AN EVALUATION OF DYNAMIC PULMONARY FUNCTION TESTS IN SICKLE CELL ANAEMIA IN RAIPUR DISTRICT, CHHATTISGARH

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Abstract: **Background and Objectives:** Sickle cell anaemia is a life-long haematological disorder characterized by red blood cells that assume an abnormal, rigid, sickle shape. It is the most widespread and numerically the most important haemoglobinopathy in the world today. The sickle cell disease (SCD) is commonest monogenic disorder in India, affects all the major organs of the body.Impairment of pulmonary function is a common complication of SCD. Hypoxaemia is the hallmark of pulmonary abnormality in SCD patients of all age groups and is said to result from the combined effects of perfusion and diffusion defect. Hence present study was carried out to determine the difference in lung volumes between male and female sickle cell disease patients (HbSS),sickle cell trait patients(Hb AS) and compare with normal controls (HbAA)non sicklers. **Method:** 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), Peak Expiratory Flow Rate(PEFR),Forced Expiratory Flow during 25%-75% of Expiration(FEF25%-75%),Forced Expiratory Volume Ratio(FEV1/FVC) were selected for the study. The data collected was subjected to statistical analysis involving computation of Mean, Standard deviation, Independent T test**. Result**: The results revealed that subjects with SCD had significantly lower mean FVC, FEV1, PEFR, FEF25-75% and FEV1/FVC compared to the controls. The lung function indices were lower in females than males of the sickle cell patients. This work also showed that the difference in FEV1, PEFR , FEF25%-75%,FEV1/FVC between HbAS and HbSS was statistically significant but the difference in FVC between HbAS and HbSS turned out to be statistically non-significant. **Conclusion**: The result of this work suggested that Pulmonary function test differs significantly in subjects with SCD compared with matched controls of a similar age and gender. It is indicative of mixed pattern (both restrictive and obstructive) lung impairment in sickle cell anaemia.

Key Words: Pulmonary Function Test, Sickle Cell Trait, Sickle Cell Disease,Forced Vital Capacity,Forced Expiratory Volume in 1 sec, Peak Expiratory Flow Rate, Forced Mid Expiratory Flow 25%-75% , Forced Expiratory Volume Ratio.

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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[2,6].

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 characterised 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:

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

Exclusion Criteria:

1. 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.
2. Patients with Hb <8gm/dl were not included in study because of compensated anaemia.
3. 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.50 subjects were compared with 50 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.

Table 1 shows that the Mean values of FVC , FEV1, PEFR ,FEF25%-75% and FEV1/FVC were less in HbSS and HbAS than their normal matched controls in both the sexes. Also FVC, FEV1, PEFR, FEF25%-75% and FEV1/FVC in HbSS were less than HbAS group in both the sexes.

Table 2 shows that Mean values of FVC,FEV1,PEFR,FEF25%-75% and FEV1/FVC 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 PEFR, FEF25%-75%, FEV1/FVC between HbAS and HbSS was statistically significant.

Table: 1 Study variables of PFTs (FVC, FEV1 ,PEFR , FEF25%-75%, FEF/FVC) between males and females of Normal Control groups and Sickle Cell Patients

CATEGORY	SEX	FVC MEAN±SD	FEV1 MEAN±SD	PEFR MEAN± SD	FEF25-75% MEAN±SD	FEV1/FVC MEAN±SD
NORMAL (n=50)	Male (n=33)	3.66±.58	3.07±.51	5.70±1.71	3.38±.85	83.96±5.27
	Female (n=17)	2.68±.32	2.24±.30	4.28±1.02	2.67±.43	83.63±2.30
HbAS (n=28)	Male (n=17)	3.29±.96	2.25±.94	4.29±1.52	2.87±1.02	72.82±27.10
	Female (n=11)	2.40±.50	1.77±.53	2.84±1.24	1.89±.80	72.94±12.39
HbSS (n=22)	Male (n=12)	3.19±.62	1.48±.83	2.41±.69	1.59±.76	47.63±25.36
	Female (n=10)	2.38±.88	1.51±.25	2.45±1.15	1.75±.72	67.55±15.90

Table: 2 Comparison of FVC ,FEV1 , PEFR , FEF25-75% and FEV1/FVC in different study group

CATEGORY	FVC		FEV1		PEFR		FEF25-75%		FEV1/FVC	
	Mean±SD	t value	Mean±SD	t value	Mean±SD	t value	Mean±SD	t value	Mean±SD	t value
NORMAL (n=50)	3.32±.69	1.96 (p<.05)	2.78±.59	4.11 (p<.05)	5.21±1.64	3.99 (p<.05)	3.31±.80	2.87 (p<.05)	83.84±4.45	2.59 (p<.05)
HbAS (n=28)	2.93±.91		2.05±.82		3.71±1.56		2.48±1.04		72.86±22.17	
NORMAL (n=50)	3.32±.69	2.47 (p<.05)	2.78±.59	8.24 (p<.05)	5.21±1.64	9.25 (p<.05)	3.31±.80	7.64 (p<.05)	83.84±4.45	5.40 (p<.05)
HbSS (n=22)	2.82±.84		1.49±.62		2.42±.90		1.66±.73		56.68±23.41	
HbAS (n=28)	2.93±.91	0.46 (p>.05)	2.05±.82	2.75 (p<.05)	3.71±1.56	3.65 (p<.05)	2.48±1.04	3.28 (p<.05)	72.86±22.17	2.48 (p<.05)
HbSS (n=22)	2.82±.84		1.49±.62		2.42±.90		1.66±.73		56.68±23.41	

p <.05 is statistically significant, p >.05 is statistically not significant

Discussion:

With improved supportive care the median age of survival has risen to 42 years for men and 48 years for women[8].As survival into adulthood has become more common in subjects with SCD, there has been an increased incidence of chronic organ failure. Lung is among the major organs involved in SCD[5,7]&pulmonary manifestations are the leading cause of morbidity and mortality in patients with SCD[8,9].

Pulmonary function tests are useful in assessing the functional status of the respiratory system both in physiological and pathological conditions. Spirometry is also the gold standard for the diagnosis, assessment, and monitoring of COPD.

Sickle Cell Trait (n=28) were found to be more common than Sickle Cell Disease(n=22). This is consistent with BEET,LEHMAN[1] 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, FEV1/FVC,FEF 25%-75%,PEFR 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, FEV1/FVC,PEFR andFEF25%-75%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 BOWEN et 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 done by Koumbourlis et al[14].

BOWEN et al [13] reported highly significant reduction in PEFR in children with mutiple episodes of acute chest syndrome.The abnormal values for PEFR are likely to result from the changes in the lung compliance. This is consistent with present study.

Conclusion:

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,PEFR,FEF25%-75% and FEV1/FVC%.Also,in restrictive impairment ,hallmark is reduction in FVC so it is mixed pulmonary impairment in sickle cell anaemia.This will help in diagnosis,treatment and prevention of Sickle Cell Chronic Lung Disease.

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