A Study of Pulmonary Function Tests in Sickle Cell Anaemia Patients in Raipur District, Chhattisgarh, India.

Karishma Singh*.

Department of Physiology, Pt. J.N.M. Medical College, Raipur 492001, Chhattisgarh, India.

ABSTRACT

The inherited disorders of haemoglobin are the commonest single gene disorder of the world population. Sickle cell anaemia being the most widespread and numerically the most important haemoglobinopathy in the world today The major features of sickle cell disease (SCD) in most patients are life-long anaemia and the consequences of recurrent vaso-occlusion. Many complications of SCD involve anaemia, vaso-occlusion etc. Impairment of pulmonary function is a common complication of SCD. The patients suffering from this disease frequently present with complaints referable to the pulmonary system although other systems are also involved. Hence present study was carried out to evaluate the pulmonary function tests in sickle cell disease patients (HbSS),sickle cell trait patients(Hb AS) with normal person (HbAA) non-sicklers.1) To study the pulmonary alterations in cases of homozygous SS & heterozygous AS Sickle Cell Disorder subjects.2) To compare the parameters with normal healthy controls & assess the importance of PFT in "Steady State"(free from complications or crisis)as an objective evidence to predict the risk of "Sickle Cell Chronic Lung Disease'' in future. A cross sectional study was done in 50 cases of SCD (22HbSS& 28HbAS) and age and sex matched normal 50 HbAA controls. From the various measured pulmonary function test(PFT)parameters Forced Vital Capacity(FVC),Forced Expiratory Volume in 1 sec(FEV1),FEV1/FVC, Forced Mid Expiratory Flow(FEF25%-75%) were selected for the study. The data collected was subjected to statistical analysis involving computation of Mean, Standard deviation, Independent T test. Mean value of FVC, FEV1, FEV1/FVC and FEF25%-75% were found to be significantly lower than normal controls, but the difference in FVC between HbAS and HbSS turned out to be statistically non-significant whereas the difference in FEV1, FEV1/FVC,FEF25%-75% between HbAS and HbSS was statistically significant. There were significant reductions in pulmonary function test parameters in sickle cell anaemia patients as compared to normal controls indicative of mixed pattern (both restrictive and obstructive) lung impairment in sickle cell anaemia.

Keywords: Pulmonary Function Test, Sickle Cell Trait, Sickle Cell Disease, Forced Vital Capacity, Forced Expiratory Volume in 1 sec, Forced Expiratory Volume Ratio, Forced Mid Expiratory Flow.

*Corresponding author

INTRODUCTION

Sickle cell anaemia is an uncompensated haemolytic anaemia in which a markedly shortened overall RBC survival is insufficiently balanced by increased erythropoiesis to maintain the normal levels of total RBCs and Hemoglobin concentration. It is most widespread and important haemoglobinopathy in the world today. The sickle cell gene was described in India in the tribal population in the south[1] but further reports indicated the high prevalence among many districts of Orissa, Chhattisgarh, Madhya Pradesh, Maharashtra and not only affecting the tribal but also non-tribal & many other backward castes [2].Chhattisgarh has the largest tribal population in the country and it lies in the sickle cell belt.

The sickle cell mutation results from a single nucleotide change GAG->GTG in the 6th codon of exon 1 of beta globin chain[3].Consequently, the normal Glutamic acid of beta 6 is replaced by Valine, thus leading to the formation of sickle Hb (HbS) causing a complex disease involving multiple organs. The inheritance of SCD obeys the principle of Mendelian inheritance[4].When one parent is heterozygous for the sickle cell gene & other is normal, the offspring would have an equal chance of having either sickle cell trait AS or a normal AA genotype. If both have AS there is a 1 in 2 chance of offspring having AS& 1in 4 chance of having normalAA or SCD SS.

The clinical course of SCD is punctuated by complications or crisis. Impairment of pulmonary function characterized by airway obstruction, restrictive lung disease, abnormal diffusion capacity & hypoxaemia [5] is a common complication of SCD. Hence the present study was undertaken to evaluate the PFT in cases of SCA visiting PT.JNM MEDICAL COLLEGE and DR BRAM HOSPITAL, RAIPUR, CHHATTISGARH for investigations.

MATERIAL AND METHODS

After taking ethical clearance from scientific committee of Pt.J.N.M Medical College, Raipur, Chhattisgarh, the present cross-sectional study was conducted in the Dept. of PHYSIOLOGY & CENTRE FOR GENETIC DISEASE & MOLECULAR BIOLOGY in the Dept. of BIOCHEMISTRY at Pt.J.N.M.MEDICAL COLLEGE, RAIPUR, C.G from 2004-2006. A total of 50 cases of SCD (22 HbSS& 28 HbAS) from 10-60 years of age were selected.

Inclusion Criteria

- All the subjects were non-smokers and none had received blood transfusions within the past 3 months.
- Normal healthy non-sicklers were selected as controls.
- Consent to participate in the study.

Exclusion Criteria

- Subjects with history of malignancy, pulmonary   Tuberculosis, Diabetes. Mellitus, Hypertension, chronic lung disease, acute chest syndrome and respiratory infection 2weeks prior to spirometry were excluded from the study.
- Patients with Hb<8gm/dl were not included in study because of compensated anaemia.
- Smokers

Sickling Test

The subjects were evaluated for sickling by Sickling Test (Sodium Meta bisulphide Slide Test) & positive results were confirmed for trait AS or disease SS by Cellulose Acetate(Hb)Electrophoresis.

Subjects were divided into 3 groups.

Group A

Homozygous (HbSS) sickle cell disease- Included   22 patients

Group B

 Heterozygous (HbAS)-sickle cell trait – Included   28 patients

Group C

Normal Controls (HbAA)-Included 50 subjects of matched age and sex group.

Spirometry (Lung Function Test)

Detail clinical history of the subjects was taken. After taking informed consent, PFT (spirometry) was performed using computerized Spirometer HELIOS-501(RMS, Chandigarh, INDIA).All the tests were done at the same time of the day to avoid diurnal variation without any tight clothing which substantially restricts full chest and abdominal expansion. The whole procedure was explained and demonstrated to the subjects then spirometry performed. They were allowed to do enough practice, as lung volume depends on subject making a maximal voluntary effort. The subject was made to sit holding the electronic spirometer in front with the mouth piece of Spirometer at the level of his lips. The nostrils were closed with nose clip. The subject was then asked to take maximum deepest possible inspiration and hold it, and then close lips around the mouth piece so as to avoid escape of any air and expire forcefully and as fast and long as much as possible into the mouth piece. By doing this value of FVC and its components were obtained. The Lung function test parameters were interpreted according to guidelines for measurement of respiratory function of American Thoracic Society and the Association of Respiratory Technicians and Physiologists. Gas volumes and flow were corrected to Body Temperature and Pressure Standards (BTPS) automatically by the instrument.50subjects were comparedwith50 normal controls of matched age and sex groups. Height &weight were also measured.

Statistical analysis

The result were expressed mean ± standard deviation and Independent Sample T test as was applied to calculate the level of significance. A p-value of 0.05 or less was considered
Statistically significant

RESULT

Following observations were made from the study of PFT in 50 normal controls, 28 HbAS and 22 HbSS cases.

In HbAA group-Maximum number of subjects were in the age group 20-49 years in both the sexes.
In HbAS group- Maximum number of cases were in the age group 20-49 years in both sexes.
In HbSS group- Maximum number of cases were in the age group 20-29 years in both sexes.

Comparison of FVC in litres among different study groups is shown in Table 1. The mean FVC in litres in the normal controls (3.32±.69)was found to be greater than HbAS cases (2.93±.91)&HbSS cases (2.82±.84),which is statistically significant(p<.05)but the difference in FVC between HbAS&HbSS turned out to be statistically non-significant(p>.05)

Comparison of FEV1 (litres) in 1st sec. among different study groups is shown in Table 2. The mean FEV1 in litres in 1sec in normal controls (2.78±.59)was greater than AS (2.05±.82)&SS(1.49±.62)which is statistically significant(p<.05)& the difference in FEV1between AS & SS is also statistically significant(p<.05).

Comparison of FEV1/FVC in % among different study groups is shown in Table 3.The mean FEV1/FVC in% in normal controls (83.84±4.45)was greater than HbAS(72.86±22.17)&HbSS(56.68±23.41) this is statistically significant(p<.05)& the difference in FEV1/FVC between HbAS&HbSS also turned out to be statistically significant(p<.05)

Comparison of FEF 25%-75% in litres/sec among different study groups is shown in Table 4. The mean FEF25%-75% in litres/sec in normal controls(3.13±0.80)was found to be greater than HbAS cases (2.48±1.04)&HbSS cases (1.66±0.73),which is statistically significant($p<.05$)and the difference in FEF25%-75% between AS & SS is also statistically significant($p<.05$).
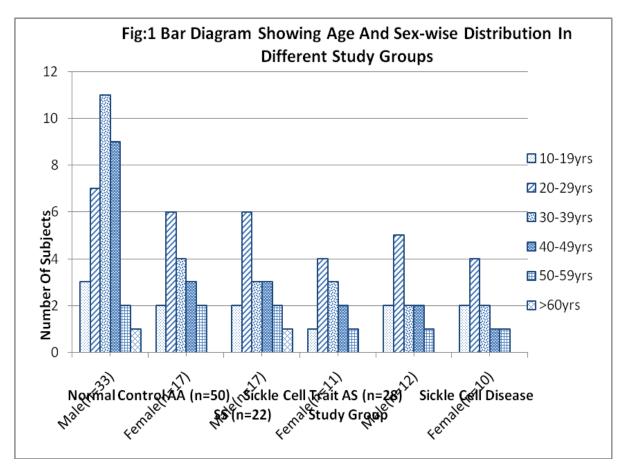

Fig:1 Bar Diagram Showing Age And Sex-wise Distribution In Different Study Groups

Table 1: Comparison of FVC in litres among different study groups

Category	Mean ±SD	t Value
Normal Controls(n=50)	3.32±0.69	
Sickle Cell Traits(n=28)	2.93±0.91	1.96($p<0.05$)
Normal Controls(n=50)	3.32±0.69	
Sickle Cell Disease(n=22)	2.82±0.84	2.47($p<0.05$)
Sickle Cell Trait(n=28)	2.93±0.91	
Sickle Cell Disease(n=22)	2.82±0.84	0.46($p>0.05$)

Table 2: Comparison of FEV1(litres)in 1st sec. among different study groups

Category	Mean ±SD	t Value
Normal Controls(n=50)	2.78±0.59	4.11($P<0.05$)
Sickle Cell Traits(n=28)	2.05±0.82	
Normal Controls(n=50)	2.78±0.59	8.24($P<0.05$)
Sickle Cell Disease(n=22)	1.49±0.62	
Sickle Cell Trait(n=28)	2.05±0.82	2.75($P<0.05$)
Sickle Cell Disease(n=22)	1.49±0.62	

Table 3: Comparison of FEV1/FVC in % among different study groups

Category	Mean ±SD	t Value
Normal Controls(n=50)	83.84±4.45	
Sickle Cell Traits(n=28)	72.86±22.17	2.59(P<0.05)
Normal Controls(n=50)	83.84±4.45	
Sickle Cell Disease(n=22)	56.68±23.41	5.40(P<0.05)
Sickle Cell Trait(n=28)	72.86±22.17	
Sickle Cell Disease(n=22)	56.68±23.41	2.48(P<0.05)

Table 4: Comparison of FEF 25%-75% in litres/sec among different study groups

Category	Mean ±SD	t Value
Normal Controls(n=50)	3.13±0.80	2.87(P<0.05)
Sickle Cell Traits(n=28)	2.48±1.04	
Normal Controls(n=50)	3.13±0.80	7.64(P<0.05)
Sickle Cell Disease(n=22)	1.66±0.73	
Sickle Cell Trait(n=28)	2.48±1.04	3.28(P<0.05)
Sickle Cell Disease(n=22)	1.66±0.73	

DISCUSSION

In Medicine, outcome which is the end result of a disease, is measured in terms of morbidity and mortality. Chhattisgarh lies in the sickling belt. It has the largest tribal population in the country& SCD is very common in the tribal & non-tribal population[6].The lung is among the major organ involved in SCD [5,7]&pulmonary manifestations are the leading cause of morbidity and mortality in patients with SCD[8,9].

The present study is an attempt to study PFT (FVC, FEV1, FEV1/FVC% and FEF25%-75%) to assess the importance of spirometry to detect abnormalities in lung function tests of sickle cell disorder patients. Sickle Cell Trait (n=28) were found to be more common than Sickle Cell Disease (n=22).This is consistent with BEET, LEHMAN [3] who in their studies recorded the higher frequency of SCT as compared to SCD. This might be due to death of SCD patients before the age of sample population. FEMI-PEARSE et al[10]reported decreased vital capacity in patients with SCD but no airway obstruction. In this study FVC, FEV1 and FEF25%-75% were reduced in SCD patients especially after the age of 20 years. This can be due to changes in lung compliance developed after repeated infections& embolic episodes. MILLER& SERJEANT [11] observed significant reduction in FEV1&FVC of SCD patients as compared to normal predicted values. This is comparable to the study conducted by PIANOSI et al[12]& the present study .POWARS et al[5] reported 28 cases of Sickle Cell Chronic Lung Disease with progressive deterioration of pulmonary functions in each stage of SCCLD.SCCLD is a prime contributor to mortality in young adult patients with SCD.

In present study, there was a progressive decrease in FVC, FEV1 with advancing age (after 20 years) in both sexes of SCD patients. This is comparable to the study done by PLATT et al[8], MILLER&SERJEANT[11],PIANOSI et al[12]and BOWENet al[13]. PIANOSI et al[12] observed either a restrictive or an obstructive pattern of PFTS in a small group of children with SCD.They used FEF 25%-75% as an indicator of small airway obstruction. This is comparable with the present study and the study conducted by KOUMBOURLIS AC et al[14].

CONCLUSION

In the different study groups, mean values of FVC, FEV1, FEF25%-75% and FEV1/FVC were highest in normal controls then followed by SCT &SCD groups. The mean difference was found to be statistically significant p<0.05 among all the study groups except for FVC where the difference between SCT & SCD cases were found to be statistically insignificant p>0.05. By this study it is concluded that sicklers show a significant reduction in PFT values compared to non sicklers indicative of both obstructive and restrictive pattern of lung diseases. In obstructive pulmonary disorder, the hallmark is reduction in FEV1, FEV1/FVC% and FEF25%-75%.Also,in restrictive impairment ,hallmark is reduction in FVC so it is mixed pulmonary impairment in sickle

cell anaemia. These results have implications for the timing of commencement of treatment aimed at reducing chronic pulmonary morbidity in patients with SCD.

REFERENCES

[1]   Lehman H, Cutbush MC. Br Med J 1952; i:404-5
[2]   Kar BC, Devis, Dash KC, Das M. Trans Roy Soc Trop Med Hyg 1987; 81:273-75.
[3]   Ingram VM. Nature 1957; 180:326-328.
[4]   Huck JG. John Hopk Hosp Bull 1923; 34:335-44.
[5]   Powars D, Weidman JA, et al. Med 1988;67:66-76.
[6]   Ghatge SG, Pradhan PK, Agrawals. Ind J Med Res 1977; 66:260-264.
[7]   Houpt HM, Moore GW, Bauer TW, et al. Chest 1982; 81:332-337.
[8]   Platt OS , Brambilla DJ, Rosse WF, et al. N Engl J Med 1994; 330: 1639-44.
[9]   Thomas AN, Serjeant GR. BMJ 1982; 285:633-635.
[10]   Femi-Pearse, et al. J Appl Physiol 1970; 28:574-77.
[11]   Miller GJ, Serjeant GR. Thorax 1971; 26:309-15.
[12]   PianosiP, et al. J Pediatric 1993; 122:366-71.
[13]   Bowen EF, et al. Arch Dis Child 1990; 65:330-32.
[14]   Koumbourlis AC, Zar HJ et al. Pediatric 2001; 138:188-92.