A study of pulmonary function tests in HIV infected children

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Abstract:

Background: If untreated, HIV mortality will be high from the cause of acute respiratory infections in neonatal stage up to one year of age. Here, the study was conducted to determine the prevalence of spirometric abnormalities in HIV positive children.

Methodology: A cohort of 20 children in the age group of 10 to18 years with a diagnosis of HIV was included. Spirometry measurements carried out to analyze the forced expiratory volume at one second (FEV1), forced vital capacity (FVC), FVC/FEV1 ratio, and forced expiratory flow 25% to 75% (FEF25-75) and pulse oximetry. The PFT data were analyzed in correlation with the age and blood parameters.

Results: 20 HIV-infected participants with a mean age 15.5 years were recruited. 17 children were on antiretroviral therapy. The mean CD4 count was 496±235.22 (151-1088) cells/µl. Mean Hb% value observed was 9.96±2.5 and mean total leucocyte count was 3785±2087.37. We found mean FEV1 as 71.05±9.2, mean FVC as 71.6±8.5 and ratio FEV1/FVC as 98%±0.11. The total lung capacity was observed as 73%-117%.

Conclusions: Clinicians evaluating HIV infected children with respiratory symptoms must first determine whether those symptoms are a result of common bacterial symptoms or opportunistic infections.

Keywords: Antiretroviral therapy (ART); Chronic lung disease; HIV; Pulmonoray function test.

Introduction

Respiratory complications could be the major cause of mortality and morbidity in HIV infected children. Even though in the presence of antiretroviral therapy (ART), the HIV epidemic remains a global health crisis with a high burden of pulmonary complications among infected patients. Respiratory disease is the most common manifestation of HIV/AIDS among children, accounting for more than 50% of HIV-associated mortality [1-3]. India has the 3rd largest population living with HIV infection. India is estimated to have around 14,500 (10,974–19,346) new HIV infections among children in 2011 [4].

Since the development of effective ART, obstructive lung diseases like asthma and chronic obstructive pulmonary disease (COPD) are becoming a growing concern in HIV infected population. In some of them, airway obstruction and diffusion defects were determined by spirometry. In recent studies, it was demonstrated that 31- 64% of HIV positive adults may have the pulmonary complications with up to 20% of airway obstruction measured by spirometry and 20% of clinically diagnosed asthma [5,6]. Likewise, a greater incidence of asthma was reported in HIV positive versus non-infected children [7]. However, there was very small data available related to pulmonary function testing in HIV-infected children in Indian population. Hence the current study designed to study the prevalence of spirometric abnormalities in HIV infected children in the current settings.

Materials and Methods:

This is a cross sectional single center study involving pulmonary function tests in HIV infected children followed at Department of Pulmonology, Narayana General Hospital on an outpatient basis. Inclusion criteria were age of 10 to 18 years, no history of smoking, and no history of previous acute/chronic lung disease.

Informed consent was taken from the child's care taker. Complete blood picture, chest X-ray, sputum for Acid Fast Bacilli staining and subclass assay of CD4 counts were analyzed by flow cytometry for all the children, prior to pulmonary function test.

PFT evaluation includes forced expiratory flows (forced viral capacity: FVC, forced expiratory volume in one second: FEV1 and forced expiratory flow during the middle half of FVC: FEF25-75), total lung capacity and carbon monoxide diffusing capacity (DLCO) using the single breath-hold method.

Results were measured as raw values and percentages of predicted values of each patient. All statistical analysis was performed using Microsoft Excel package. P value <0.05 was considered statistical significant.

Results:

Twenty HIV positive children were included: 10 boys and 10 girls, with a mean age of 15.5 ± 1.8 years. None of the children suffered from acute or chronic respiratory disease or had any respiratory symptoms determined by respiratory questionnaire and clinical examination.

Table 1: Demographic characteristics

Characteristic	Mean±SD(range)
Age in years	15.5±1.8 (10-18)
Sex, female (%)	10 (50%)
CD4 counts (cells/µL)	496±235.22 (151-1088)
On ART (%)	17 (85%)
Duration of ART (n=17)	5.9y (2-8)
BMI Males	15.7±2.57
BMI Females	16.97±1.70

Table 2: Spirometric and laboratory indices

Indices	Mean±SD Value
Hb	9.96±2.5 (5.7-14.2)
Total leucocyte count	3785±2087.37 (2000-11,600)
FEV1	71.05±9.2 (56-90)
FVC	71.6±8.5 (61-93)
FEV1/FVC	98%±0.11 (73%-117%)
Total lung capacity	78.45±15.5 (46-111)
DLCO	69.03%±0.20 (36%-109%)

All the children's FEV1/FVC ratio was more than 70%. Hence no obstruction was noted. But FEV1 and FVC predicted values are reduced in almost all the children. 12 children's test results were considered restrictive (TLC<80%). In all these 12 evaluations DLCO was also reduced (<80%) indicating the disease process within the lung parenchyma.

10 evaluations showed ditstal obstruction (FEF 25-75% <70%). We found weakly positive correlation between Hb% and TLC, and also between CD4 counts and TLC. We observed no correlation between duration of ART and TLC.

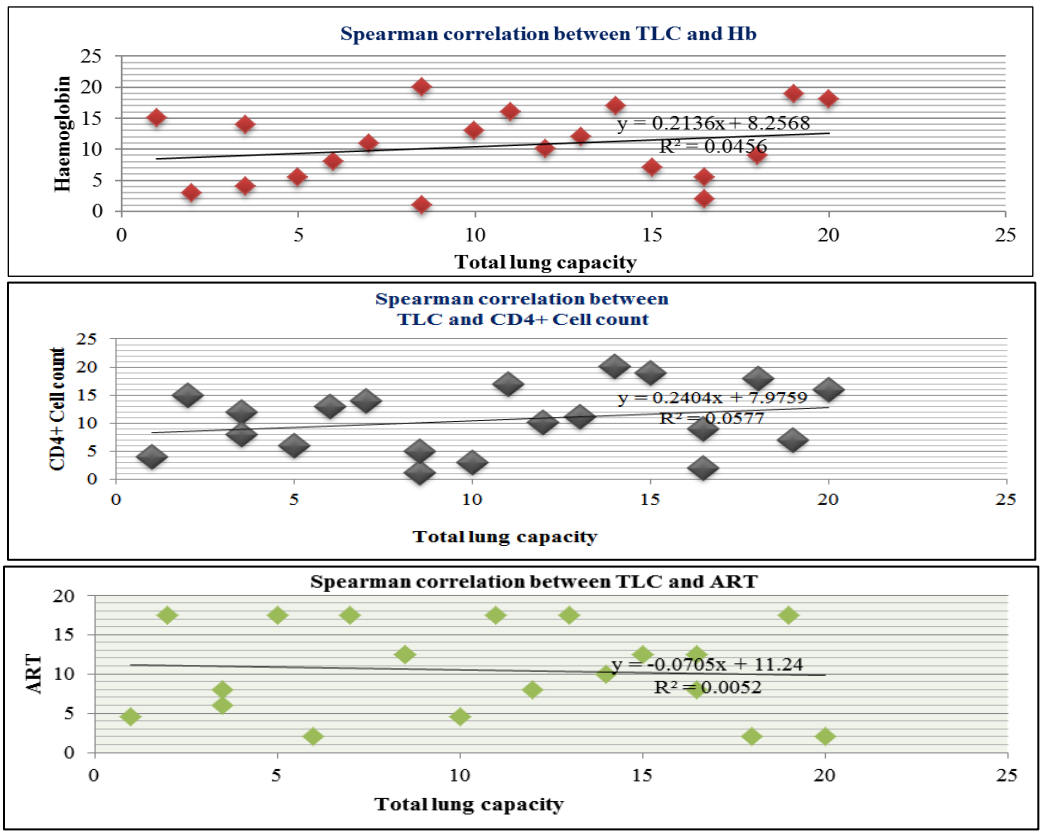

Fig. 1: Observation of correlation between TLC, Hb, CD4 count in ART children

Discussion:

Our data shows that in HIV infected, non-smoking children spirometry and DLCO values show restrictive disease with positive correlation between CD4 counts and TLC. Rosen et al., demonstrated that patients with advanced HIV infection, characterized by CD4 count <

200/mm^3 were associated with reduced TLCO values [8]. Conversely, Nieman et al., demonstrated that patients with reduced DLCO progressed more rapidly to AIDS [9]. Two main mechanism involved in reduced DLCO measurements; diffuse alveolar destruction (as observed in pneumonia, pulmonary hypertension or fibrosis) or a decrease in alveolar expansion (as observed in neuromuscular disease). Patients with HIV infection receiving HAART may suffer from each of these mechanisms.

In a previous study involving HIV-infected Zambian children, low hemoglobin level (<8 g/dL) also was identified as an independent predictor of mortality [10]. Whereas, in our study, Hb level doesn't shown any correlation with lung capacity in HIV positive children.

Despite the fact that our patients were HAART-treated, none of the patients developed asthma and we could not find significant relationship between FEV1 or FEV1/FVC and CD4 T-cell counts or percentages. This may be due to small sample size of our population. Rubio et al., found evidence of small-diameter bronchi obstruction (whereas in our study, reduction in FEF_{25-75} was noted in 4/17 patients), and a positive correlation between CD4/CD8 ratio and FEF_{25-75}. It is possible that in pediatric patients, alterations of FEF_{25-75} may reflect or precede those observed in adult larger bronchi. Unfortunately none of these HIV positive children underwent broncho-alveolar liquid fluid analysis or high resolution CT-scan [11]. The mechanisms behind the emergence of these diseases are largely unknown, but may result from HIV infection itself, the effect of long-term ART and immune reconstitution or the development of autoimmunity, the effects of repeated pulmonary infections or simply due to extended periods of time living with HIV. In the developing populations of Africa, Asia and the Indian subcontinent, where the vast majority of global HIV disease burden lies, mortality from HIV infection is still dominated by infectious diseases [12].

As these children may progress rapidly to AIDS, they need to go through higher modalities like CT scan and bronchoscopy (for BAL fluid analysis) to confirm the diagnosis and to start necessary treatment earlier which helps in decreasing morbidity and mortality. Avoidance of smoking, routine influenza and pneumococcal vaccinations and careful pulmonary follow-up must therefore be combined to decrease the risk.

Conclusions:

In this study, 12 out of 20 children are having restrictive lung disease as both TLC and DLCO decreased than predictive normal values. Unlike recent studies, we did not find any obstruction in the major airways. But, distal obstruction was noted in 10 children. It may progress as the age of children increases. We found some positive correlation between CD4 counts and total lung capacity and no correlation between duration of ART and the TLC.

Conflicts of Interest: None declared.
Acknowledgements: None.

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