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RESEARCH ARTICLE

EVALUATION OF TUBERCULAR PLEURAL EFFUSION IN HIV SEROPOSITIVE PATIENTS AND ITS CORRELATION TO CD4 COUNT

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Abstract

Aim:- To observe the characteristic of tubercular pleural effusion in HIV seropositive patients and its correlation to CD4 count.

Material Method:-This study was conducted in the department of Pulmonary Medicine VSS Medical College Burla, Sambalpur , Odisha during the period of November 2014 to 2016. 44 HIV seropositive patients with pleural effusion were studied in correlation to CD4 counts.

Results:-Out of 44 HIV seropositive patients with pleural effusion were studied of which 84% were males and 16% females. Maximum number of patients belonged to the age group 31-40 yrs males 16 & female 1(38.6%) followed by 21-30 yrs 25%(males 7 and females 4). Maximum number of males were in age group 31-40 whereas maximum females were in age group 21-30. Commonest occupation was driver 10 (22.7%) followed by labourers 9(20%). Commonest constitutional symptoms were fever and generalized weakness in 26 patients (59%) and cough was the commonest respiratory symptoms in 84% of cases followed by chest pain in 63% and breathlessness in 50% of cases. Majority of effusion were Right side 22 cases(50%), Left side 15(34%) and bilateral in 7(15.9%) cases. Most of the effusions were moderate in 31(70.4%) cases, minimal in 9(20%) and massive in 4(9%).Pleural fluid was straw coloured in 39 cases(89%) and haemorrhagic in 5(11%) cases.Maximum patients (23 ie 52.3%) were having CD4 count in range of 201-500, followed by 11 cases in range of 101-200. 2 patients were having CD4 count >500/cumm and 4 below <50/cumm.ADA level was >100 in 1 case ,<40 in 1 (2.27%), >60 in 23 (52%) and between 40 to 60 in 19 cases(43.18%).Out of 44 patients, 39 showed predominantly lymphocytic pattern, 5 cases showed neutrophilic pattern. In 5 cases, RBCs were also found in pleural fluid.Out of total 44 cases, number of patients having pleural fluid positive for AFB was 6 ie 13.6% of cases. Pleural fluid

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for AFB was positive at lowest CD4 count of 48 and highest at CD4 count of 304/cumm.Corrected Chi-square test showed that there was significant association between CD4 RANGE and TUBERCULIN TEST (p=0.12).Corrected Chi-square test showed that there was no significant association between CD4 RANGE and radiological findings (p=0.68).

Conclusion:- Tuberculosis is one of the most common opportunistic infection associated with HIV irrespective of CD4 status. So, high degree of clinical suspicion, early and rapid diagnostic methods like CB NAAT MTB/RIF and appropriate antitubercular therapy should be instituted to improve quality of life.

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Introduction:-

Tuberculosis (TB) and HIV have been closely linked since the emergence of AIDS. Worldwide TB is the most common opportunistic infection affecting HIV-seropositive individuals[1] and it remains the most common cause of death in patients with AIDS. It is estimated that there are 2.1 million people living with HIV in India with estimated adult HIV prevalence of 0.27%(range: 0.2-0.4)[2]. TB accounts for 25% of deaths among People living with HIV and AIDS(PLHIV)in India. It ranks second in the world and accounts for about 10% of the global burden of HIV associated TB[2]. HIV infected patients have approximately 8 times greater risk of TB than persons without HIV and the risk continues to increase with drop in CD4 count. CD4 cells (often called T-cells or T-helper cells) are a type of white blood cells that play a major role in protecting our body from infection. They send signals to activate body's immune response when they detect "intruders," like viruses or bacteria. They are made in spleen, lymph nodes and thymus. Once a person is infected with HIV, the virus begins to attack and destroy the CD4 cells of the person's immune system. HIV uses the machinery of the CD4 cells to multiply (make copies of itself) and spread throughout the body. This process is called the HIV life cycle. HIV can destroy entire family of CD4 cells. HIV and TB work together to shorten life span. The presentation of TB in HIV infected patient may vary with degree of immunosuppression. As the HIV disease progresses the clinical presentation is more likely to be extrapulmonary or smear negative than in HIV uninfected person[7]. Unlike other opportunistic infections which occur over a particular range of CD4 counts, it can occur throughout the course of HIV. Clinical presentation however depends on the level of immunosuppression. Typical manifestations such as upper lobe disease, sputum positivity and cavitation are frequently seen in early HIV infection when the CD4 count is >200/cumm. Atypical features begin to occur as the immunity declines and CD4 count goes <200/cumm with more extrapulmonary manifestations[8]. Extrapulmonary TB is the commonest cause of pyrexia of unknown origin(PUO) among HIV positive individuals in developing countries.[8] Lymph nodes are the most common site of involvement followed by pleural effusion and virtually every site of the body can be affected. The other forms of tuberculosis include pericardial effusion, abdominal TB and TB meningitis[9]. The majority of pleural effusions in patients with HIV infection are caused by infections; however, about a third are due to noninfectious causes[10]. Pleural effusion is usually unilateral and asymmetric, may be associated with parenchymal opacities. Interestingly, among patients with AIDS, the percentage of tuberculosis cases that have a pleural effusion is higher in patients with CD4+ counts above 200 cells·μL-1 than in those with CD4+ counts below 200 cells·μL-1 [11]. This observation supports the hypothesis that tuberculosis pleuritis is predominantly due to delayed hypersensitivity rather than a direct infection of the pleural space. The pleural fluid acid-fast bacillus (AFB) stain is positive in ~15% of patients with AIDS[12] but in only ~1% of patients without AIDS[13]. The pleural fluid and the sputum culture are each positive in 40–50% of patients with AIDS but in only 10–15% of patients without AIDS[14]. In patients with tuberculous pleuritis, the purified protein derivative (PPD) skin test is less likely to be positive if the patient has AIDS. It has been shown that pleural fluid characteristics are similar in HIV-positive and negative patients with TB pleurisy[15,16], and that particularly ADA is not affected by HIV-status[17]. This study is done to evaluate the tubercular pleural effusion in HIV seropositive patient and its correlation to CD4 count.

The aim of study is to observe the characteristic of tubercular pleural effusion in HIV seropositive patients and the impact of CD4 count on pattern of tubercular pleural effusion in HIV patients

Materials And Methods:-

This study was conducted in the department of Pulmonary Medicine VSS Medical College Burla, Sambalpur ,Odisha from NOV 2014 to SEP 2016. All work was performed according to the international guidelines for human experimentation in clinical research.This is a cross sectional observational study. The HIV seropositive patients with pleural effusion were included in this study. Patients having co existing immunocompromised conditions such as Diabetes Mellitus, Chronic Kidney Disease, patient on long term immunosuppressive therapy and patient not willing to give consent or participate in the study were excluded from the study. In all patients, initially detailed clinical examination was done alongwith chest x ray. Based on chest x ray pleural effusion was classified as mild , moderate and massive. Patients with pleural fluid level upto 5^{th} rib anteriorly were classified as mild, upto 2^{nd} rib anteriorly as moderate and above the second rib as massive pleural effusion.The procedure was explained carefully to the patient, and a signed consent form was obtained.Pleural fluid aspiration was done under all aseptic precautions and local anaesthesia. An 18G needle attached to 3 way cannula and 50 ml syringe was inserted in pleural cavity. Pleural fluid was analysed both macroscopically and microscopically. The colour, odour and turbidity was noted and fluid was sent for biochemical investigation for adenosine deaminase(ADA) , glucose, protein and AFB in plane tube and in an ethylenediaminetetraacetic acid tube for total and differential count. Exudates and transudates were classified based on Light's criteria.HIV serological status was assessed using three recombinant enzyme linked immunoassay(ELISA) methods as per NACO guidelines. Testing positive by all 3 methods was considered as diagnostic of HIV infection. CD4 T lymphocytes counts in HIV seropositive patients were assessed using CYSFLOW counter based on flow cytometry technique.PTB was diagnosed among HIV seropositive and seronegative patients by clinical history and examination , sputum smear examination for AFB by ZiehlNeelsen and fluorescent staining methods as per RNTCP and chest X ray. Pleural fluid analysis - Diagnostic aspiration was done and diagnosis of tubercular pleural effusion was made by cytological evaluation of pleural fluid, estimation of pleural fluid ADA, glucose, protein, LDH and demonstration of pleural fluid AFB. Routine baseline investigations like complete hemogram, blood glucose level, serum electrolyte, LFT and RFT, Sputum for AFB, Chest X ray lateral view, Tuberculin skin test with 5 TU, FNAC or Excisional biopsy, CT Scan of thorax and abdomen. All data were statistically analyzed and a p value of less than 0.5 was considered significant.

Observation:-

A total of 44 HIV seropositive patients with pleural effusion were studied in correlation to CD4 counts. The age of the study population ranged from 15-65 yrs. The mean age of male were 37.51±10.05 and female were 34.85±14.15. Considering the total population, maximum number of patients belonged to the age group 31-40 yrs (males 16 & female 1,38.6%) followed by 21-30 yrs 25% (males 7 and females 4). Maximum number of males were in age group 31-40 whereas maximum females were in age group 21-30. The commonest occupation was driver 10 (22.7%) followed by labourers 9(20%) . Farming was occupation of 15.9% of the patients. All the females included in study were housewives and their number was 7 (15.9%). Other occupations included hotel staffs (6.8%), weaver (2.27%), vendor (2.27%), businessman(4.5%) and student(2.27%). The mean BMI of the patients was 18.38±2.28 **kg/m^2** with range 14.10 – 25.80 **kg/m^2** & there was no patient with obesity (0.0%). Most of the patients were underweight (42.0%) followed by with normal body weight (39.6%) which was significantly higher ($Z=5.98;p<0.0001$).

The Commonest constitutional symptom was fever and generalized weakness in 26 patients (59%). Of the respiratory symptoms, cough was the commonest presenting problem in 84% of cases followed by chest pain in 63% and breathlessness in 50% of cases. GI symptoms like pain abdomen, abdomen distension and diarrhea was present in about 10% of cases. Neurological symptoms like disorientation , quadriparesis and headache was seen in 11%. The majority of effusion in Right side with 22 cases(50%), in Left side 15(34%) and bilateral in 7(15.9%) cases. The most of the effusions were moderate in 31(70.4%) cases, minimal in 9(20%) and massive in 4(9%). The pleural fluid was straw coloured in 39 cases(89%) and haemorrhagic in 5(11%) cases. The coexistence of other parenchymal or systemic lesions with pleural effusion were lymphadenitis in 7 cases(15.9%), parenchymal lesion associated in 6(13.6%) and disseminated tuberculosis in 5(11.3%). The associated lung parenchymal lesion in chest x-ray in addition to pleural effusion were upper zone infiltration in 3(6.8%), fibrocavitory lesion in 1(2.27%) patient ,miliary shadows and mediastinal lymphadenopathy was seen in 2 (5%) cases each. The tuberculin test was negative in 24 cases(54.5%) i.e. induration <5mm and 20 patients had positive tuberculin test i.e. induration >5mm. The maximum patients (23 ie 52.3%) were having CD4 count in range of 201-500, followed by 11 cases in range of 101-200. 2 patients were having CD4 count >500/cumm and 4 below <50/cumm. Thus proportion of CD4 count in range of 201-500 cumm was significantly higher ($Z=3.96;p<0.001$). The overall mean CD4 count was 223.81±179.81.

Among males mean CD4 count was 225.43±188.43 and in females it was 215.28±208.28. The ADA level was >100 in 1 case ,<40 in 1 (2.27%), between 40 to 60 in 19 cases(43.18%), between 60 to 80 in 16 (36.30%) cases and between 80 to 810 in 7 (15.90%) cases. Proportion of patient with ADA between 40-60 U/L (43.18%) and 60-83 U/L (36.3%) were significantly higher ($Z=3.28;p<0.001$). The cellular pattern of pleural fluid were predominantly lymphocytic pattern in 39 cases, neutrophilic pattern in 5 cases and RBCs were also found in 5 cases.

Table 1:- Correlation Of Pleural Fluid AFB Positivity With CD4 Count.

SL. NO	CASE NO	BACILLARY LOAD	CD4 COUNT(/cumm)
1	19	1+	48
2	11	1+	291
3	25	2+	126
4	33	1+	304
5	35	2+	68
6	42	1+	128

Out of total 44 cases, number of patients having pleural fluid positive for AFB was 6 ie 13.6% of cases. Pleural fluid for AFB was positive at lowest CD4 count of 48 and highest at CD4 count of 304/cumm

Table 2:- Correlation Of Tuberculin Positivity With CD4 Count.

CD4 RANGE (/cumm)	TUBERCULIN TEST		TOTAL
	POSITIVE (>5mm)	NEGATIVE (<5mm)	
<50	0	4	4
51-100	1	3	4
101-200	3	8	11
201-500	14	9	23
>500	2	0	2
TOTAL	20	24	44

χ^2 =11.14 ; p<0.0011 S-Significant. Corrected Chi-square test showed that there was significant association between CD4 RANGE and TUBERCULIN TEST (p=0.12). In this study, tuberculin test was negative in all 4 cases having CD4 count <50/cumm and positive in 16 out of 25 cases ie 68% having CD4 count >200/cumm. In patients having CD4 between 51-100/cumm, 25% were TST positive and in range of 101-200/cumm , 36% were TST positive.

Table 3:- Correlation Of CD4 Count With Radiological Features In Addition To Pleural Effusion.

CD4 RANGE (/cumm)	RADIOLOGICAL FINDINGS			
	INFILTERATION	CAVITY	LYMPHADENOPATHY	MILIARY SHADOW
<200	0	0	0	1
200-500	3	0	1	1
>500	0	1	1	0

χ^2 =1.12 ; p=0.68 NS-Not Significant. Corrected Chi-square test showed that there was no significant association between CD4 RANGE and radiological findings (p=0.68).

Discussion:-

Coinfection with TB and HIV has already been reported as one of the most significant global publichealth concerns.[14] Tuberculosis is the commonest opportunistic disease in HIV positive persons in India irrespective of the CD4 count[15] . HIV/AIDS pandemic has caused a resurgence of TB, resulting in increased morbidity and mortality worldwide[16]. With decrease in CD4 count in HIV seropositive patients, atypical presentation are more common.The high frequency is related to the failure of the immune response to contain M. tuberculosis, thereby enabling haematogenous dissemination and subsequent involvement of single or multiple non-pulmonary sites[17]. Diagnosis and treatment should be done promptly to prevent the emergence of MDR and XDR TB.

In this study, 44 HIV seropositive patients with pleural effusion were studied out of which 84% were males and 16% females. This is comparable to the study by Sunita H et al[18] in which 90% were males and 10% females. Patel et al[19]

showed 82% males were involved and 18% females.NACO report also shows 61% males and 39% females[20]. Male preponderance is seen as they are more exposed to outdoor activities and travelling. Most of the patients belonged to age group 21-40 yrs(68%) with mean age of male being 37.3±10.01 yrs and females 34.8 ±14.15yrs.This is the productive age group causing financial and social burden. Sunita H et al[18] found most of the patients in age group of 20-30 yrs. In study done by Manjareeka et al[21], majority of the patients belonged to age group 30-45 yrs in accordance with my study. This reflects that persons who are sexually more active are at increased risk for HIV infection and thereby for tuberculosis[22]. However , there were no females in the age group 15-20 yrs in our study. In present study, most common occupation was driving (22.7%) followed by labourers(20%), farmers and housewives 15.9% each,hotel staffs(6.8%), businessman(4.5%), weaver,vendor and student constituting 2.27% each. Ninan et al[23] showed most common occupation of labourers(54%) followed by drivers(22%). In study by Patel et al[19] most common occupation was farmers(30%), manual labourers(22%) and driver (16%) The percentage of the professions is thus seems to vary in different studies, largely due to the differences in geographical distribution in the occupational patterns and the source from where the patients were selected. Most of the patients in my study belonged to lower socioeconomic class similar to the study by Manjareeka et al[21]. Interestingly, in my study all the 7 females were housewives and married, not involved in any outdoor occupation and their spouse were also HIV seropositive except one who had history of blood transfusion thrice for some systemic illness. Similar results were found in study by Soumya Swaminathan et al[24] in which except in one case, both the husband and wife were affected. A vast majority of patients(75%) in my study were addicted to one or more substance regularly. 13(27.2%) patients were alcoholic, 1 smoker and 19(43%) were addicted to both alcohol and smoking. Ninan et al[23] showed 88% patient were using intoxicating substance in one way or other.

In this study, the most common presenting symptom was cough (84%) followed by chest pain(63%) , fever and generalized weakness(59%). Cough is an alarming sign making the patient alert to seek medical advice. These findings are supported by Manjareeka et al[21] study in which cough was predominant symptom in 90% patients. Patel et al[19] found cough to be main symptom in 94% of patients followed by fever in 86% , wt loss in 78% and loss of appetite in 62% cases. Fever was the most common symptom followed by wt loss and cough in 42% cases in a study by Sharma et al[25]. In my study, 11% of patients showed neurological symptoms like headache,disorientation and quadriparesis which was a significant finding, as it was indicative of disseminated form of tuberculosis. 57% of the patients in my study were underweight, out of which 2 were very severly underweight. 39% patients were having BMI within normal limit and 2.27% were overweight. HIV and TB both being a chronic disease lead to weight loss because of metabolic alterations, anorexia, malabsorptive disorders, hypogonadism, and excessive cytokine production[26]. This can be explained as generalized weakness and weight loss was a common finding in my study. In this study, 84% of the effusion were unilateral, confined to right side in 50% cases and left side in 34% cases. 16% of the pleural effusion was bilateral. Sunita H et al[18] also showed similar results with predominance of rt side effusion followed by left side, however incidence of bilateral effusion in their study was 22% which is greater than this study. Less number of bilateral pleural effusion in my study may be due concomitant minimal parenchymal lesion. Miller et al[27] also showed bilateral plef in 25% of cases. In a study by Ahmed Z et al[28], 13.85% of the patients presented with bilateral pleural effusion. In all the studies,rt side was more commonly involved, except that by Frye et al[17] in which Lt side effusion was common in 59% of the cases. Bilateral pleural effusion indicates disseminated form of TB in HIV which occurs with decreasing CD4 count. It was observed that 31(70%) of the effusions were moderate, 20% minimal and 9% presented with massive effusion, Thus proportion of moderate effusion was significantly higher ($Z=7.16; p<0.0001$) In contrast to the study by Miller et al[27] where 7 out of 8 tubercular effusion were small and only one was moderate. Frye et al[17] found that 50% of the effusion were massive and 45% were moderate and only one was small effusion. In this study, 26 patients(59%) had pleural effusion without any parenchymal or systemic involvement. Lymphadenitis was associated in 7 (15.9%), coexistent parenchymal lesion was seen in 6 cases(13.6%) and disseminated form of tuberculosis was present in 5(11.3%). These parenchymal lesions were in form of infilteration in 3(6.8%), fibrocavitory lesion 1(2.27%) and miliary shadows in case of 2 cases(4.5%)Bhattacharya et al[29] showed that pleural effusion may be isolated or associated with parenchymal infilterate and miliarypattern.In a study by Frye et al[17] 16(73%) out of 22 patients were having parenchymal infilterate in addition to pleural effusion, mostly lower lobe in 12 cases followed by upper lobe and adenopathy in 2 patients each. Adenopathy was found in 4(17%) patients as compared to present study where 2 patients(4.5%) were having mediastinal/paraortic lymphadenopathy, which is quite high in comparison to present study. Corrected Chi-square test showed that there was no significant association between CD4 RANGE and radiological findings ($p=0.68$). Mean induration after tuberculin test in this study was 5.13±4.33mm. It was positive ie induration > 5mm was seen in 20 patients(45%) with induration 5-10 mm in 16(36%), 10-15mm in 3(6.8%) and one patient with induration >20mm. 24(54.5%) patients were found to have negative tuberculin test, which was significantly higher ($Z=2.62; p=0.0088$) Sunita H et

al[18] and Patel et al[19] reported 26.6% and 32% tuberculin test positivity. The cut off value of induration in their study was 10mm to be regarded as positive. Other studies[29,17,30,31] show tuberculin positivity to vary between 20 to 64%. Although, a positive tuberculin skin test increases the likelihood of tuberculosis, a negative test reflects the immunodeficiency status and does not rule out the presence of active tuberculosis[32]. So, tuberculin test is not of much value in HIV-infected persons, particularly those with advanced disease. The mean CD4 count in my study was 223.81±179.81/cumm with males having mean CD4 of 225.43±188.43 and females 215.28±208.28. the degree of immunosuppression was almost equal for both sexes. Minimum CD4 count in males and females was 28 and 84 respectively. Frye et al[17] mean CD4 count was 259±51 with range in between 28-740. CD4 count > 200/cumm was seen in 25(57%) and <200/cumm in 19(43%) of cases. 4(9%) were having CD4<50/cumm and in 2 (4.5%), CD4>500/cumm. . Thus proportion of CD4 count in range of 201-500 cumm was significantly higher (Z=3.96;p<0.001).Interestingly, among patients with AIDS, the percentage of tuberculosis cases that have a pleural effusion is higher in patients with CD4+ counts above 200 cells·μL-1 than in those with CD4+ counts below 200 cells·μL-1[33]. The prevalence of pleural effusion in tuberculous HIV patients with CD4+ T-lymphocyte (helper-inducer) counts >200 cells/mL was 27%, while it was only 10% in HIV patients with tuberculosis and CD4+ T-lymphocyte counts <200 cells/mL[33]. Macroscopic appearance of the pleural fluid revealed 39(89%) to be straw colour while 5(11%) were haemorrhagic in contrast to study by Frye et al[17] where 69% was straw coloured and 31% serosanguinous. The value of pleural fluid ADA was < 60 U/l in 46% cases and >60 in 54% with mean ADA of 65.06 U/l. Riantawan P, et al[13] reported mean ADA in tubercular pleural effusion to be 110/cumm. Levine H, et al[34] found Pleural fluid ADA (adenosine deaminase) to be a cost-effective alternative and exhibits good sensitivity and specificity. A pleural fluid ADA level of 60 or more in HIV positive patients gives a sensitivity of 95% and specificity of 96%[35]. However Baba et al [36] showed that In all HIV-infected patients regardless of CD4 counts, the sensitivity of ADA was 94% when the cutoff value of 30 U/l was used and specificity of 95%. Adenosine deaminase (ADA) a T lymphocyte enzyme that catalyzes the conversion of adenosine and deoxyadenosine to inosine and deoxyinosine, respectively. Two different molecular forms of ADA, ADA 1, and ADA2 have been identified [17] ADA1 is found in all cells, with its greatest activity in lymphocytes and monocytes. ADA2 isoenzyme is found mainly in monocytes/macrophages. Most of the ADA found in tuberculous pleural fluid is ADA2, whereas most of the ADA found in other causes of pleural fluids is ADA1. Testing ADA levels in the pleural fluid is an easy, inexpensive, and useful test to establish the diagnosis of pleural TB. ADA retains its high utility in all HIV-infected patients[13] even patients with low CD4 counts[36]. All the pleural fluid in this study were exudative by Light's Criteria of >3g/dl with mean value of 5.39 ± 1.31. This is comparable to the study by Soe Z et al[37] where the pleural fluid protein 4.91 ± 1.22 g/dl was reported and Sunita H et al[18] where only one sample was transudative and rest exudative. Riantawan et al[13] found mean protein value in pl fluid to be 5.2 g/dl quite similar to present study. Range of Pleural fluid glucose was 29 - 140 mg/dl with mean value of 73.59 ± 23.63 mg/dl which was low as compared to Riantewan et al[13] analysis showing mean glucose of 92mg/dl. The pleural fluid glucose ranged from 29 to 101 mg/dl in study by Sunita H et al[18] in accordance with present study. This is in contrast to study by Light et al[38](114), they reported pleural fluid glucose <60 mg/dl. In this study, value of LDH ranged from 55-1640 with a mean of 664.01±433 in contrast to Frye et al[17] study showing mean LDH 1184±309. In 39 (88%) patients, pleural fluid was lymphocytic predominant. A lymphocytic pleural effusion is most often the result of tuberculosis[38]. Neutrophils were predominantly seen in 5(12%) cases reflecting an acute process[34]. Among these, 5 patients had RBCs in pleural fluid present. Frye et al[11] found lymphocytic predominance in 66% ranging from 3 – 100% with a mean of 69±8% and polymorphonuclear cells in 33% cases. Bhattacharya et al[29] also showed lymphocyte predominance inspite of low number of blood lymphocyte in concordance with present study. Sunita H et al[18] also had similar findings with 80% lymphocytic predominance and 11% haemorrhagic. In this study, pleural fluid for AFB was positive in 6 (13.6%) cases. This is comparable to Bhattacharya et al[29] where positivity was 15%. Other studies by Richter et al[39]and Heyderman et al[40] showed pleural fluid AFB positivity ranging from 5 to 18%. In my study, in 4 out of 6 AFB positive for pleural fluid CD4 count <200/cumm implying greater positivity with decreasing CD4 count.Heyderman et al[40] found that the more immunocompromised the patient, the higher chance of finding TB organisms in the pleural fluid and the pleura itself. A CD4 count of < 200×106/L was associated with a positive pleural fluid smear. Increased pleural fluid AFB positivity may be attributed to increased bacillary load in immunocompromised patients leading to direct invasion by mycobacterium as compared to non HIV patients where delayed hypersensitivity appears to be the main etiology of pleural effusion. One patient in this study having CD4 count 264/cumm and concomitant parenchymal lesion was found to be sputum positive for AFB. However his pleural fluid for AFB was negative with pleural fluid analysis of ADA 52 U/l, glucose 74mg/dl and protein 6.2g/dl. Similarly tuberculin positivity in this study was also found to be decreasing with decreasing trend of CD4 count. Out of 8 patients having CD4< 100, only 1 was having positive tuberculin test. Positivity increased with increase in CD4 count and was positive in 16 of 25 patients with CD4> 200/cumm.The limitations of this study were less number of patients in study

and in TB HIV coinfection, inspite of high burden of bacillary load, we found less number pleural fluid AFB positivity. The yield could have increased with CBNAAT MTB/RIF assay.

Conclusion:-

HIV TB coinfection has significant impact on the patient as well as to the society. Tuberculosis is one of the most common opportunistic infection associated with HIV irrespective of CD4 status. So, high degree of clinical suspicion, early and rapid diagnostic methods like CB NAAT MTB/RIF and appropriate antitubercular therapy should be instituted to improve quality of life.

References:-

1. Mayer KH, Hamilton DK. "Synergistic Pandemics:confronting the global HIV and Tuberculosis Epidemics. Clin Infect Dis. 2010 May15;50suppl 3:S67-70.
2. Integrated training module for HIV/TB collaborative activities 2015, Govt. of India MoHFW.
3. Denis, Marie F., "Extrapulmonary tuberculosis in HIV-positive and HIV-negative children in Haiti: A hospital-based Investigation" (2005). Graduate Thesis and Dissertations.
4. Soumya Swaminathan and G Nagendran. HIV and tuberculosis in India. Biosci.2008 Nov;33(4):527-37.
5. Review article Indian J Med Res 120, October 2004, pp 316-353 Extrapulmonary tuberculosis, S.K. sharma & A. Mohan – Department of Medicine, All India Institute of Medical Sciences, New Delhi & Department of Emergency Medicine, Sri Vnkateswara Institute of Medical Sciences, Tirupati.
6. Joseph J, Strange C, Sahn SA. Pleural effussions in hospitalised patients with AIDS. Ann Intern Med 19993; 118:856.
7. Jones BE, Young SMM, AntoniskisD, Davidson PT, Kramer F, Barnes PF. Relationship of the manifestations of tuberculosis to CD4 cell counts in patients with human immunodeficiency virus infection. AM Rev Respir Dis 1993; 148: 1292-1297.
8. Relkin F, Aranda CP, Garay SM, Smith R, Berkowitz KA, Rom WN.Pleural tuberculosis and HIV infection. Chest 1994; 105: 1338-1341.
9. Light RW. Pleural Diseases. Third Edition. Baltimore, Williams and Wilkins, 1995.
10. Cordero PJ, Gil Suay V, Greese JV, et al. The clinical characteristics of pleural tuberculosis in patients with and without human immunodeficiency virus infection. (translated from spanish). Arch Bronchoneumol 1995; 31: 512-518.
11. Frye MD, Pozsik CJ,Sahn SA. Tuberculosis pleuricy is more common in AIDS than in non-AIDS patients with tuberculosis. Chest 1997: 112: 393-397.
12. Richter C, Perenboom R, Mtoni I, et al. Clinical features of HIV-seropositive and HIV-seronegative patients with tuberculosis pleural effusion in Dar es Salaam, Tanzania. Chest 1994; 106: 1471-1475.
13. Riantawan P, Chaowalit P, Wongsangiem M, Rojanaraweewong P. Dagnostic value of pleural fluid adenosine deaminase in tuberculous patients with reference to HIV coinfection and a Bayesian analysis. Chest 1999; 116: 97-103.
14. Berger HW, Megia E.. Tuberculosis pleurisy. Chest 1973; 63:88-92.
15. Levine H, S zanto PB, Cugell DW. Tuberculosis pleurisy: an acute illness. Arch Intern Med 1968; 122: 329-332.
16. www.who.int/tb/publications/who_htm_tb2004_329/en.
17. Michael D. Frye, Carol J. Pozsik and Steven A. Sahn. Tuberculous Pleurisy is More common in AIDS than in Non-AIDS Patients With Tuberculosis.Chest.1997 Aug;112(2):393-7.
18. Sunita H, GB doddamani, Iinganand I Pujari, CVB Prasad. Pleural fluid Analysis in HIV-associated Tuberculosis Patients: A Retrospective Study. Ind J Clin practice, Vol.23,No.1June2012.
19. Anand K Patel, Sandip J Thakrar, Feroz D Ghanchi. Clinical and laboratory profile of patients with TB/HIV coinfection: A case series of 50 patients. Lung India.2011 Apr;28(2):93-6.
20. National AIDS Control Organization Report 2012. Dept of AIDS Control. Ministry of Health and Family Welfare, Govt of India. P4-5.
21. Manjareeka M, Nanda S. Prevalence of HIV infection among tuberculosis patients in Eastern India. J Infect Public Health 2013 Oct,6(5);358-62.
22. Barnes PF, et al. Tuberculosis in patients with HIV infection. Med Clin North Am 1993; 77(6): 1369-89.
23. Mathew Ninan, Doye George, P Sukumaran, Gunanidhi sahu, RN Mania, Philip Mathew. Pattern of extra-pulmonary tuberculosis in patients with human immunodeficiency virus infection, At a tertiary care centre in eastern India. Int J med Research & Health Science,July 2015;4(3):572-577.

24. Soumya Swaminathan, M Sangeetha, N Arunkumar, PA Menon, Beena Thomas, K Shibi, Ponnuraja and S Rajasekar. Pulmonary Tuberculosis in HIV positive individuals: preliminary report on clinical features and response to treatment. Indian J Tub 2002;49: 189-193.
25. Sharma SK, Kadhiravan T, Banga A, Goyal T, Bhatia I, Saha PK. Spectrum of clinical disease in a series of 135 hospitalised HIV infected patients from north India. BMC Infect Dis 2004;4:52.
26. Nutrition and HIV Infection: Review of Weight Loss and Wasting in …cid.oxfordjournals.org >…> Medicine & heaith > Clinical Infectious Disease.
27. Robert F Miller, Sarah J Howling, Anrdew J Reid, Penny J Shaw. Pleural effusions in patients with AIDS. Sex Transm Infect.2000 Apr;76(2):122-5.
28. Ahmad Z, et al. Manifestations of tuberculosis in HIV infected patients. JIACM 2005;6(4):302-5.
29. A K Bhattacharya. Pleural effusion in AIDS. Lung India 2005; 22:101-104.
30. Relkin F, Aranda C P, Garay S M, et al. Pleural tuberculosis and bHIV infection. Chest 1994; 105:1338.
31. Kitinya J N, Richter C, Perenboom R, et al. Influence of HIV status on pathological changes in tuberculous pleuritis. Tuber Lung Dis 1994; 75:195-198.
32. Prasad R, et al.A clinico-radiological study of patients of tuberculosis with HIV co-infection. Curr Med Trends2006;10:1971-7.
33. Jones BE, Young SMM, Antoniskis D, Davidson PT, Kramer F, Barnes PF. Relationship of the manifestation of tuberculosis to CD4 cell count in patients with human immunodeficiency virus infection. Am Rev Respir Dis 1993; 148: 1292-1297.
34. Levine H, Metzger W, Lacera D, et al. Diagnosis of tuberculous pleurisy by culture of pleural biopsy specimens. Arch Intern Med 1970; 126(2):269-71.
35. Burgess LJ, Leroux I, Taljaard JJF. Combined use of pleural adenosine deaminase with lymphocyte/ neutrophil ratio. Chest 1996;109:414-9.
36. K. Baba, A.A. Hoosen, N. Langeland, and A.M. Dyrhol-Riise. "Adenosine deaminase activity is a sensitive marker for the diagnosis of tuberculous pleuritis in patients with very low CD4 counts," PloS ONE, vol. 3, no. 7, Article ID e2788, 2008.
37. 37.Soe Z, et al. A study on tubercular pleural effusion. Int J Collab Res Int Med Pub Health 2010;2(3):32-48.
38. Light RW, et al.Pleural effuision: the diagnostic separation of transudates and exudates. Arch Intern Med 1972; 77(4):507-13.
39. C. Richter, R. Perenboom, A. B. M. Swai et al., "Diagnosis of tuberculosis in patients with pleural effusion in an area of HIV infection and limited diagnostic facilities, "Tropical and Geographical Medicine, vol. 46, no. 5, 1994; 293-297.
40. R. S. Heyderman, R. Makunike, T. Muza et al., "Pleural tuberculosis in Harare, Zimbabwe: the relationship between human immunodeficiency virus, CD4 lymphocyte count, granuloma formation and disseminated disease," Tropical Medicine and International Health, vol. 3, no. 1, p-14-20, 1998.