

A Study on the Radiological Presentation of HIV –Tb Coinfection and Its Correlation with Cd4 Count

DR.S.Geetha MD.*, DR.S.Malathi MD.*, DR.V.Madhavan,MD*.,
DR.Vijay Usharaj.MD*.,

*Assistant Professor, Department Of General Medicine, Government Royapettah Hospital/Kilpauk Medical College, Chennai, Tamilnadu, India.

Abstract:

Objectives: The aim of this study was to determine and compare the radiological appearance of pulmonary tuberculosis (PTB) and its correlation with CD4 count in groups of patients with and without human immunodeficiency virus (HIV) infection in ART & CHEST clinic in Kilpauk Medical College Hospital, Chennai, Tamilnadu, Chennai.

Materials and Methods: A total number of 60 patients of HIV + ve TB and 30 patients HIV –veTB were enrolled in this study.

The diagnosis of PTB was made on the basis of clinical history, physical examination, Ziehl-Neelsen microscopy on three sputum samples and chest radiography. The following issues were recorded for each radiograph: the number of zones involved with consolidation, cavitation, pleural effusion, bronchopulmonary pattern of spread; miliary disease; hilar and mediastinal lymphadenopathy.

Results: Out of all participant males are commonly infected (68%). The diffuse pulmonary involvement was more common in PTB / HIV confection group than PTB without HIV infection (27.7% vs 12%). Mediastinal lymphadenopathy and lower zone infiltration are common on chest X- ray in PTB / HIV group than HIV-ve group (35.5% vs 0%). However, HIV positive patients less commonly had cavitary lesion (0% vs 57.69%).. On analyzing the CD4 count with radiological pattern , when the count goes below 200 typical pattern chest x ray findings are more common. When CD4 count more than 200 typical pattern may occur.

Conclusion: Atypical chest x-ray findings are common in HIV- TB co infection. The most common atypical presentations are mediastinal adenopathy, lower zone infiltrations and military mottling. Cavitation is rare in HIV-TB co infection. When the CD4 count is more than 200, upper zone infiltration is more common. When the CD4 count less than 200, atypical x ray findings are common. Lymphnodes, meninges and pleura are the common sites of extra pulmonary TB involvement. Tuberculosis can occur at any level of depletions of CD4 count. But when the CD4 count is grossly low extra pulmonary TB is more common. Since TB-HIV fuel each other , early diagnosis And proper effective management are essential to reduce the morbidity and mortality.

I. Introduction

The burden of TB and HIV/ AIDS poses unprecedented challenges on the public health system in India. TB and HIV are overlapping epidemics. They are closely interlinked .untreated HIV infection leads to progressive immunodeficiency and increased susceptibility to infections including TB. TB is the leading cause of HIV related morbidity and mortality. HIV is the most important factor fuelling the TB epidemics in populations with a high HIV prevalence in many countries especially in sub Saharan Africa and increasingly in Asia and South America. Studies have shown that there is close association between HIV and TB. Evidence of this interaction included several observations repeatedly made by WHO, National governments and funding partners. These observations are the areas that have been mostly affected by HIV epidemics also report the greatest increase in the incidence and prevalence of the TB. The largest increase in TB cases has occurred among people aged 25-40 years. The very same age group mostly affected by HIV/ AIDS.TB is the most common opportunistic infection among AIDS patients. (between 60-75% of AIDS patients will develop TB) HIV prevalence among TB patients is higher than in the general population. (it is estimated a prevalence of 5.2% of HIV in adult TB in India. This study is focused to know about various Radiological presentations of tuberculosis in HIV infected patients and its correlation with CD4 count. As HIV-TB co-infection leads to increased morbidity and mortality diagnosis of HIV-TB co-infection should be done at the earliest and thereby proper treatment, adequate care and support to be given all patients with HIV/ AIDS.

Aim

To study the radiological presentation of tuberculosis in HIV positive patients and its correlation with CD4 count

II. Materials And Methods

Place of study; department of medicine , KMCH, Chennai.

Type of study; cross sectional study

Collaborating department; chest clinic, ART clinic

Duration of study; January 2016 to January 2017

Case Selection

Inclusion Criteria

1. patients who have been diagnosed as HIV positive either by Rapid test or ELISA and who have clinical and investigatory evidence of pulmonary TB or Extrapulmonary TB are enrolled in the study. These patients are picked up from ART clinic.
2. Those patients who sought medical attention for any form of tuberculosis at chest clinic OP, are chosen as controls
3. Patients between the age group of 15 to 55 are enrolled in the study.

Exclusion Criteria

1. Patients below the age of 15 and above the age of 55 are excluded in the study.
2. HIV positive individuals who did not have clinical or investigatory evidence of any form of TB were excluded.
3. Patients who had other causes of immune suppression such as diabetes, lymphoma, leukemia, visceral malignancy, malnutrition, on immune suppressive drugs were excluded.

Methodology

Clinical Examination

All HIV positive patients were meticulously examined for the presence of Pulmonary and Extra pulmonary tuberculosis. Their symptoms were analyzed in a detailed manner. Complete general examinations for the presence of opportunistic infection and respiratory system and other system examination were done All of them were subjected to the following investigations. Basic blood investigation, sputum smear for AFB, chest x ray PA view, PPD reactivity by Mantoux test and CD4 count. Special investigations were done in patients with extra pulmonary TB like FNAC of lymph node , biopsy, and CSF analysis.

Sputum Smear For Afb

Done by ZiehlNeelsen technique;

- Fix the the smear on the slide
- Cover the fixed smear with carbolfuchsin for 3 minutes
- Heat , rinse with tap water and decolorize with acid alcohol for 3-5 seconds
- Counterstain with methylene blue for 3-5 seconds
- Rinse again with tap water
- Observe under microscope by using oil immersion lens

The bacilli appears as red ,beaded rods, 2-5 μm long and 0.25-0.5 μm wide. Minimum of three sputum samples (2 spot +1 early morning sample) should be examined . results are read as follows.

If the slide has	Results	Positive (grading)
More than 10 AFB per oil immersion field	Positive	3+
1-10 AFB per oil immersion field	Positive	2+
10-99 AFB per 100 oil immersion field	positive	1+
1-9 AFB per 100 oil immersion field	Scanty	Record exact figure
No AFB per 100 oil immersion field	negative	-

In case of TB Lymphadenitis FNAC smear of the Lymphnode done and look for AFB.

Chest Skiagram

All the patient were taken x-ray chest PA views and if necessary lateral view. Infiltrations are carefully looked and also looked for cavitation, lymphnode enlargement either in mediastinum and /or hilar region.

Ppd Reactivity By Mantoux Test

ml of purified protein derivative -5TU injected intra dermally into the left forearm of the patients. The results are read at 48-72 hours later. In duration in the transverse axis is measured. Positive reactions indicate that the patients had been exposed to TB bacilli. In duration of more than 5mm is indicative of TB infection in HIV infected patients.

1. Csf Analysis

In patients who had presented with signs of meningeal irritation or altered sensorium lumbar puncture was performed under aseptic precautions. CSF was subjected to cytology and bio chemical analysis. CSF analysis favoured TB meningitis.

2. Cd4 Count Analysis

Blood was collected in heparinized bottles for flow cytometry analysis. Blood was drawn in the morning and heparinized and was sent to Chennai Medical college for analysis of CD3, CD4 and CD8 counts by flowcytometry. Flow cytometry is used in the phenotyping of T cell subsets for monitoring of HIV patients.

Procedure

The heparinized blood of about 100 µl of whole blood is simultaneously stained and analyzed for CD3 , CD4 and CD8 by FACS Count Cytometry using LASER.

III. Results And Observations

A total number of 60 patients of HIV + ve TB and 30 patients HIV –veTB were enrolled in this study. All the data were fed into a computer and the results were collected using an epidemiology incorporated software.

The following test statistics were used

- 1) Two sample t test
- 2) Wilcoxon Rank Sum test / Mann- Whitney test
- 3) Chi-square test
- 4) Fisher- exact

Table 1- Sex Distribution Analysis

	MALE		FEMALE	
	No	%	no	%
Total no of cases HIV POSITIVE TB	41	68.33	19	31.67
Total no of HIV NEGATIVE TB	23	76.67	7	23.33

On analyzing the sex distribution , males are more commonly infected than females in both groups.

Table 2- Clinical Presentation Of Tuberculosis

	Total no of cases	No of pulmonary tuberculosis	No of extra pulmonary tuberculosis
HIV +ve	60	45	15
HIV –ve	30	26	4

On analyzing the presentation of TB, pulmonary tuberculosis is most common than extra pulmonary TB.

Table 3- Presenting Sites Of Extra Pulmonary Tb

Presenting sites	HIV +ve		HIV – ve		P' valve
	No	%	No	%	
TB lymphadenitis	7	46.67	1	25	0.4257
Tuberculous pleural effusion	5	33.33	1	25	0.6272
Tuberculous meningitis	1	6.67	2	25	0.9701
G.I. tract TB	1	46.67	0	0	0.7895
Bone	1	46.67	0	0	0.7895

The sites of extra pulmonary TB are in the following order of occurrence- lymphnode, pleura, pericardium, meninges, GIT, GUT, bone and others.

Table 5- Radiological Manifestion Of Pulmonary Tuberculosis

S1 no	Radiological findings	HIV+ve No (45)	HIV +ve % (45)	HIV –ve No (26)	HIV –ve % (26)	P'
1	Cavitating lesions	0	0	15	57.69	1.1E-07
2	Upper zone infiltrations	7	15.56	7	26.92	0.1234
3	Mid zone infiltrations	2	4.44	1	3.85	0.6986

4	Lower zone infiltrations	11	24.44	1	3.85	0.03636
5	Combined	3	6.67	1	3.85	0.5331
6	Bilateral extensive	2	4.44	1	3.85	0.6986
7	Mediastinal lymphadenopathy	16	35.56	0	0	0.00202
8	Military mottling	1	2.22	0	0	0.6338
9	Normal study	3	6.67	0	0	0.2483

On analyzing the radiological pattern in HIV-TB patients, mediastinal adenopathy and lower zone infiltrations are common. There is no cavitating lesions.

Radiological manifestation of pulmonary TB

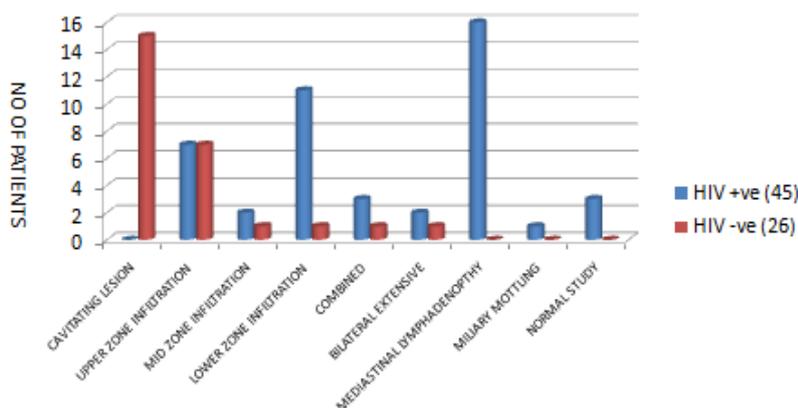
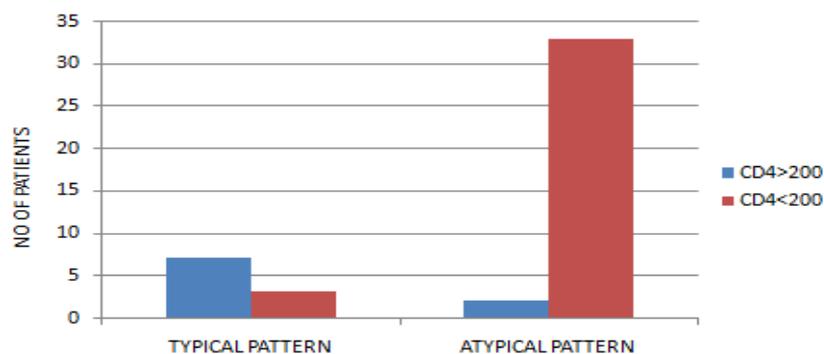


Table 6- Cd4 Count With Radiological Patterns Of Pulmonary Tuberculosis

CD4 count	Total no of pulmonary tuberculosis (45)	Typical pattern	Atypical pattern
➤ 200	10	7	3
< 200	35	2	33

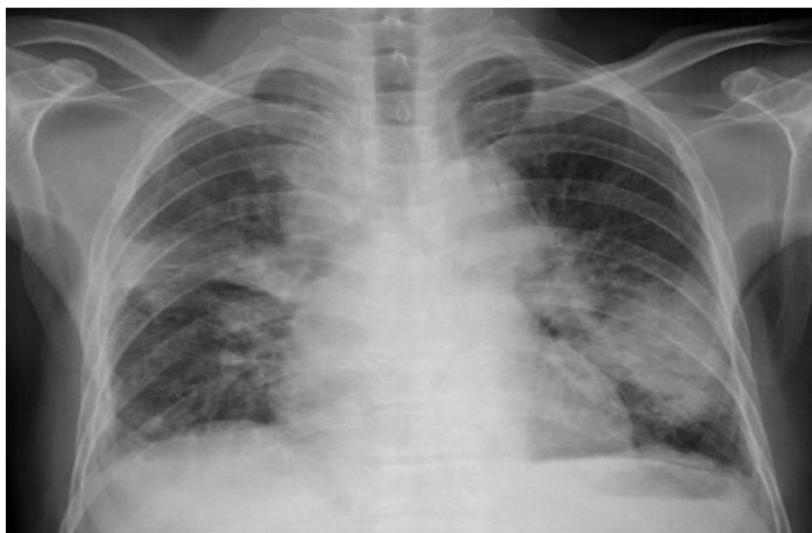
On analyzing the CD4 count with radiological pattern , when the count goes below 200 typical pattern chest x ray findings are more common. When CD4 count more than 200 atypical pattern my occur.

CD4 CORRELATION WITH RADIOLOGICAL PATTERNS OF PULMORY TUBERCULOSIS





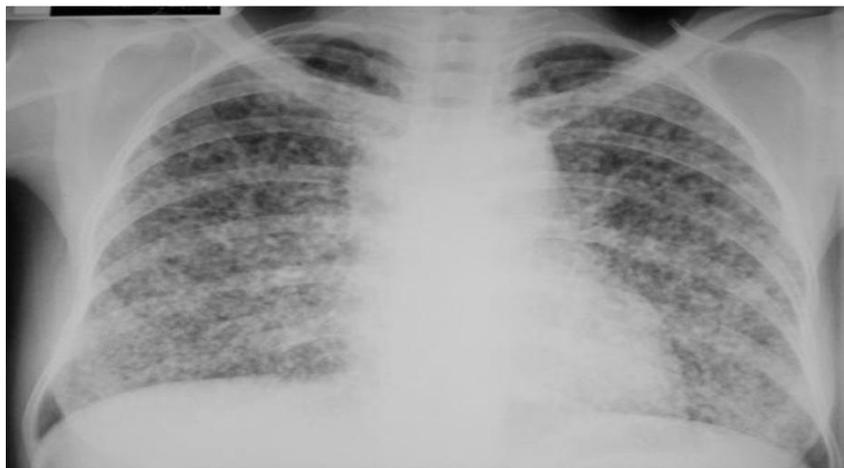
Picture 1- Chest X Ray In Hiv-Tb Co Infection – Midzone Infiltration



Picture 2- chest x ray in HIV-TB co-infection-mediastinum, hilar adenopathy with bilateral pneumonia



Picture 3- chest x ray in HIV-TB co infection- Bilateral alveolar and Interstitial opacities without excavation



Picture 4- chest x ray In HIV-TB coinfection –miliary pattern

IV. Discussion

TB is the most common opportunistic infection in HIV / AIDS patients. TB and HIV fuel each other, hence untreated HIV-TB co infection further increases the morbidity and mortality in HIV/ AIDS patients. So early diagnosis is very necessary to prevent the morbidity and mortality. This study documents the various radiological presentations of TB among HIV and non HIV patients. The x- ray presentation, sputum AFB, mantoux reactivity were analysed in both these groups. The observations made in these studies that males were commonly infected when compared to females. The mean age group for male 35.95 and female 28.84 in the HIV group and mean age group for male is 33.78 and female is 27.71 in non HIV –TB group. Out of 60 cases of HIV-TB , 45 cases are pulmonary TB , 15 cases are extra pulmonary TB and among 30 cases of non HIV-TB, 26 cases are pulmonary TB, 4 cases are extra pulmonary TB. There is no significant correlation. But various studies show that even in HIV / AIDS pulmonary TB is the most common. It basically depends on the level of patients immunosuppression. When TB occurs in the earlier period of HIV infection, pulmonary TB is more common. When TB occurs late in the period HIV infection ,i.e after a significantly depressed CD4 count , extra pulmonary TB is more common. Sometimes both pulmonary and extra pulmonary TB may co-exist in the same patient.

On analyzing the extra pulmonary TB , out of 15 cases, 7 cases are TB Lymphadenitis, 5 cases are pleural effusion, 1 is TBM, 1 is GIT, 1 is bone. The various studies also document the site of EPTB are in the same order of occurrence like lymphnode, pleura, pericardium, meninges, GIT, GUT, bone and others. Dr. Fitz Gerald, Dr.Stan et al university of coloumbia have noted these points. There are interesting observations on made in the x-ray chest. In HIV –TB the most common x-ray presentation are mediastinal adenopathy, lower zone infiltration, combined bilateral extensive infiltration and millary mottling. Out of 45 cases , 16 cases are found to be mediastinal adenopathy whereas no cases of mediastinal adenopathy was found in non HIV group. The p' value is 0.00020 which is significant. Lower zone infiltration was 10 out of 45 patients in HIV-TB group whereas 1 Case was found in non HIV-TB . The p' valve is 0.03636 which is significant. Various other studies also shown this atypical presentation in high percentage. This is very much consistent with observation made by ZumlaMalon and Henderson et al. They have found 50% of cases are having mediastinal adenopathy. Similar observation also documented by DianevHavlir, Peter F. Branes M.D. et al.

Another interesting finding In these studies are absence of cavitation in HIV TB whereas 58% are cavitating in non HIV group. The p' value is 0.00 which is significant. This finding was consistent with observation made by Decker CF and Lazarus A et al mentioned in that post graduate medical journal 2000. Upper lobe cavitating lesions is not common is noted by several other authors also and including ZumlaMalon and Henderson et al. There is 1 case of miliary mottling in HIV whereas no millary mottling in non HIV. The p' value is 0.6338 which is not significant. Dr.Sowmyaswaminathan et al TRC has noted 11 case out of 78 HIV – TB . This incidence is quite higher than made in the study.

3 cases are normal chest x-ray in spite of sputum AFB positivity in HIV/ TB group. This normal chest x-ray in HIV patient is also noted by DianevHavlir, Peter F. Branes M.D et al. ideally all HIV patient with normal chest x-ray should be subjected to HRCT thorax because the finding of low density lymphnode with peripheral enhancement on a contrast CT is highly predictive of tuberculosis. On analyzing the radiographic pattern with CD4 count, it is very well noted when the count > 200 upper zone infiltration is common .when the count is < 200 atypical presentation like mediastinaladenopathy, lower zone infiltration are common. This has significant p' valve . Various studies also proved this statement.

On analyzing CD4 count the mean CD4 count of 45 out of 60 cases of pulmonary HIV-TB is 174.2 whereas the mean CD4 15 out of 60 cases of extra pulmonary HIV-TB IS 114.6. The p' value is 0.0285 which is significant. This is consistent with the observation made out of Post FA , Wood R , Pillay GP et al in south Africa and various other authors also.

Infect tuberculosis can develop at any CD4 count. If the CD4 count is moderately low pulmonary tuberculosis is common. But when the CD4 count is very much lowered extra pulmonary tuberculosis is more common than pulmonary TB. Moreover atypical mycobacterial lesions and opportunistic infections are common.

V. Conclusion

As TB is the most common opportunistic infection in all HIV positive individuals , hence all HIV patients should be screened for TB and all TB patients should be screened for HIV status. Atypical chest x-ray findings are common in HIV- TB co infection. The most common atypical presentations are mediastinal adenopathy, lower zone infiltrations and military mottling. Cavitation is rare in HIV-TB co infection. When the CD4 count is more than 200, upper zone infiltration is more common. When the CD4 count less than 200, atypical x ray findings are common. Lymph nodes, meninges and pleura are the common sites of extra pulmonary TB involvement. Tuberculosis can occur at any level of depletions of CD4 count. But when the CD4 count is grossly low extra pulmonary TB is more common. Since TB-HIV fuel each other , early diagnosis and proper effective management are essential to reduce the morbidity and mortality.

Bibliography

- [1]. Corbett EL, Watt CJ, Walker N, Maher D, Williams BG. The growing burden of tuberculosis; global trends and interactions with HIV epidemic (Archives of int medicine 2003, 163;1009-1021)
- [2]. A clinical manual on HIV / TB (second edition) by WHO , GENEVA, 2004.
- [3]. UNAIDS- Updated on Global facts and figures (Dec 2006).
- [4]. http://data.unaids.org/pub/epi_report/2006.
- [5]. WHO Global tuberculosis control: surveillance, planning, financing report 2007, Geneva, WHO, 2007(WHO/HTM/TB/2007/376)
- [6]. TB India 2007-RNTCP status Report published central TB division, directorate general of public services, Ministry of Health & Family Welfare, New Delhi.
- [7]. Impact of HIV on tuberculosis in Zambia; a cross sectional study –A M Elliott, N Luo, G Tembo, B Halwiindi, G Steenberg, L Machiels, J Pobee, P Nunn, R J Hayes ,and K P Mc Adam. BMJ 1990 September 1: 301(6749); 412-415.
- [8]. Jamal LF, Moherdau F (2007) Tuberculosis and HIV infection in Brazil: magnitude of the problem and strategies for control. Rev Saúde Pública 41: 104-110.
- [9]. Greenberg SD, Frager D, Suster B, Walker S, Stavropoulos C, et al. (1994) Active pulmonary tuberculosis in patients with AIDS: spectrum of radiographic findings (Including a normal appearance). Radiology 193: 115-119.
- [10]. Long R, Maycher B, Scalcini M, Manfreda J (1992) The chest roentgenogram in pulmonary tuberculosis patients seropositive for human immunodeficiency virus type I. Chest 99: 123-127.
- [11]. Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents Morbidity and Mortality. Weekly Report 58: 5. (2011) Tuberculosis National Institute for Health and Clinical Excellence.
- [12]. 11. Elliott AM, Halwiindi B, Hayes RJ, Luo N, Tembo G, et al. (1993) The impact of human immunodeficiency virus on the presentation and diagnosis of tuberculosis in a cohort study in zambia. J Trop med hyg 96: 1-11 .
- [13]. Bakari M, Arbeit RD, Mtei L, Lyimo J, Waddell R, et al. (2008) Basis for treatment of tuberculosis among HIV-infected patients in Tanzania: the role of chest x-ray and sputum culture. BMC Infect Dis 8: 32.
- [14]. Noronha D, Pallangyo KJ, Ndosi BN, Lweno H, Sabuka SR (1991) Radiological features of pulmonary tuberculosis in patients infected with human immunodeficiency virus. East Afr Med J 68: 210-215.
- [15]. Saks AM, Posner R (1992) Tuberculosis in HIV positive patients in South Africa: a comparative radiological study with HIV negative patients. Clin Radiol 46: 387-390.
- [16]. Padyana M, Bhat RV, Dinesha M, Nawaz A (2012) HIV-Tuberculosis: A Study of Chest X-Ray Patterns in Relation to CD4 Count. N Am J Med Sci 4: 221-225.
- [17]. Keiper MD, Beumont M, Elshami A, Langlotz CP, Miller WT Jr (1995) CD4 T lymphocyte count and the radiographic presentation of pulmonary tuberculosis. A study of the relationship between these factors in patients with human immunodeficiency virus infection. Chest 107: 74-80
- [18]. Post FA, Wood R, Pillay GP (1995) Pulmonary tuberculosis in HIV infection: radiologic appearance is related to CD4+ T-lymphocyte count. Tuberc Lung Dis 76: 518-521.
- [19]. Ahmad Z, Shameem M (2005) Manifestation of tuberculosis in HIV infected patients. JIACM 6: 302-305
- [20]. Prasad R, Saini JK, Gupta R, Kannaujia RK, Sarin S, et al. (2004) A comparative study of Clinico-radiological spectrum of tuberculosis among HIV Seropositive and HIV seronegative patients. Indian J Chest Dis Allied Sci 46: 99-103
- [21]. Mabilia Babela JR, Makosso E, Senga P (2006) Radiological Specificity of pulmonary tuberculosis in Congolese children: effect of HIV infection. Med Trop 66: 255-259.
- [22]. Awoyemi OB, Ige OM, Onadeko BO (2002) Pattern of active pulmonary tuberculosis in human immunodeficiency virus seropositive adult patients in University College Hospital, Ibadan, Nigeria. Afr J Med Med Sci 31: 25-31.
- [23]. Bellamy R, Ruwende C, Corrah T, McAdam KP, Whittle HC, et al. (1998) variations in the NRAMPI gene and susceptibility to tuberculosis in West Africans. N Engl J Med 338: 640-644.