecules affecting people of African descent.¹ The homozygous state referred to as sickle cell anaemia (SCA) is the commonest form, with a prevalence rate of 2% in Nigeria.²

Recent findings have revealed that chronic inflammatory processes occurring in these patients may account for chronic complications seen in this disease.³ Abnormality

of lung function is one such chronic complication that can occur in all age groups.⁴⁻⁶ The chronic lung abnormalities in SCA are usually collectively referred to as sickle cell chronic lung disease (SCCLD). The early stages of SCCLD are usually asymptomatic.⁷ New therapies⁸ that are now available to ameliorate the natural history of SCA, can be used in asymptomatic stages of SCCLD to prevent further progression to symptomatic stages. This is very important because the well-established symptomatic stages can only be treated symptomatically. Pulmonary function tests are important in detecting the early stages of SCCLD so that appropriate measures can be taken to prevent their progression to symptomatic stages. Ventilatory function tests are among the very important parameters that can be used to assess the pulmonary function in order to detect early SCCLD.^{5,6,9} Sometimes there may be obstructive lung dysfunction initially⁵ but restrictive lung disease usually develops later.⁹

This paper is designed to study the ventilatory function of SCA patients in comparison with that of healthy controls.

Materials and methods

Fifty-seven (30 male and 27 female) patients with haemoglobin genotype SS and 60 (37 male and 23 female) normal subjects with haemoglobin genotype AA were studied. The sickle cell patients were consenting patients selected by ballot from the adult Sickle Cell Clinic of the University of Ilorin Teaching Hospital in the north-central region of Nigeria. The healthy controls were consenting age- and sex-matched medical students and hospital health workers. The ages of the patients ranged from 18 to 32 years and those of the controls from 17 to 30 years. The controls were all lifelong non-smokers with no clinical evidence of cardiopulmonary disease and normal chest radiographs. The patients were also lifelong non-smokers with no clinical or radiological evidence of pulmonary tuberculosis or asthma.

The ethical clearance for the study was obtained from the ethical committee of the University of Ilorin Teaching Hospital.

Diagnosis of sickle cell anaemia

Sickle cell anaemia was diagnosed by performing haemoglobin electrophoresis (using cellulose acetate strips) on venous blood samples collected from the patients as described by the International Committee for Standardization in Haematology.¹⁰ The healthy controls also had haemoglobin electrophoresis performed on their venous

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blood samples. The anthropometric and ventilatory measurements were performed by AEF. The height (in centimetres) was measured without shoes, and weight (in kilograms) was measured in light clothing.

The forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV₁) were measured in litres at BTPS (body temperature, (ambient) pressure, saturated (with water vapour)) with a computerised spirometer (Spirolite®) and the forced expiratory ratio (FEV%) was calculated from these values. Peak expiratory flow rate (PEFR) in litres/min was measured with a Wright's peak flow meter at ATPS (ambient temperature and pressure, saturated (with water vapour)). The techniques for the test were explained and demonstrated to subjects. All the ventilatory tests were done in the sitting position. The reproducibility of the ventilatory testing was determined using the American Thoracic Society criteria (largest FVC within 0.2 L of the next one and largest FEV₁ within 0.2 L of the next one).¹¹ The best of three trials was recorded. The predicted FVC and FEV₁ values were obtained using the prediction equations of Patrick and Femi-Pearse,¹² while the predicted PEFR values were obtained from prediction equations of Elebute and Femi-Pearse.¹³

Statistical analysis

This was carried out with an IBM equivalent computer using version 10.0 of the SPSS programme. The numerical quantitative variables were expressed as mean $\pm$ SD while the categorical variables were expressed as percentages. The means of all numerical variables were compared using analysis of variance; $p \leq 0.05$ was taken as significant.

Results

Table 1 shows a summary of the anthropometric characteristics of the subjects. The mean age in both groups was similar. However, the mean height and weight of the sickle cell patients were significantly less ($p < 0.001$) than those of the healthy controls. Further analysis revealed that there were no significant differences ($p > 0.05$) in the mean height and weight between male and female sickle cell patients, whereas the values obtained in the male controls were significantly higher ($p < 0.05$) than

those in the female.

The percentage age distribution of the sickle cell patients revealed that 46 (81%) of them were in the 18–24 year age group, 11 (19%) in the 25–34 year group, and none in the older age group.

The observed FVC and FEV₁ in the sickle cell subjects were significantly lower ($p < 0.001$) in both sexes than the predicted values and those obtained from the healthy controls, as highlighted by Figure 1. Likewise, Figure 2 shows that the mean values of PEFR in the sickle cell patients were significantly lower ($p < 0.001$ in males and $p < 0.05$ in females) than values predicted by equations and observed values in the controls. Quantitatively, the observed FVC, FEV₁, and PEFR were lower in the male sickle cell patients than the values observed in the male controls by 1430 mL, 1200 mL, and 114.46 L/min respectively, while the differences between these parameters in the female sickle cell patients and female controls were 380 mL, 400 mL and 28.02 L/min respectively. These differences were all large enough to be clinically significant (except for the PEFR in females). The mean FEV% was above 80% in all age groups and the differences observed

Figure 1 Comparison of mean FVC and FEV₁ in male and female sickle cell patients with predicted values (Nigerian equations) and with observed values from controls

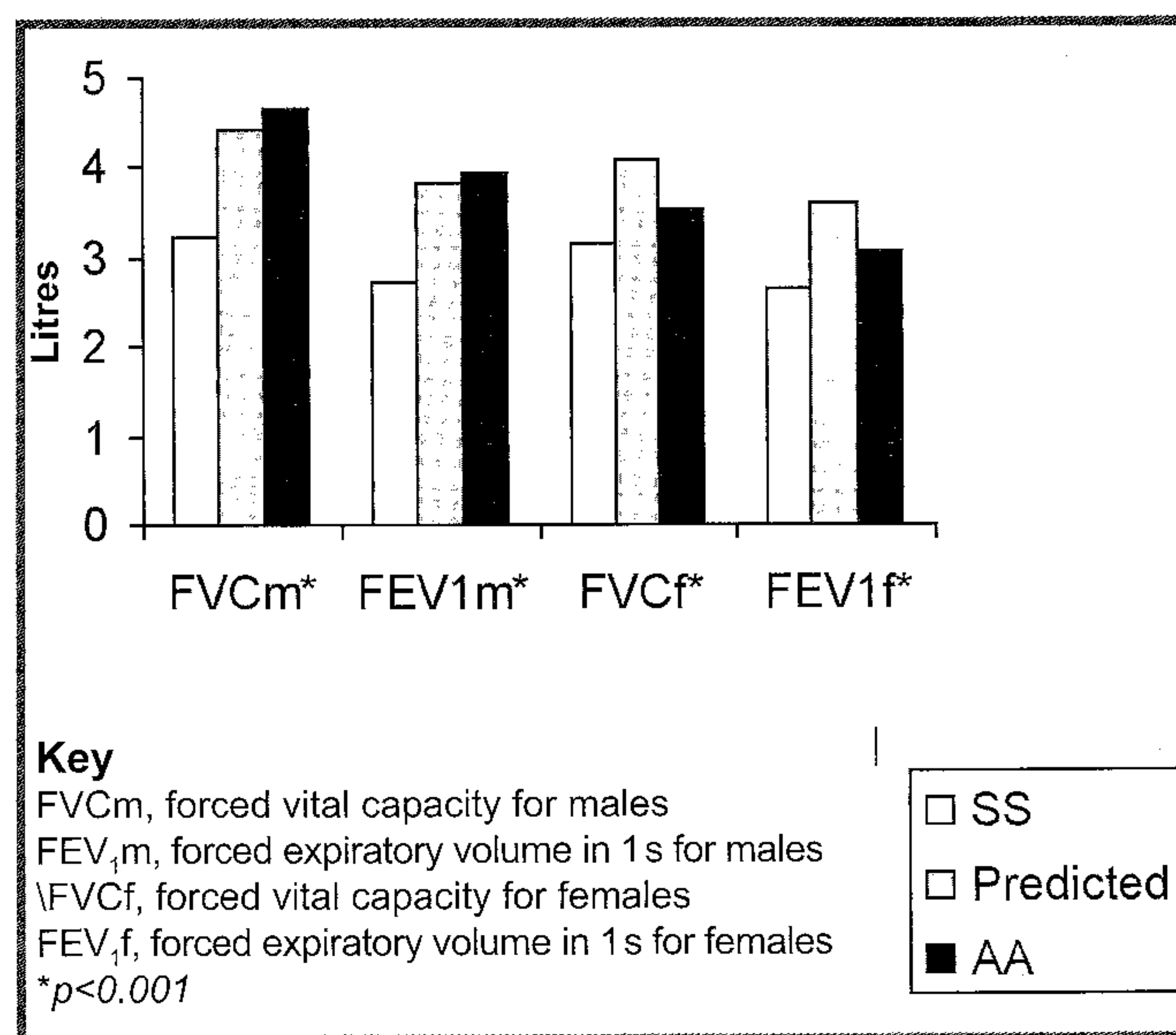
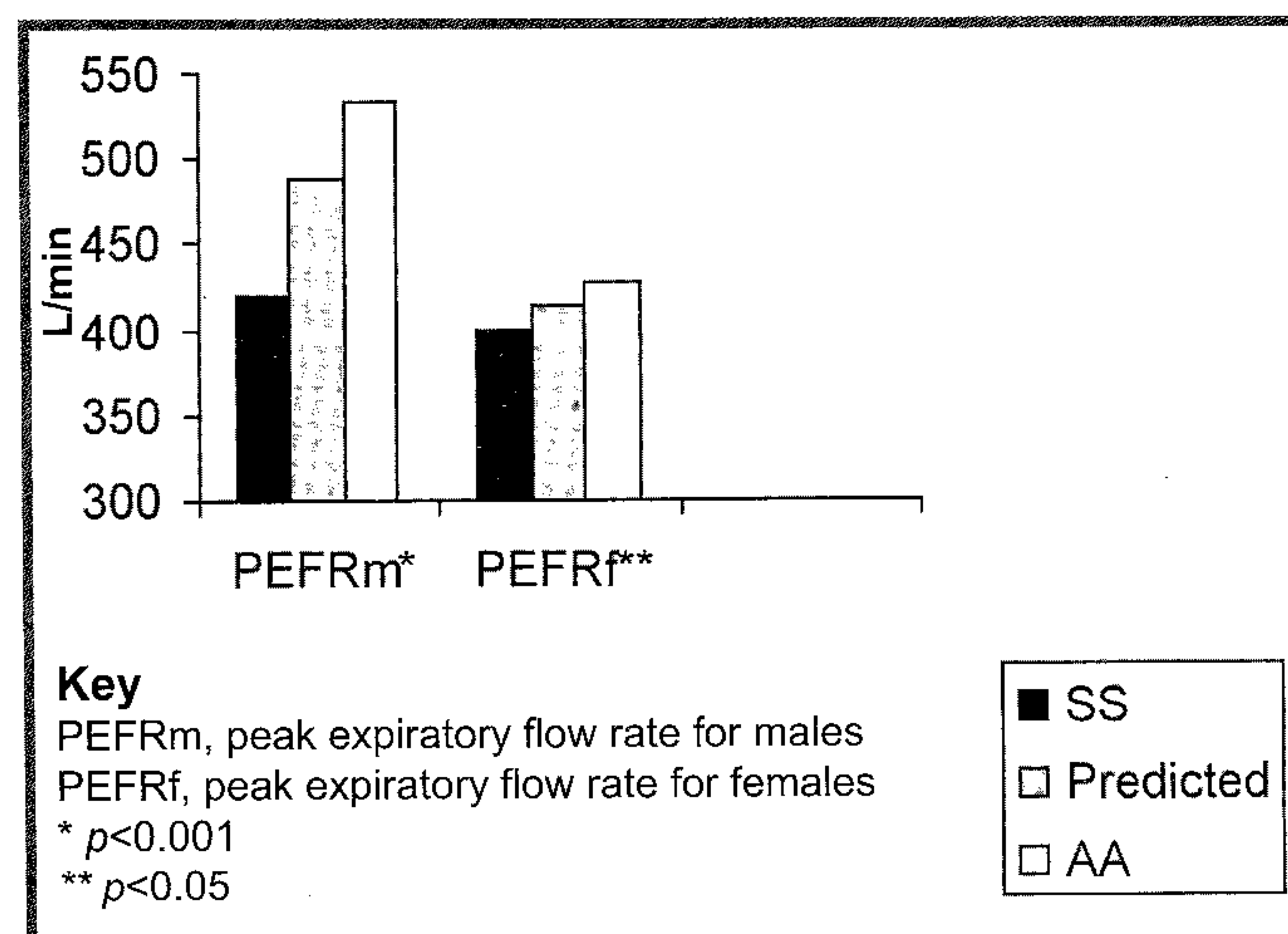


Table 1 Anthropometric characteristics of the subjects

Parameters	SS				AA				p value
	No.	Mean	SD	Range	No.	Mean	SD	Range	
Age (years)	57	22.6	3.23	18–32	60	23.5	3.18	17–30	NS
Height (cm)	57	163.0	6.97	147–181	60	170.1	5.81	158–188	<0.001
Weight (kg)	57	50.7	5.65	35.8–62.1	60	61.9	9.16	45.0–95.6	<0.001

Key: SS, sickle cell patients; AA, control subjects; SD, standard deviation; NS = not significant.

Figure 2 Comparison of mean PEFR in male and female sickle cell patients with values predicted (Nigerian equations) and observed from controls



between them were not statistically significant ($p > 0.05$). However, ten (17.5%) of the patients (five males and five females) had an FEV% that was less than 80% with the lowest being 58.6% in one of the females, whereas none of the controls had values less than 80%.

No significant differences ($p > 0.05$) were noticed in FVC, FEV₁, and PEFR observed in the male and female sickle cell patients. However, in the controls the values in the males were significantly higher ($p < 0.01$ for FVC and PEFR, $p < 0.001$ for FEV₁) than in the females (see Table 2). In absolute terms, the lung function parameters were just marginally lower (clinically insignificant) in the female sickle cell patients than their male counterparts (difference of 80 mL for FVC, 80 mL for FEV₁ and 29.59 L/min for PEFR), unlike the clinically significant difference in lung function between male and female controls (difference of 1130 mL for FVC, 880 mL for FEV₁ and 106.01 L/min for PEFR).

Discussion

It was observed in this study that although the mean age of the sickle cell patients was similar to those of the controls, the patients were smaller in stature – as shown by their lighter weight and shorter height. This is a confirmation of earlier findings.^{9,14} However, there were no significant differences in the stature of male and female sickle cell patients. The observation that most of the SCA patients were in the 18–24 year age group is similar to results of a previous national survey by the Federal Ministry of Health in Nigeria.¹⁶ This finding suggests a reduced survival beyond early adulthood.

Observed FVC, FEV₁, and PEFR in the sickle cell patients were statistically and clinically lower than the values obtained from predicted equations and those in the healthy controls. This is in keeping with observation from earlier studies.^{13,16} The disparities may be due to differences in stature as documented by this report and noted by earlier studies.^{9,13,16} Other factors that may account for the lower lung function in the SCA patients include repeated acute chest syndrome as documented by Powars et al,⁹ sickle cell related vasculopathy as reported by Faller,¹⁷ and chronic oxygen desaturation with or without sleep hypoventilation as noted by Samuels et al.¹⁸

The reduced mean FVC and FEV₁ values together with observation of a normal FEV% suggested a restrictive defect of pulmonary function in the sickle cell patients. This is similar to observations by Powar et al.⁹ Despite the restrictive ventilatory defect suggested by the mean values of the lung parameters, it was observed that 17.5% of the sickle cell patients had results consistent with obstructive defect. This proportion of patients with obstructive defect in this study is lower than that reported by Koumbourlis and co-workers.⁵ This may be because they measured respiratory resistance directly, unlike this study which relied on the FEV%. The reasons for the restrictive defect may be related to the predisposition

Table 2 Comparison of ventilatory function among the sickle cell patients and the controls by sex

	Sickle cell patients										Controls									
	Males					Females					Males					Females				
	No.	Mean	SD	Range		No.	Mean	SD	Range	p value	No.	Mean	SD	Range		No.	Mean	SD	Range	p value
FVC (L)	30	3.22	0.36	2.50–4.60		27	3.14	0.6	1.76–4.71	NS	37	4.65	0.66	2.75–6.53		23	3.52	0.39	2.50–3.86	<0.01
FEV ₁ (L)	30	2.7	0.5	1.98–4.11		27	2.66	0.54	1.45–3.60	NS	37	3.94	0.50	2.58–4.86		23	3.06	0.36	2.24–3.86	<0.001
PEFR (L/min)	30	419.27	74.26	258–550		27	399.68	64.40	275–598	NS	37	533.73	68.04	400–680		23	427.71	33.06	330–480	<0.01

Key: FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 second; PEFR, peak expiratory flow rate; SD, standard deviation; NS = not significant.

to recurrent acute chest syndrome.⁹

Despite the ventilatory defect demonstrated in these patients, all of them had chest radiographs that were reported as normal by two consultant radiologists at different times. This may be because the patients were in the early asymptomatic stages. Powars et al⁹ noted that chest radiograph findings in the early stages are often interpreted as normal because the interstitial changes may be so subtle that they can be missed.

Although the lung function indices were lower in females than males among the sickle cell patients, the differences were not statistically or clinically significant. This is contrary to previous observation by Miller et al.¹⁹ The exact reason for this is not known. It may be related to the lack of significant differences in stature between male and female sickle cell patients. It is also possible that the disease was more severe in the patients in this study, thereby overshadowing the effect of normal variation between males and females.

In conclusion, this study has revealed that young adult Nigerians with sickle cell anaemia have lower ventilatory function (predominantly restrictive type) compared with healthy subjects and this is probably due to their smaller stature.

Learning points

1. The ventilatory function of the sickle cell patients was lower than that of healthy subjects and the difference was both statistically and clinically significant.
2. The predominant ventilatory defect in the sickle cell patients was a restrictive defect.
3. The ventilatory defect in the sickle cell patients was not associated with any appreciable radiological defect.
4. There was no significant (statistical or clinical) difference in lung function between male and female sickle cell patients.

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