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Chest Radiograph Patterns and their Correlation with CD4 Count in Adults with Human Immunodeficiency Virus (HIV) in Lagos University Teaching Hospital, Nigeria

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Abstract

The only available treatment for Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) at the moment is antiretroviral therapy (ART). The chest radiograph patterns in adults with HIV could be used as an alternative or surrogate to CD4 count in monitoring the progress of treatment in resource poor settings where these tests and expertise are not available. This study was aimed at evaluating chest the radiograph patterns in HIV sero-positive adults and correlating with the CD4 cells count. This was a cross-sectional study conducted among patients diagnosed of HIV using the National algorithm at the HIV Clinic of the Lagos University Teaching Hospital. A purposive sampling method was employed and three hundred and twenty (320) HIV sero-positive adult participants were recruited. Postero-anterior chest x-ray projection was performed on all the participants and the radiographs were reported by two consultant Radiologists and the CD4 counts was determined. Pulmonary TB was the most frequent finding (22.1%) while bronchitis was the least frequent finding (0.9%). and normal radiograph (52.6%). The CD4 count was less than, 200 cells/mm^3 in 38.3% of the participants. There was a strong correlation between chest radiograph patterns and CD4 cells count (r=-0.53; p=0.001). This study revealed that the most predominant radiographic patterns are Pulmonary Tuberculosis. A strong negative correlation was observed between chest radiograph patterns and CD4 count. The Chest radiograph patterns may be recommended as a measure of immunosuppression in adults with HIV in Nigeria.

Keywords: HIV, Chest radiograph patterns, CD4 counts

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INTRODUCTION

The Human Immunodeficiency Virus (HIV) infection is a huge global public health challenge with an estimated 36.7 million people living with the disease worldwide (WHO, 2020). Almost 1.2 million individuals have died of AIDs-related illness (WHO, 2020). The burden of HIV epidemic varies considerably between countries and regions. Sub-Saharan Africa remains the most severely affected region (WHO, 2020). Although the continent of Africa is about 15.8% of the world's population, Sub-Saharan Africa is singularly responsible for about 69% of all people living with HIV and 70% of Acquired Immune Deficiency syndrome (AIDS) related deaths (WHO, 2020). Nigeria has the second largest number of people living with HIV in the World (Punch, 2019). In Nigeria, about 1.9 million people were estimated to be living with HIV according to the National HIV / AIDS indicator and Impact Survey.

The virus (HIV) causes a chronic infection that leads to severe immunosuppression due to severe decline in the CD4 count of the affected individual, which is usually below, 500 cell/mm^3 (Akinbamni *et al*., 2012l; Ford *et al*., 2017 & Kaplan, 2019). The Acquired Immune Deficiency syndrome (AIDS) is a systemic disorder caused by HIV and characterized by severe impairment and progressive damage to both cellular and humoral immune responses (Rajeev *et al*., 2014). The immunological complications have been documented as strong independent predictors of morbidity and mortality in HIV infected individuals (Akinbami *et al*., 2012). The low CD4 count is linked with mortality in HIV infected individuals (David, 2001). In the majority of African countries, the cost of routine CD4 cells count measurement is quite expensive and establishing sophisticated laboratory services at relatively poorly equipped health facilities remains a main challenge for effective management of HIV infected individuals in Nigeria.

The CD4 cell count has been an important component for the treatment of individuals infected with HIV treatment and care programmes since the virus was identified as a disease compromising the immune system. The CD4+ lymphocyte counts are routinely used globally, including many parts of Sub-Saharan Africa, to determine eligibility for, and monitoring response to antiretroviral therapy (ART) in HIV-positive. They are used as a measure of the risk of development of opportunistic infections (Akinbami *et al*., 2012).

The chest radiography is an important tool in assessing the pulmonary complications as well as manifestations of HIV/AIDS (Akinbami *et al*, 2012). It has a sensitivity and specificity of 98% and 93% respectively in detecting pulmonary complications in patients with HIV (Umar *et al*., 2021). Several studies have documented the spectrum and pattern of chest radiographic findings in patients with HIV (Ahidjo *et al*., 2012; Atalabi *et al*., 2012 & Umar *et al*., 2019). The common chest findings documented include but not limited to pulmonary nodules, interstitial pulmonary infilterates, reticulonodular shadows, bronchial wall thickening, consolidation, cavitation, atelectasis, lung collapse, enlarged lymphnodes, pneumothorax, pleural effusions and normal findings (Umar *et al*., 2021). Most chest pathologies reported are immunological complications in HIV infection.

The study was aimed at evaluating chest radiograph patterns among HIV sero-positive adults in relation to CD4 cells count and possibly establish chest x-ray findings as an alternative measure of immune-suppression and possible monitoring tool for progress of antiretroviral treatment.

MATERIALS AND METHODS

This study was a cross-sectional conducted among patients diagnosed with HIV using the National algorithm at the HIV Clinic of the Lagos University Teaching Hospital from October, 2019 to June, 2021. Ethical approval to conduct the study was obtained from the Human Research and Ethics committee of Lagos University Teaching Hospital (LUTH), Lagos State, Nigeria. Consent was obtained from all the participants, after providing them with all necessary information about the procedures required in the study in clear and simple language. Their consent to participate in the study was strictly voluntary and had the right to withdraw from the study at any time they wish without any consequences. They were also informed about the confidentiality of the data obtained from them. A purposive sampling method was employed and three hundred and twenty (320) HIVsero-positive participants were recruited.

The sample size was calculated based on Yamane's formula (Yamane, 1967).

$$n = \frac{N}{1 + Ne2}$$

Where n = Sample size,
N = population,
e = proportion of sampling error (error limit).

1600 HIV patients presented at the HIV clinic from January, 2018 to November, 2018. Hence, N = 1600; e = 0.05. This gives

$$n = \frac{1600}{1 + 1600(0.05)2}$$

$$n = \frac{1600}{1 + 4.000}$$

$$n = 320$$

Hence, the sample size for this study was 320 subjects**.**

Non-probability purposive sampling method was adopted

Postero-anterior chest x-ray projection was conducted on all participants and sample of blood was collected for CD4 count determination. The obtained data was analyzed using SPSS version 23. The mean±SD was obtained using descriptive statistics. The difference in CD4 count between males and females was obtained using independent 2 samples t-test. Analysis of variance (ANOVA) was used to investigate significant differences in CD4 count between the various chest radiographic patterns. The relationship between the chest radiographic patterns and CD4 count was evaluated using Chi-square. P value of < 0.05 was considered statistically significant.

RESULTS

Demographic variables of the participants

A total of 320 patients participated in this study, comprised females (62%); the males comprised and males 38%. Following the various age categories as shown in Table 1, 8.1% of the patients were below 20 years; 17.8% between 20-29 years; 28.4% between 30-39 years; 27.8% between 40-49 years; 12.5% between 50-59 years; only 5.3% above 60 years.

Table 1: Distribution of studied population according to gender and age

Variable	Options	Frequency *n* (%)
Gender	Male	122 (38)
	Female	199 (62)
Age (years)	<20	26 (8.1)
	20-29	57 (17.8)
	30-39	91 (28.4)
	40-49	89 (27.8)
	50-59	40 (12.5)
	60-69	17 (5.3)

As presented in Table 2, majority of the patients had CD4 count less than 200 cells/mm^3 (38.3%); followed by patients who had at least 500cells/mm^3 (25.2%). Of the patients, 19.3% had CD4 count between 350-499cells/mm^3; 17.1% had between 200-349cells/mm^3. Similarly, majority (42.1%) had low viral load (<10,000 copies/mL); 40.8% of patients had high viral load (>100,000 copies/mL), while 17.1% had intermediate viral load (10,000-100,000 copies/mL). Distribution according to chest X-ray findings revealed that the highest percentage of the HIV patients showed normal chest with no abnormal findings on X-ray (52.6%). The abnormal findings that was observed on the chest X-ray were; pulmonary tuberculosis (22.1%), pneumonia (9.7%), cardiomegaly (6.2%), pleural effusion (4.4%), consolidation (4.1%), and bronchitis (0.9%).

Table 2: Distribution of studied population according to HIV status and chest X-ray findings

Variable	Options	Frequency *n* (%)	X^2	p-value
CD4 count (cells/mm^3)	<200	123 (38.3)	34.875	<0.001
	200-349	55 (17.1)		
	350-499	62 (19.3)		
	> 499	81 (25.2)		
Chest X-ray finding	Normal	169 (52.6)	449.589	<0.001
	Bronchitis	3 (0.9)		
	Cardiomegaly	20 (6.2)		
	Consolidation	13 (4.1)		
	Pleural effusion	14 (4.4)		
	Pneumonia	31 (9.7)		
	Pulmonary TB	71 (22.1)		

As shown in Table 3, the result comparing mean values between the male and female patients showed no significant difference in age (t = 3.252; p = 0.675) and CD4 count (t = 0.285; p = 0.776).

Table 3: Comparison of mean values of some parameters between males and females

Variable	Sex	Mean ± SD	T	p-value
Age (years)	Male	38.79 ± 15.38	3.252	0.675
	Female	38.10 ± 13.19		
CD4 count (cells/mm^3)	Male	343.01 ± 271.65	0.285	0.776
	Female	352.04 ± 331.87		

No significant difference in mean value of age was found when the various CD4 count groups were compared (F = 2.157; p = 0.093). In Table 4, mean age was highest among patients whose CD4 count was less than 200 cells/mm^3 (40.64 years); The mean age of patients whose CD4 count was between 200-349 cells/mm^3 was 37.98 years, while those who had between 350-499

cellss/mm^3 was 38.24 years; mean age was least among patients whose CD4 count was at least 500 cell/mm^3 (35.58 years). Viral load showed significant difference when its mean value was compared between the various CD4 count groups (F = 2.946; p = 0.033). The highest viral load was seen among patients who had CD4 count less than 200 cells/mm^3 (590545 copies/mL) and between 200-349 cells/mm^3 (263103 copies/mL)

Table 4: Comparison of mean values of some parameters according to CD4 count categories

Variable	CD4 Category	Mean ± SD	F	p-value
Age (years)	> 499	35.58 ± 17.08	2.157	0.093
	350-499	38.24 ± 11.72		
	200-349	37.98 ± 12.72		
	<200	40.64 ± 13.06		
CD4 count (cells/mm^3)	> 499	695.38 ± 324.01	210.440	<0.001
	350-499	415.39 ± 40.33		
	200-349	279.48 ± 47.23		
	<200	84.98 ± 56.69		
Viral load (copies/mL)	> 499	194353 ± 132801	2.946	0.033
	350-499	136896 ± 39801		
	200-349	263103 ± 120342		
	<200	590545 ± 134688		

Following the result presented in Table 5 above, CD4 count showed significant difference in mean value when compared between the various chest X-ray findings (F = 18.835; p < 0.05). The mean CD4 count determined for patients who showed Bronchitis, Cardiomegaly, Consolidation, Pleural effusion, Pneumonia and Pulmonary TB, where each compared with mean CD4 count of patients who had normal chest X-ray finding. Each showed a significant lower mean value when compared with the normal (p < 0.05 in each case). The highest mean CD4 count was found among patients who showed normal finding on chest X-ray (425.45 cells/mm^3); the least was among patients who showed Pulmonary TB on chest X-ray (136.10 cells/mm^3). The mean CD4 count of patients who showed cardiomegaly was 318.55 cell/mm^3; pneumonia was 276.84 cell/mm^3; consolidation was 241.23 cells/mm^3; pleural effusion was 240.00 cell/mm^3; bronchitis was 221.00 cells/mm^3.

Table 5: Comparison of mean values of CD4 Count between various chest X-ray findings

Variable	Chest X-ray findings	Mean ± SD	F	p-value
CD4 count (cells/mm^3)	Normal	474.13 ± 20.99	18.835	-
	Bronchitis	221.00 ± 55.61		<0.001
	Cardiomegaly	318.55 ± 43.72		0.006
	Consolidation	241.23 ± 58.77		0.001
	Pleural effusion	240.00 ± 90.92		<0.001
	Pneumonia	276.84 ± 16.08		<0.001
	Pulmonary TB	136.10 ± 16.08		<0.001

As shown in Table 6, there was no significant difference in mean value of CD4 count found between the various age categories (F = 1.247; p = 0.287). CD4 count was highest among patients aged below 20 years (446.42 cells/mm^3), and least among those aged between 40-49 years (296.79 cells/mm^3).

Table 6: Comparison of mean values of CD4 count according to age

Variable	Age (years)	Mean ± SD	F	p-value
CD4 count (cells/mm^3)	<20	446.42 ± 53.69	1.247	0.287
	20-29	373.42 ± 33.18		
	30-39	351.87 ± 41.11		
	40-49	296.79 ± 24.68		
	50-59	329.90 ± 35.08		
	60-69	381.53 ± 86.91		

Table 7: Correlation of chest X-ray findings with CD4 count

	Spearman's Correlation	CD4 count	Viral load	X-ray finding
CD4 count	**Rho**	1	-0.530	-0.578
	p-value		<0.001	<0.001
X-ray finding	**Rho**	-0.578	0.626	1
	p-value	<0.001	<0.001	

DISCUSSION

The Human Immunodeficiency Virus infection commonly presents with a broad variety of respiratory and cardiac manifestations that may be associated with high mortality rates. The conditions often manifest radiographically, sometimes associated with some degree of overlap, changeability and non-specificity. Chest radiograph has been demonstrated to be an essential diagnostic tool with high sensitivity and specificity. Human Immunodeficiency Virus disease results in compromised immunity. Currently, the CD4 count is one of the immunological markers employed in HIV disease progression and assessment (Akinola *et al.,* 2014).

A total of three hundred and twenty patients participated in this study. A greater percentage of the participants were females (62%), males comprised 38% of the studied population. The current study showed female preponderance with female to male ratio of 3:2. This is in agreement to the research findings of Umar *et al*., (2021), Ibinaiye *et al*., (2014) Akinola *et al.,* (2014) and Akinbami *et al.,* (2012) in Kano, North-Western Nigeria, Maiduguri, North-Eastern Nigeria and Lagos-South Western Nigeria respectively. The higher susceptibility of females to contracting HIV could be as a result of early marriage, polygamous relationships and pelvic inflammatory disease (PID) which predisposes to micro-ulcerations of the genital tract thus increasing the risk of HIV infection. Furthermore, sexual intercourse during menstruation and presence of genital ulcers and the use of oral contraceptive which could induce cervical ectopia due to replacement of squamous by columnar epithelium, also increases the risk of women for HIV infection. In addition, female freedom to marry and re-marry when divorced could be a contributing factor in this environment. Contrary to the findings of this study, Oguntoyibo *et al*., (2008) Desalu *et al*., (2010) Ahidjo *et al.,* (2005) and Kitara *et al*., (2015) reported male preponderance in their studies in Ilorin, North-Central Nigeria, Yola, North-Eatern Nigeria, Maiduguri, North-Eastern Nigeria and Uganda respectively. This variation could be due to the restriction of their studies to only HIV patients with Pulmonary Tuberculosis (PTB) co-infection. Pulmonary Tuberculosis has been reported by Akhigbe *et al.,* (2019) as more males participated in his research work.

A total of 52.6% of the study population had normal chest radiograph. Abnormal chest raiographic findings were recorded in less than half of our study participants. The research finding is in agreement with Akinola *et al*., (2014) Akinbami *et al.,* (2013) and Ahidjo *et al.,*

(2005) from Lagos and Maiduguri respectively. In contrast, Atalabi *et al*., (2012) and Adeyekun *et al*., (2002) from Ibadan- South Western Nigeria and Benin-South-South Nigeria respectively reported abnormal chest radiograph findings in more than half of the study population. The chest radiograph may be normal in HIV- infected patients despite active infection because of their weak immunity that could not mount a granulomatous reaction to invading organisms. The disparity in the prevalence of normal chest radiographs in the above studies may be associated with the different degrees of immunosupression of the study populations. The sample size and geographical location could also be contributing factor to this variation. For this study, six major abnormal chest radiograph patterns were recorded; bronchitis (0.9%), cardiomegaly (6.2%), consolidation (4.1%), pleural effusion (4.4%), pneumonia (9.7%) and pulmonary tuberculosis (22.1%). Pulmonary Tuberculosis was the most common abnormal chest radiograph pattern. In contrast, Umar *et al.,* (2021) reported ten major abormal chest radiograph patterns; consolidation (15.8%), pulmonary infilterates (16.3%) , reticulonodular opacity (10%) , plate atelectasis (0.7%), lung collapse (0.7%), emphysematous bullae (0.7%), hilar adenopathy (4.3%) , pleural effusion (1.4%) , lung fibrosis (1.4%) and cardiomegally (4.3%).

This variation in number of abnormal radiograph patterns reported could be as a result of the sample size and pattern of reporting adopted by the radiologists. It is worthy of note, that some participants had a combination of these findings. For instance, pulmonary TB as reported in our research finding could be a combination of consolidation, hilar adenopathy, pleural effusion with fibrosis. This could be the reason for having smaller abnormal chest radiograph patterns in our study. There was an obvious variation in prevalence of various abnormal chest radiograph patterns.

In this study, pulmonary Tuberculosis was the most common abnormal chest radiograph patterns, which corroborates that reported by Umar *et al.,* (2021) in a study conducted in Sokoto to show the baseline chest radiographic findings among HIV positive adults in a poor resource economy and equally similar to the research finding reported by Atalabi *et al*., (2012) in a study conducted in Ibadan to show the baseline chest radiographic features among antiretroviral therapy naïve HIV positive children in a pediatric care program. The concordance in these studies may be due to similarity in the average immune status of the study groups as all the three study groups were HAART naïve HIV/AIDS patients coming to the hospital for the first time.

This study showed a prevalence of Pulmonary TB in 22.1% of the patients. This was less than the finding reported by Adeyekun *et al*., (2002) in Benin City, Nigeria and greater than that obtained by Akinbami *et al.,* (2013) in Lagos, Nigeria. The difference could be as a result of the smaller sample size used compared to this study. Pneumonia was reported as the second most common chest radiographic abnormality in our study, this is in contrast with the research finding carried out by Benito *et al.,* (2004) in Spain where Brochopneumonia was reported as the most common infection in HIV infected patients, this could be as a result of risk factors such as smoking and intravenous drug abusers which is prevalent in European population (Benito *et al.,* 2004).

The result of the chest X-ray patterns in patients with HIV in relation to CD4 cells count showed that patients with normal chest X-ray findings had the highest CD4 cell count. A significant difference was noted between CD4 cells counts across the various patterns of chest x-ray findings. In abnormal chest X-ray patterns, CD4 cells count was highest in those with Brochitis and the least was found in those with pulmonary TB. This implies that different chest

diseases patterns have great influence on the CD4 cells counts of the affected individual. This finding is consistent with the findings of the studies conducted by Keiper *et al.,* (1995), Akinbanmi *et al.,* (2011), Padyana *et al.,* (2012) and Ravi *et al.,* (2017), which also reported differences in the CD4 cells count across the various chest x-ray patterns in HIV patients. In Keiper *et al.,* (1995) study, which was conducted to determine the association between the radiographic presentation of pulmonary tuberculosis and CD4 T lymphocyte count in HIV-infected patient in order to provide an empirical approach for early diagnosis, treatment and isolation of infected subjects, reported different CD4 cells counts across the various chest X-rays observed. According to Keiper *et al.,* (1995), AIDs patients presenting with CD4 less than 0.20×10^9 cells/L and atypical radiographic pattern for pulmonary tuberculosis are at-risk for tuberculosis infection. Furthermore, the study conducted by Akinbanmi *et al.,* (2011), which evaluated the radiological features seen on chest radiographs of HIV/AIDs patients in relation to their corresponding CD4 count, also reported variations in the CD4 cells count across the various chest X-ray patterns. In their study, those with normal chest x-ray findings had CD4 count of < 100 cells/il and patients with lobar pneumonia chest x-ray findings had CD4 count between 100-200cells/il. According to Akinbanmi *et al.,* (2012), the CD4 count level may not be a good indicator of pulmonary infections. In Padyana *et al.,* (2012) study in India, which was evaluated chest X-ray patterns in HIV patients with tuberculosis in relation to CD4 count, also noted a variation of the CD4 count across the different chest x-ray patterns. Despite the similarities in the finding of this study and that of the aforementioned authors, there are discrepancies in the actual values of the CD4 count and the chest X-ray patterns and these differences could be attributed to the sample sizes and the natures of the various studies. According to Taylor *et al.,* (1995) and Beck *et al.,* (2001), the lungs are one of the main organs for HIV-associated disease, and approximately 70% of the patients suffer at least one respiratory complication during the course of their illness. It was observed that the majority of chest radiographic abnormalities were observed below the CD4 count of 200 cells/mm^3, it then implies that CD4 count is a true measure of immunosppression in HIV patients, contrary to the submission by Akinbami *et al*., (2012). Furthermore, a strong negative correlation was observed between chest radiograph patterns and CD4 count.

CONCLUSION

The major abnormal chest radiographic findings in HIV patients were pulmonary TB, pneumonia, pleural effusion, cardiomegaly, consolidation, and bronchitis. Major abnormal chest radiographic findings were discovered at the CD count below 200 cells/mm^3. There was a strong correlation between various chest radiograph patterns and CD4 counts in patients with HIV infection.

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