

## **CD<sub>4</sub> COUNT LEVELS AND PATTERN OF RESPIRATORY COMPLICATIONS IN HIV SEROPOSITIVE PATIENTS IN CALABAR, NIGERIA.**

**\* E. J. PETERS<sup>1</sup>, O. E. ESSIEN<sup>1</sup>, K. K. IMMANANAGHA<sup>3</sup>, G. A. INAH<sup>2</sup>, E.  
E. PHILLIP-EPHRAIM<sup>1</sup>, R. E. AGBULU<sup>1</sup>**

<sup>1</sup>*Department of Medicine, UCTH, Calabar*

<sup>2</sup>*Department of Radiology, UCTH, Calabar*

<sup>3</sup>*Federal Medical Centre, Yenagoa.*

**Summary:** A prospective observational study was carried out to describe the pattern of pulmonary complications in hospitalized patients with Human Immune-deficiency Virus (HIV) infection at the University of Calabar Teaching Hospital, Calabar between January 2005 to December 2006. One hundred and twenty-four patients which consists 60 males and 64 females, aged between 20 – 60 who met the inclusion criteria formed the subjects for the study. The mean age of the subjects was 34.60± 1.2 years. A structured questionnaire was used to obtain the demographic data, clinical information and CD<sub>4</sub> lymphocyte count. Radiological analysis of chest was done with the chest X-ray of each subject. Chronic productive cough topped the list of respiratory symptoms (89%) followed by chest pain (74%) and dyspnea (62%). Lung consolidation was the commonest respiratory sign as seen in 44% of the cases. Hilar lymphadenopathy was seen in (35%), Pleural effusion (32%), lung fibrosis (21%) and finger clubbing (15%). The clinical and radiological pattern of most patients with chronic cough was highly suggestive of mycobacterial infection such as tuberculosis, although only 40% of cases had positive Acid Fast Baccilli. The mean CD<sub>4</sub> lymphocyte count level was 174.8 ± 5.4 cells/μl and this may be responsible for the respiratory findings as opportunistic lung infections are said to be commoner at CD<sub>4</sub> count levels below 200 cells/μl. However, four patients had mediasternal masses which may suggest neoplasms. Concerted efforts and continuous evaluation of these patients are needed to determine the spectrum of respiratory illnesses among HIV positive patients in Calabar.

**Key Words:** CD<sub>4</sub>, Respiratory, complications, HIV/AIDS, Calabar.

### **Introduction**

Pulmonary complications have been one of the commonest causes of morbidity and mortality since the advent of Acquired Immune-deficiency Syndrome (AIDS) (Afessa, 2001 and Murray *et al*, 1984). Seropositive patients nonetheless, are also prone to other infectious and non-infectious conditions. However, the type of pulmonary complications that develop depend on the degree of immuno suppression (Huang, 1998). The pulmonary complications are also likely to vary according to geographical location, HIV risk factors, gender, race or ethnicity and social habits of patients.

Respiratory symptoms which are frequent in HIV infected individuals may be due to a wide spectrum of diseases (GroupTpcHis, 1993). The spectrum of pulmonary illnesses in HIV infected patients include both opportunistic infections and neoplasms (Wallace *et al*, 1997). The opportunistic infections are caused by

bacterial, mycobacterial, viral, fungal and parasitic pathogens. A pilot study conducted in USA on the pulmonary complications of HIV infected patients demonstrated that respiratory symptoms are frequent complaints in HIV infected individuals and there was increase in frequency as the CD<sub>4</sub> cell count declines below 200cells/μl (Wallace *et al*, 1993). However, such study has not been carried out in our environment, which has one of the highest prevalent rates of HIV infection in the country (FMOH, 2004).

This study is therefore aimed at evaluating the pattern of respiratory complications amongst HIV seropositive patients seen at the University of Calabar Teaching Hospital over a 2-year period. Knowledge of the pattern of pulmonary complications in patients with HIV infection will help clinicians develop faster diagnostic and therapeutic approach to patients management.

### Subjects and Methods

A two-year prospective study (January, 2005 – December, 2006) was carried out in Calabar to evaluate CD<sub>4</sub> lymphocyte count levels in HIV seropositive patients and pattern of respiratory complications amongst these patients. Confirmed HIV positive patients with CD<sub>4</sub> count levels below 500cells/ $\mu$ l who were receiving free Antiretroviral (ARV) treatment from Pepfar Clinic and subsequently admitted at the University of Calabar Teaching Hospital with respiratory complications were enrolled for the study within the period.

A total of 124 patients, which consisted 60 males and 64 females aged between 20 – 60, were used for the study. The mean age of patients was  $34.60 \pm 1.2$  years. Data on gender, age, marital status, occupational history, respiratory symptoms/signs, chest radiograph findings and CD<sub>4</sub> lymphocyte count were collected. The investigators, physicians and radiologist reviewed all chest radiographs and the pattern of respiratory complications were

noted after thorough clinical examination of the patients. Mycobacterial organisms were identified by Ziehl-Neelson stain only. Other bacterial organisms were cultured. However, it was not possible to culture mycobacterial, fungal, viral and parasitic organisms as there were no facilities in the hospital.

Similarly, bronchoscopic examination on the subjects could not be done to ascertain definitive lung pathology due to lack of such facility. Antibiotic susceptibility tests were reviewed for cultured cases. Information on the bio-data, past medical history, social habits, and respiratory symptoms/signs were obtained using a prepared structured questionnaire administered to all patients. Data obtained were carefully documented in an information sheet prepared for each patient and analyzed with an Epi info version 6.0 software. All means were expressed with their standard deviation. However, no statistical analysis was done.

Table 1: Demographical characteristics of the subjects

Sex:	Total No. (n)/Percentage (%)		
Male	60 (48)		
Female	64 (52)		
Marital status:			
Single	66 (53)		
Married	44 (34)		
Widowed	10 (8)		
Separated	6 (5)		
Age distribution:			
	Total	Male	Female
<20 years	(n/%)	(n/%)	(n/%)
21 – 25	13 (10)	-	12 (10)
26 – 30	16 (13)	4 (3)	12 (10)
31 – 35	18 (15)	6 (5)	12 (10)
36 – 40	36 (29)	24 (19)	12 (10)
41 – 45	16 (13)	10 (8)	6 (5)
46 – 50	10 (8)	10 (8)	- (0)
51 – 55	8 (6)	4 (3)	4 (3)
>55	4 (3)	2 (1.5)	2 (1.5)
	4 (3)	- (0)	4 (3)
Occupational status:			
Students	30 (24)		
Businesspersons	52 (42)		
Civil servants	12 (9.5)		
Drivers	22 (18)		
Housewives	8 (6)		

Mean CD<sub>4</sub> count =  $173.85 \pm 5.4$ cells/ $\mu$ l

Mean age =  $34.6 \pm 1.2$  years

Positive AFB =  $\frac{25}{62}$  (40%)

Negative AFB =  $\frac{32}{62}$  (53%)

## Results

One hundred and twenty-four patients which consisted of 60 males and 64 females were enrolled for the study after meeting the inclusion criteria. The mean age of patients was  $34.60 \pm 1.2$  years. Table I shows the demographic characteristics of the subjects. Unmarried patients formed the bulk of the patients (53%) while the remaining patients were married, widowed or separated. Majority of the patients (29%) were in the age group 31 – 35 and about (80%) were below forty years of age. Students accounted for 24% of the patients surveyed, while private businesspersons were 42%. Twenty-two (18%) of the subjects were drivers. Table II illustrates the pattern of respiratory symptoms amongst the subjects surveyed. Chronic productive cough topped the list with 89%, followed by chest pain 74%, dyspnea 62% and sinusitis 37%. Non-productive cough was seen in only 11% of the subjects surveyed while 18% had cough with haemoptysis.

The pattern of respiratory signs and complications is shown in Table III. Lung consolidation was the commonest complication seen in 44% of the subjects surveyed and this was followed by hilar lymphadenopathy (35%), pleural effusion (32%), lung fibrosis (26%) and finger clubbing (15%). Mediasternal mass was seen in 4 (3%) of the patients. Positive AFB sputum examination was confirmed in only 40% of the cases surveyed while 53% were negative.

The CD<sub>4</sub> lymphocyte count levels distribution of the subjects is as shown in Table IV. The mean CD<sub>4</sub> count level was  $173.85 \pm 5.1$  cells/ $\mu$ l. The bulk of the patients (27%) had a CD<sub>4</sub> count level between 151-200 cells/ $\mu$ l followed by a count between 101-150 cells/ $\mu$ l as seen in 21% of patients. Less than 20% of the cases surveyed had a CD<sub>4</sub> count level greater than 200 cells/ $\mu$ l. 83% of the patients had a CD<sub>4</sub> count of less than 200 cells/ $\mu$ l.

Table 2: Respiratory symptoms

	Total %	Male (n/%)	Female (n/%)
Chronic productive cough	110 (89)	54 (44)	56 (45)
Non-productive cough	14 (11)	6 (4)	8 (7)
Chest pain	92 (74)	44 (35)	43 (39)
Dyspnea	78 (62)	38 (30)	40 (32)
Haemoptis	22 (18)	12 (10)	10 (8)
Sinusitis	46 (37)	22 (18)	24 (19)

Table 3: Respiratory signs and diagnosis or complications

	Total %	Male (n/%)	Female (n/%)
Fibrosis	32 (26)	16 (13)	16 (13)
Pleural effusion	40 (32)	22 (18)	18 (14)
Consolidation	54 (44)	26 (21)	28 (25)
Lymphadenopathy	44 (35)	24 (19)	20 (16)
Finger clubbing	30 (24)	16 (13)	14 (11)
Mediasternal mass	4 (3)	-	4 (3)

Table 4: CD<sub>4</sub> Lymphocyte count level distribution (cells/ $\mu$ l)

	Total %	Male (n/%)	Female (n/%)
0 – 50	24 (19)	14 (11)	10 (8)
51 – 100	20 (16)	16 (13)	4 (3)
101 – 150	26 (21)	8 (6)	18 (15)
151 – 200	34 (27)	14 (11)	20 (16)
201 – 250	6 (5)	4 (3)	2 (1.5)
251 – 300	4 (3)	2 (1.5)	2 (1.5)
>300	10 (8)	6 (5)	4 (3)

## Discussion

This study collected clinical, laboratory and radiological data in a prospective and standardized form to access the pattern of respiratory complications in HIV seropositive patients in Calabar over a period of two years. The study intended to provide useful source of information on the pattern of respiratory illnesses in HIV infected patients in our environment. Subjects who reported chronic productive cough were 89%, chest pain 74% and shortness of breath 62%. These figures are higher than that reported by studies on the pulmonary complications of HIV infection in USA (Wallace, 1997; Moore and Charsson, 1996).

However, only 11% of the subjects had non-productive cough, which may clinically suggest infection by fungal infection such as *pneumocystis carinii*. This finding is quite different from studies reported in North America and Europe where *P. carinii* infection is the commonest type of non-mycobacterial infection seen in HIV infected patients (Stansell *et al*, 1997 and Delorenzo *et al*, 1991).

Mycobacterial infection such as tuberculosis still remains the commonest type of respiratory infection in Nigeria as documented in other studies (Idoko *et al*, 1994; Idigbe *et al*, 1994 and Peters *et al*, 2005). This was also amply demonstrated in our study in which a significant percentage of the patients presented with chronic productive cough, haemoptysis and other constitutional symptoms suggestive of mycobacterial infection. Indeed, tuberculosis is the most common opportunistic infection associated with HIV worldwide (Daley *et al*, 1992). The study also revealed that upper respiratory tract illnesses such as sinusitis and upper respiratory infection were not as common as documented in the pulmonary complications of HIV infection study in USA. These illnesses were found to be even more common than bacterial pneumonia and tuberculosis in that study (Wallace *et al*, 1997).

However, lung consolidation was the commonest pattern of respiratory pathology elicited among the patient surveyed (44%). This may suggest the higher prevalence of pneumonia, which may be largely bacterial in origin than opportunistic pneumonia, which has the highest prevalence in other studies (Delorenzo *et al*, 1991 and Koracs *et al*, 1984).

Pleural effusion was seen in 32% of the case while lung fibrosis was seen in 26%. These findings coupled with chronic productive cough in these patients may strongly suggest tuberculosis, which has been documented to be fairly common amongst HIV patient (Charsson *et al*, 1987). In this study, more than 50% of

patients surveyed had negative AFB smear and this was similar to findings by Afessa on survey of African-American Patients in Pulmonary Complication study in USA (Afessa, 2001). However, tuberculosis can affect people with HIV no matter what level of their CD<sub>4</sub> count, which means that tuberculosis can often occur years before other problems associated with HIV develop. Lymphadenopathy was seen in 35% of the subject while mediasternal mass was found in only four patients with HIV but is more likely in those with CD<sub>4</sub> count of less than 200cells/ $\mu$ l. In patients with HIV infection, about 20% may develop a malignancy (Beral and Weiss, 1991).

The mean CD<sub>4</sub> lymphocyte count in patients surveyed was  $173.85 \pm 5.4$ cells/ $\mu$ l. In patients not treated with highly active antiretroviral drugs, the CD<sub>4</sub> cell count is an excellent indicator of an HIV infected patient's risk of developing a specific opportunistic infection or neoplasm, presumable because it reflects the stage of HIV disease and degree of immuno compromise. Many respiratory illnesses such as upper respiratory tract infection, sinusitis, bacterial pneumonia and tuberculosis are more common in HIV infected persons than in immuno-competent ones. These diseases have occurred in HIV infected patients at all CD<sub>4</sub> count ranges (Huang, 1998).

However, studies have shown that there is a higher prevalence of diseases such as bacterial pneumonia and tuberculosis as the CD<sub>4</sub> count level declines (Wallace *et al*, 1997, and Hanson *et al*, 1995). This is consistent with findings in our study in which the mean CD<sub>4</sub> count was below 200cells/ $\mu$ l and about 90% of patients presented with chronic productive cough. Thus, knowledge of the CD<sub>4</sub> count level in HIV patients is extremely useful in making differential diagnosis and suggesting a diagnostic and therapeutic plan.

In addition, it is likely that demographic and regional differences will affect the spectrum of illnesses seen in our environment. This is because, few patients may be injection drug users, or on illicit drugs and homosexuality is still very uncommon. It has been well documented that a patient's HIV transmission category and habits provide insights into the relative frequency of various HIV-related opportunistic infections and neoplasm (Afessa, 2001 and Selwyn *et al*, 1997).

A travel and residence history may provide further information about exposures to HIV infection and certain organisms. This may explain why a significant percentage of patients surveyed in our study were long distance drivers. This study had several limitations. Some important data such as cigarette smoking

and use of chemoprophylaxis were not collected. Similarly, invasive investigation like diagnostic bronchoscope was not performed and moreover there was no facility for culture and isolation of mycobacterial, viral, fungal and parasitic organisms.

In conclusion, the study has described the spectrum of respiratory illnesses seen in HIV infected patients in Calabar. Respiratory infection still remains the commonest type of respiratory illnesses. The application of highly active antiretroviral treatment is likely to be associated with changes in type and severity of pulmonary complications that we see in these patients. The pulmonary complications are also likely to vary according to geographical locations, HIV risk factors and severity of immuno-suppression. It is therefore recommended that continuous monitoring of these patients be performed in order to ascertain the pulmonary complications that may develop.

#### References

- Afessa, B. (2001). Mycobacterial and non-bacterial pulmonary complication in hospitalized patients with Human Immune-deficiency Virus infection. A prospective, cohort study. *BMC Pulm Med.* 1:1 (published online).
- Beral, V., Jaffe, H., Weiss, R. (1991). Cancer surveys: cancer, HIV and AIDS. *Eur. J. Cancer.* 27:1057 – 1058.
- Chaison, R. E., Schechter, G. F., Theor, C. P. (1987). Tuberculosis in patients with Acquired Immune-deficiency Syndrome, clinical features, response to therapy and survival. *Ann Rev. Respir Dis.* 136 (3):570 – 574).
- Daley, C. C., Small, P. M., Schechter, G. F., School, G. K., McAdam, R. A., Jacobs, W. R. Jr, Hopewell, P. C. (1992). An outbreak of tuberculosis with accelerated progression among persons infected with human immune-deficiency virus. An analysis using restriction – fragments-lengths – polymorphism. *N. Eng J. Med.* 326:231-233.
- Delorenzo, L. J., Huang, C. T., Magure, G. P., Stone, D. J. (1991). Roentgenographic patterns of *Pneumocystis Carinii Pneumonia* in 104 patients with AIDS. *Chert* 100:1462 – 1464.
- Federal Ministry of Health (FMOH) Abuja, Nigeria. (2004). Technical Report of the 2003 National HIV/AIDS sentinel sero-prevalence survey, Abuja, Nigeria: FMOH.
- Group T pcoHis. (1993). Design of a prospective study of the pulmonary complication of human immune-deficiency virus infection. The pulmonary complication of HIV infection study group. *J. Clin Epidemiol.* 46(6), 497 – 507.
- Hanson, D. E., Chu, S. T., Farizo, K. M. (1995). Distribution of CD<sub>4</sub><sup>+</sup> lymphocytes at diagnosis of acquired immune-deficiency syndrome – defining and other human immune-deficiency virus related illnesses. The adult and adolescent spectrum of HIV Disease project group. *Arch. Intern Med.* 155 (14): 1537 – 1542.
- Huang, L. (1998). Pulmonary manifestation of HIV. HIV in-site publication, University of California (Published online).
- Idigbe, E. O., Nasidi, Anyiwo, C. E. (1994). Prevalence of human immune-deficiency virus antibodies in tuberculosis patients in Lagos, Nigeria. *J. Trop Med. Hgy.* 97: 91 – 92.
- Idoko, J. A., Antei, A. E., Idoko, L. O. (1994). HIV and associated TB in Jos, Nigeria. *Nig. Med Pract.* 28:48 – 50.
- Koracs, J. A., Hiemenz, J. W., Macher, A. M. (1984). *Pneumocystis Carinii Pneumonia*. A comparison between patients with the Acquired Immune-deficiency syndrome and patients with other immune-deficiencies. *Ann Intern Med.* 100 (5) 663 – 671.
- Moore, R. D., Charsson, R. E., (1996). Natural history of pulmonary disease in an HIV infected urban clinical cohort. *Ann Intern Med.* 124:633-642.
- Murray, J. F., Felton, C. P., Garay, S. M., Gohlies, M. G., Hopewell, P. C., Stover, D. C., Teirstein, A. S. (1984). Pulmonary complications of the Acquired Immune-deficiency Syndrome. Report of a National Heart, Lung and Blood Institute Workshop. *N. Eng J Med.* 310:1682 – 1688.
- Peters, E. J., Ekott, J. U., Eshiet, G. A., Anyanechi, C.C. (2005). Tuberculosis in Calabar: a ten-year review (1994 – 2003). *Nig. J. Med.* 14 (4) 381 – 385.
- Selwyn, P. A., Sekell, B. M., Alcebeb, P., (1992). High risk of active tuberculosis in HIV infected drug users with cutaneous energy. *JAMA,* 268 (4) 504 – 509.
- Stansell, J. D., Osmond, D. H., Charebois, E., Lavange, L., Wallace, J. M., Alexander, B. V., (1997). Predictors of *Pneumocystis Carinii Pneumonias* in HIV infected persons. *AM J. Respir Crit Core Med.* 155:60 – 66.
- Wallace, J. M., Han, N. I., Lavange, L. (1997). Respiratory disease trends in the pulmonary complication of HIV infection study cohort. Pulmonary complication of HIV infection study group. *Am. J. Respir Crit Core Med.* 155(1) 72 – 80.
- Wallace, J. M., Rao, A.V. Grassroth (1993). Respiratory illnesses in person with Human Immune-deficiency Virus infection: The pulmonary complication of HIV infection study group. *Am. Rev. Respir Dis,* 148 (6 pt 1) 1523 – 1529.

Received: 29/6/2007

Accepted: 15/11/2007