



**A COMPARATIVE STUDY OF CLINICAL, RADIOLOGICAL AND LABORATORY
PARAMETERS OF COMMUNITY ACQUIRED LRTI OF LESS THAN 2 WEEKS
DURATION AND ASSESSING THE RESPONSE TO STANDARD TREATMENT
GUIDELINES AMONG HIV-INFECTED AND HIV-NON INFECTED ADULTS
ATTENDING A TERTIARY CARE CENTRE IN KOLKATA**

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ABSTRACT

RTI are a substantial cause of morbidity and mortality in young children and the elderly. Every year RTI in young children is responsible for an estimated 3.9 million deaths worldwide. Acute respiratory infections (ARI) may cause inflammations anywhere in the respiratory tract from nose to alveoli with a wide range of combinations of symptoms and signs. In India, during the year 2011, about 26.3 million cases ARI were reported. During 2011 about 2492 people died of ARI and 2770 died of pneumonia. Pneumonia affects approximately 450 million people globally per year, (seven per cent of population) and results in about 4million deaths mostly in the third world countries. A reasonable number of LRTI patients require in-patient treatment. Our study revealed increased age is a significant risk factor for morbidity in LRTI. Our study also showed LRTI in HIV-R group is more common in younger age group as compared to HIV-NR group in which it is more common after 50 years of age with male preponderance in both the groups. It also proved that the severity criteria given by BTS guideline i.e. CURB-65 is pretty useful in a set up like us. It helps to recognize the severely ill patients early. CD4 level has a good predictive value in determination of causative organisms, outcome and prognosis in the HIV reactive group. The most common single organism found in sputum culture of patients of LRTI in HIV-R group is Staphylococcus aureus whereas in HIV-NR group it is Klebsiella pneumoniae.

KEYWORDS: LRTI, HIV, NON HIV.

MATERIALS AND METHODS

1) STUDY AREAS: OPD of School of Tropical Medicine, Kolkata/ Inpatient Department of Carmichael Hospital for Tropical Diseases, Kolkata.

2) STUDY POPULATION: HIV- infected & HIV-non infected adults with community acquired LRTI of less than 2 weeks duration attending OPD or are admitted at CHTD, School of Tropical Medicine.

3)STUDY PERIOD: July-2013 to June-2014.

4) SAMPLE SIZE: 50 (25 in each group)

5) SAMPLE DESIGN: SELECTION OF THE PATIENT: Adult patients presenting with fever, cough with respiratory distress for less than two weeks duration will be selected. All the patient will be referred to

ICTC.HIV antibody non-reactive people will comprise the HIV non-infected group and HIV antibody reactive people will comprise HIV infected group. Both the groups will be screened and finally recruited for the study using, following inclusion and exclusion criteria after taking informed consent.

a) Inclusion Criteria

HIV non-infected adults of both sexes with fever, cough, chest pain, breathlessness etc.
HIV infected adults of both sexes with fever, cough, chest pain, dyspnoea etc.

b) Exclusion criteria

Infant, children and adolescents (<18years). HIV infected and non-infected adults with cough, fever, dyspnoea for more than 2 weeks duration. History of hospitalisation within last three months

6) STUDY DESIGN- DESCRIPTIVE, CROSS SECTIONAL COMPARATIVE STUDY which includes.

METHODS

Every patient selected by the inclusion criteria had undergone the following

- Informed consent of the patient
- Detailed medical history
- Physical examination
- ICTC screening
- Routine investigations

(a) Complete haemogram (b) sputum for Gram stain, culture and sensitivity (c) sputum for AFB (d) sputum for fungal stain, culture (e) Blood culture (f) fasting and post prandial blood sugar (g) urea, creatinine (h) LFT (i) chest X-RAY (j) ECG.

Others as deemed necessary e.g. routine urine & stool examination, Mantoux test, lipid profile, serum ANA, RF and ACE estimation, throat swab culture, CT chest and guided FNAC, USG whole abdomen, Bone Marrow aspiration, abdominal CT.

7)PARAMETERS TO BE STUDIED

PARAMETERS SPECIFIC FOR OBJECTIVE 1- Clinical parameters include specific medical history along with findings on physical examinations of the patients, laboratory investigations including radiological findings etc.

PARAMETERS SPECIFIC FOR OBJECTIVE 2- All clinical findings, microbiological and pathological examination findings.

PARAMETERS SPECIFIC FOR OBJECTIVE 3- Progress of clinical findings, biochemical, microbiological, radiological findings with treatment.

8)STUDY TOOLS

Pre-designed and pre-tested schedule for data collection.
Prescription used by the patient.
Other allied instruments required during physical examinations
Consent forms in Bengali, Hindi and English languages.

9) STUDY TECHNIQUES All patients after selection were asked for the history and examined thoroughly, and then the sputum was collected and processed. Blood was collected for culture and sensitivity, complete blood count, and other relevant investigations. Patients were directed to go to our radiology department for chest radiograph.

Sputum collection and processing

Sputum was collected at early morning of admitted patients. For ODP cases patients were sent to department of bacteriology for giving sample. Patients were asked to deeply cough out the sample. If they were unable to do

that, a sputum induction by nebulisation with hypertonic saline was undertaken. The sample was collected in a wide neck screw cap sterile container and transported to bacteriology department. Then the quality of the sputum was assessed by Bartlett's grading system. If the sample had epithelial cell more than 10/ low power field, then it was discarded and the patient were asked to produce another sputum sample. If the sample was not acceptable the patient were excluded from our study.

The gram stained sputum were examined under microscope to detect the pus cell count and predominant bacteria. All acceptable samples were further processed for culture. The rest of the sputum was liquefied by freshly prepared solution of 1% dithioerythrol (1:1) and incubated at 37°C for 30 min. Then it was serially diluted with normal saline. Samples having 10⁻⁴, 10⁻⁵, 10⁻⁶ dilutions were inoculated in MacConkey, Blood and Chocolate agar and incubated for 48 hours. 2 days later media was examined for growth and if colony count ≥ 10 then further identification were undertaken by standard bacteriological methods.

Blood culture

For collection of blood culture after proper cleansing of venepuncture site with povidone iodine 10 ml of blood was drawn and inoculated in blood culture bottle. It was then incubated for 2 days and if growth of some organism were detected then subsequently subcultured on Blood agar and MacConkey agar.

10) PLAN FOR ANALYSIS OF DATA

Adult patients attending OPD or admitted at CHTD, School of Tropical Medicine, Kolkata with history of fever, cough, and respiratory distress with less than 2 weeks duration selected as HIV non-infected and HIV infected groups based on ICTC screening and also considering their inclusion and exclusion criteria.

Interviewing the patient for proper medical history.

Clinical examination.

Scrutiny of biochemical, radiological, microbiological examinations.
management as per standard guideline.

RESULTS AND ANALYSIS

For this study a total of 50 patients who attended the Tropical Medicine OPD or admitted to the Carmichael Hospital for Tropical Diseases were eligible as their clinical presentation fulfilled the inclusion criteria.

A)AGE AND SEX AND OTHER DEMOGRAPHIC FACTORS,

Table 1: Age distribution of HIV-R and HIV-NR patients (n=50).

Age (in yrs)	HIV-R (% out of n)	HIV-NR (% out of n)
18 to 30	9(18%)	4(8%)
31 to 40	6(12%)	3(6%)
41 to 50	7(14%)	1(2%)
51 to 60	3(6%)	7(14%)
61 to 70	0	1(2%)
71 to 80	0	5(10%)
80 and above	0	4(8%)

There were 50 patients in our study. Among them 25 patients were HIV infected and 25 patients were HIV non- infected. Most common HIV infected was in the age group of 18 to 30 yrs and HIV-NR in the age group of 51 to 60 yrs. The range of age was 19 to 55 in HIV-R and 19 to 85 in HIV-NR patients.

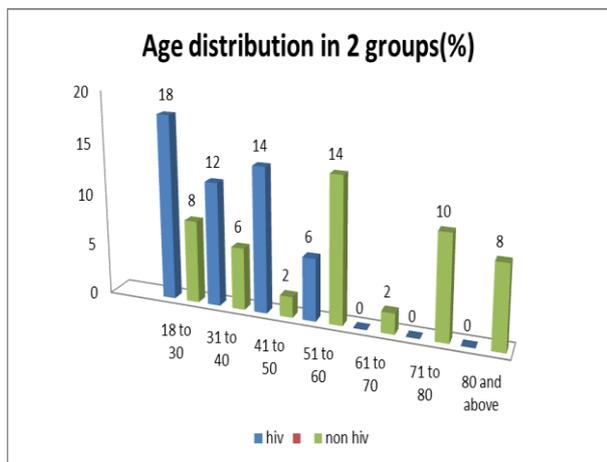


Figure 1: Bar-diagram showing age distribution of HIV-R and HIV-NR patients.

Table 2: Showing patient profile of HIV-R and HIV-NR patients (n=50).

	HIV-R (% out of n)	HIV-NR (%out of n)
a)Sex		
Male	17(68%)	14(56%)
Female	8(32%)	11(44%)
b)Residence		
Urban	10(40%)	16(64%)
Rural	15(60%)	9(36%)
c)Place of treatment		
Indoor	17(68%)	13 (52%)
OPD	8(32%)	12(48%)

From the above table we can see that, among the HIV infected patients 68% are male and 32% are female. Among the HIV Non-infected patients 56% are male and 44% are female. Major portion of our study population in HIV- Reactive patients were urban people 40% and rural people 60%. And in HIV-Non Reactive

patients urban people were 64% and rural people were 36%.68% of the patients were admitted and 32% were treated in OPD in HIV-R group. 52% of the patients were admitted and 48% were treated in OPD in HIV-NR group. Most of the admitted patients were severely ill and fulfilled CURB-65 criteria.

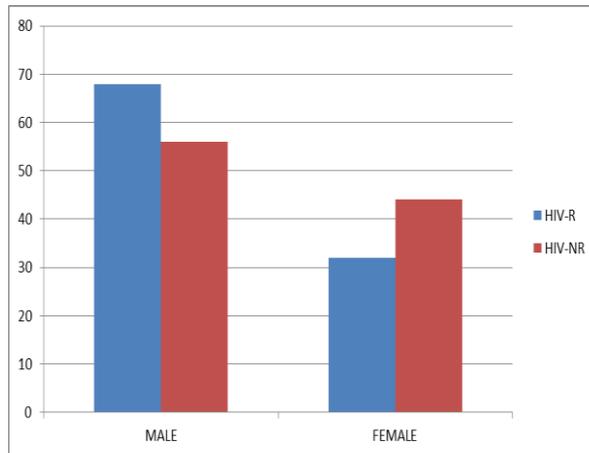


Figure 2a: Bar-diagram showing sex distribution of HIV-R and HIV-NR patients.

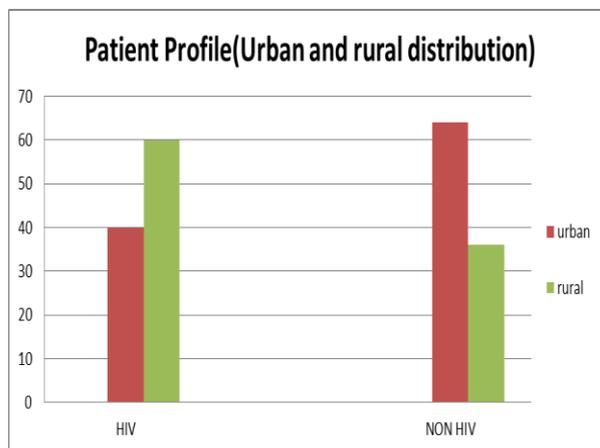


Figure 2b: Bar-diagram showing residence distribution of HIV-R and HIV-NR patients.

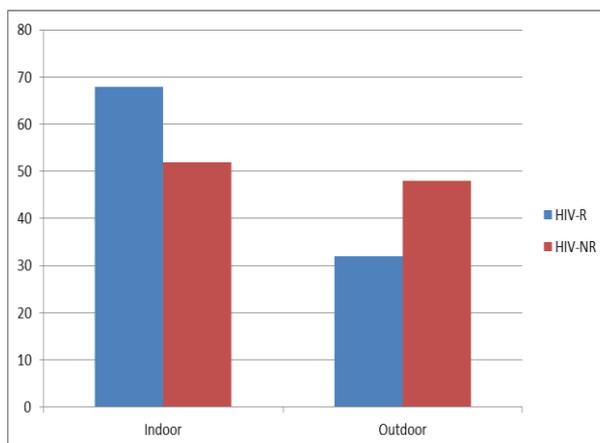
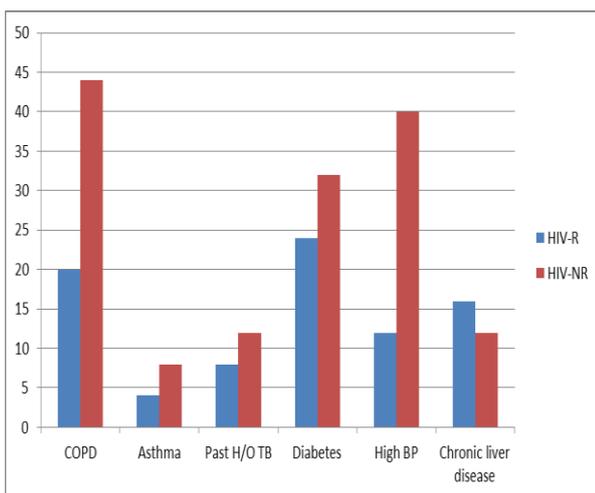


Figure 2c: Bar-diagram showing place of treatment distribution of HIV-R and HIV-NR patients.

B) ASSOCIATED DISEASES**Table 3: Showing associated co-morbid illness in HIV-R patients and HIV-NR patients.**

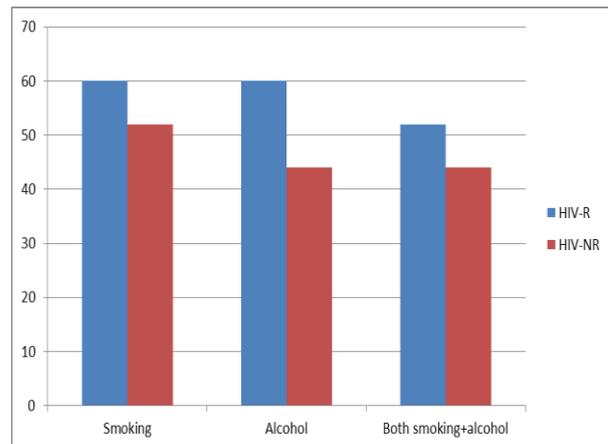
Comorbidity	HIV-R(%)	HIV-NR(%)
COPD	5(20%)	11(44%)
Asthma	1(4%)	2(8%)
Past history of TB	2(8%)	3(12%)
Diabetes	6(24%)	8(32%)
High B.P	3(12%)	10(40%)
Chronic Liver disease	4(16%)	3(12%)

The most commonly associated condition with LRTI in our study was COPD which was present in 20% HIV-R patients and 44% in HIV-NR patients. The next common disease prevalent by decreasing order is diabetes, hypertension, CLD, past H/O of TB and asthma.

**Figure 3: Bar-diagram showing associated co-morbid illness distribution of HIV-R and HIV-NR patients.****C) ADDICTION IN HIV-R AND HIV-NR PATIENTS****Table 4: Showing data of personal habits in HIV-R patients and HIV-NR patients**

Personal habits	HIV-R patients	HIV-NR patients
Smoking	15 (60%)	13 (52%)
Alcohol Intake	15 (60%)	11 (44%)
Both smoking and alcohol	13 (52%)	11 (44%)

Smoking and intake of alcohol were found to be very common in both groups of our study. 60% of HIV-R patients and 52% of HIV-NR patients were smoker. 60% of HIV-R and 44% of HIV-NR patients were alcoholic. 52% of HIV-R and 44% of HIV-NR patients were both smoker and alcoholic.

**Figure 4: Bar-diagram showing personal habits distribution of HIV-R and HIV-NR patients.****D) CLINICAL PROFILE****Table 5a: Showing clinical symptoms in HIV-R patients and HIV-NR patients.**

Symptoms	HIV-R (%)	HIV-NR (%)
Cough with expectoration	15(60%)	17(68%)
Cough without expectoration	10(40%)	8(32%)
Fever	25(100%)	23(92%)
Chest Pain	18(72%)	13(52%)
Shortness of breath	13(52%)	8(32%)
Altered mental status	0(0%)	0(0%)

The most common symptom in HIV-R patients was fever (100%) followed by chest pain(72%), cough with expectoration(60%), cough without expectoration (40%) and shortness of breath (52%). The most common symptoms in HIV-NR patients was also fever(92%) followed by cough with expectoration(68%), chest pain(52%), cough without expectoration(32%) and shortness of breath (32%). Altered mental status was not found in any HIV-R or HIV-NR group.

Table 5b: Showing No/percentage of patients presenting with different physical findings.

Physical findings	HIV-R GROUP	HIV-NR GROUP
Pallor	22(88%)	19(76%)
Cyanosis	2(8%)	3(12%)
Clubbing	5(20%)	8(32%)
Oedema	8(32%)	10(40%)
Cervical lymphadenopathy	17(68%)	11(44%)
Tachycardia	20(80%)	22(88%)
Icterus	9(36%)	12(48%)
Hypothermia	0(0%)	0(0%)
Hyperthermia	25(100%)	22(88%)
Hypertension	3(12%)	11(44%)
Normal B.P	22(88%)	14(56%)
High respiratory rate	17(68%)	19(76%)
Confusional state	0(0%)	0(0%)
Unconscious	0(0%)	0(0%)

Hyperthermia(94%) was the most common overall general survey finding followed by pallor(82%).

80% of HIV-R group had tachycardia and high respiratory rate(68%).Around 17 HIV-R patients had cervical lymph node palpable. High blood pressure was recorded in 3 patients. Clubbing(16%),oedema(56%) were present in HIV-R group.

In HIV-NR patients, the most common symptom was hyperthermia (88%) and tachycardia (88%). Next common was pallor (76%).High respiratory rate was detected in 19 patients. Oedema (40%), clubbing (28%) and high blood pressure (40%). Cervical lymphadenopathy was present in 44% of patients in HIV-NR group.

Table 6a: Showing respiratory system examination findings in HIV-R patients and HIV-NR patients.

Trachea	HIV-R (%)	HIV-NR (%)
Central	23(92%)	23(92%)
Deviated	2 (8%)	2(8%)
Movement of chest		
Normal	17(68%)	9(36%)
Diminished	7(28%)	2(8%)
Indrawing	1(4%)	11(44%)
Percussion note		
Dull	6(24%)	3(12%)
Breath sounds		
B/L VBS	19(76%)	20(80%)
Diminished VBS	6(24%)	3(12%)
Bronchial	1(4%)	1(4%)
Rhonchi	20(80%)	18(72%)
Crepitations	18(72%)	20(80%)
Complications		
Pleural Effusion	3(12%)	3(12%)
Empyema	1(4%)	0(0%)

Table 6b: Showing No/percentage of patients with various respiratory clinical findings.

	HIV-R	HIV-NR
Shifting of Trachea	2(8%)	2(8%)
Restricted movement of chest	7(28%)	2(8%)
Impaired/ dull percussion note	6(24%)	3(12%)
Hyperresonant percussion note	0(0%)	1(4%)
Normal VBS	19(76%)	20(80%)
Diminished VBS	6(24%)	5(20%)
Bronchial breath sound	1(4%)	1(4%)
Increased vocal fremitus /resonance	1(4%)	1(4%)
Decreased vocal fremitus /resonance	6(24%)	3(12%)
Adventitious sound	18(72%)	20(80%)
Crackles	16(64%)	15(60%)
Wheeze	12(48%)	12(48%)
Pleural rub	0(0%)	0(0%)
Chest indrawing	1(4%)	11(44%)

On examination of respiratory system of HIV infected patients-92% had trachea central.Deviated trachea was seen in 8% of the patients.68% of the study group had normal movements of the chest wall. Excessive work by accessory muscles of respiration (indrawing) was evident in 4% patients. Diminished movement found in 7 patients. Percussion note was dull in 6 patients. Most of the patients had bilateral vesicular breath sound(76%). 6 patients had diminished vesicular breath sound and 1 patient had bronchial breath sound. Among the added respiratory sounds, crepitation was heard in 18 patients. Rhonchi or wheeze was presents in 20 patients. Parapneumonic pleural effusion developed in 3 patients. Empyema was found in 1 HIV-R patients.

On examination of the respiratory system in HIV-NR patients-92% had trachea central.Nearly less than half of the study group had normal movements of the chest wall (36%). Excessive work by accessory muscles of respiration (indrawing) was evident in 11 patients,all of whom were diagnosed cases of COPD. Diminished movement was found in 2 patients. Percussion note was dull in 3 patients. Most of the patients (80%) had bilateral vesicular breath sound(20%). 3 patients had diminished vesicular breath sound and 1 patient had bronchial breath sound with increased vocal resonance. Among the added respiratory sounds, crepitation was heard in 20 patients. Rhonchi or wheeze was present in 18 patients. Parapneumonic pleural effusion developed in 3 patients. Empyema was also not detected in HIV-NR patients.

E) LABORATORY EVALUATION

Table 7a: Showing Hb and TLC level in HIV-R and HIV-NR.

Hemoglobin level l(gm/dl)	HIV-R	HIV-NR
<8	7(28%)	3(12%)
8.1-10	12(48%)	13(52%)
10.1-12	5(20%)	3(12%)
>12.1	1(4%)	6(24%)
TLC(cells/cu.mm)		
<8000	16(64%)	3(12%)
8001-10000	1(4%)	1(4%)
10,001-12000	3(12%)	9(36%)
12001-14000	3(12%)	6(24%)
14,001-16000	1(4%)	4(16%)
>16001	1(4%)	2(8%)

From the above table we can see that 48% of patients in HIV-R group had Hb level between 8.1-10 mg/dl and 52% of patients in HIV-NR group had Hb level between 8.1-10 mg/dl.64% of patient in HIV-R group had TLC <8000 cells/cu.mm and 36% of patients in HIV-NR group had TLC >10000 cells/cu.mm.

Table 7b: Showing comparison of wheeze and raised Eosinophil count in HIV-R and HIV-NR groups.

	HIV-R	HIV-NR
Wheeze	20	18
Raised Eosinophil count	7	12

In our study 7 out of 20 HIV-R patients with wheeze had raised eosinophil count (>4%). In HIV-NR group 18 patients had wheeze out of which 12 had raised eosinophil count.

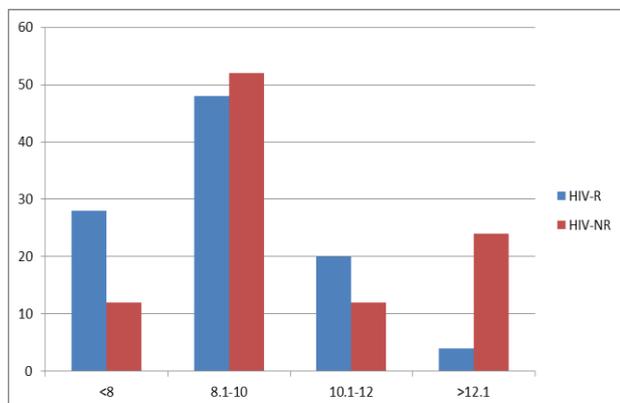


Figure 5: Bar-diagram showing Hb level in both groups.

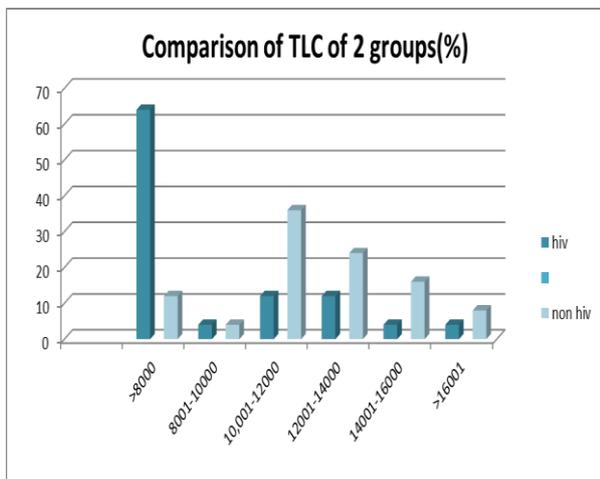


Figure 6: Bar-diagram showing TLC level in both groups.

F) CD4 level

Table 8a: Showing result of CD4 count in HIV(R) patients.

CD4 count	No of pts	Percentage
0-50	5	20%
51-100	2	8%
101-150	7	28%
151-200	1	4%
>200	10	40%

The above table shows that 40% of the HIV-R patients had CD4 count above 200 cells/ μ l.

Table 8b: Showing microorganisms found in sputum at different CD4 levels of HIV-R patients.

CD4 count	Microorganisms
0-50	Pseudomonas, K. pneumoniae, E.coli, Acinetobacter
51-100	K.oxytoca, K.pneumoniae, Acinetobacter, Pseudomonas, E.coli, A.fumigatus, A.niger
101-150	Klebsiella, Pseudomonas, Acinetobacter, Candida spp.
151-200	S.aureus, S.pyogenes, S.pneumoniae
201-250	S.aureus, S.pneumoniae, S.pyogenes,

The above table shows that Gram negative bacteria are more common in CD4 count less than 150 cells/ μ l as compared to Gram positive bacteria which are more common in CD4 count more than 150 cells/ μ l.

G) Sputum Culture

Table 9a: Showing comparison of sputum culture in HIV-R and HIV-NR patients.

Organism	HIV-R	HIV-NR
Single organism	20(80%)	21(84%)
Mixed organism	3(12%)	3(12%)
Other organism	3(12%)	2(8%)

The above table shows result of sputum culture which were acceptable considered for this study. On gram staining 20 sample(80%) had shown single organism in HIV-R patients. In HIV-NR patients it is 21 sample(84%). Mixed organism were found to be 3% in each group.

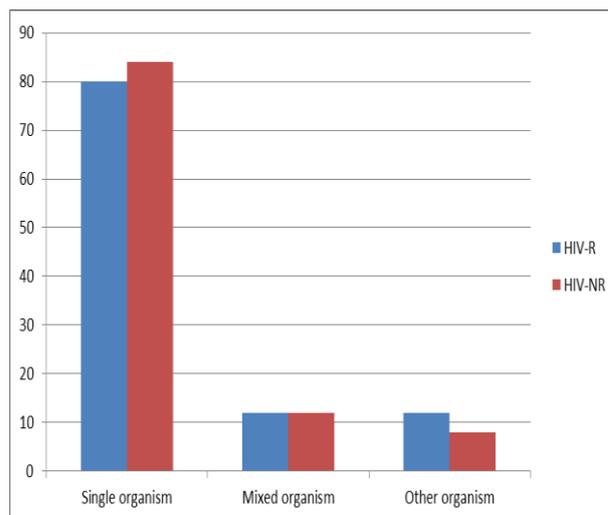


Figure 7: Bar-diagram showing comparison of sputum culture in HIV-R and HIV-NR patients.

Table 9b: Showing number of patients showing culture of specific bacteria in HIV-R and HIV-NR patients

Single organism	HIV-R	HIV-NR
S.aureus	6(24%)	4(16%)
S.pneumoniae	2(8%)	2(8%)
K.pneumoniae	4(16%)	7(28%)
S.pyogenes	5(20%)	3(12%)
Pseudomonas aeruginosa	3(12%)	3(12%)
K.oxytoca	0(0%)	2(8%)
E.coli	0(0%)	1(4%)
Mixed organism		
K.pneumoniae+s.aureus	1(4%)	1(4%)
S.pyogenes+s.aureus	1(4%)	0(0%)
Pseudomonas spp + Acinobacter spp	1(4%)	0(0%)
S.pneumoniae+K.pneumoniae	0(0%)	1(4%)
K.pneumoniae+pseudomonas	0(0%)	1(4%)

The above table shows Gram positive cocci (staphylococcus aureus) were more commonly isolated in direct smear in HIV-R patients which was 6 in number(24%), next common was streptococcus pyogenes(20%). Klebsiella spp were found in 16% of the HIV-R patients.12% patients were found to be Pseudomonas spp.

On the other hand 28% of the HIV-R patients had Klebsiella spp. Next common was Staphylococcus aureus (16%). Pseudomonas spp was found in 12% of the patients. Klebsiella oxytoca 2% and E. coli found in 1% of patients.

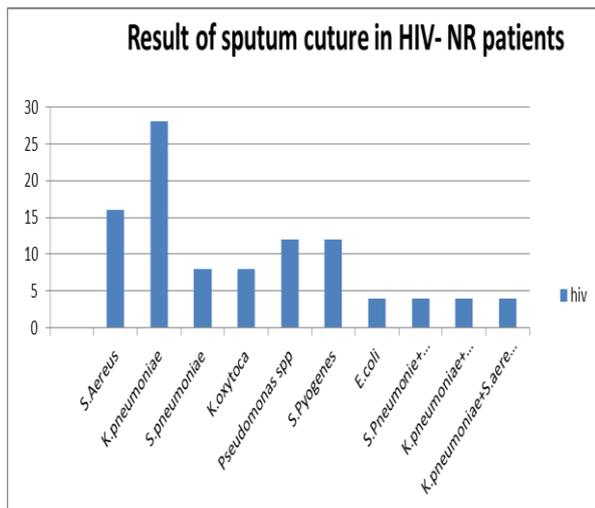


Figure 8a: Bar-diagram showing comparison of sputum culture specific bacteria in HIV-NR patients.

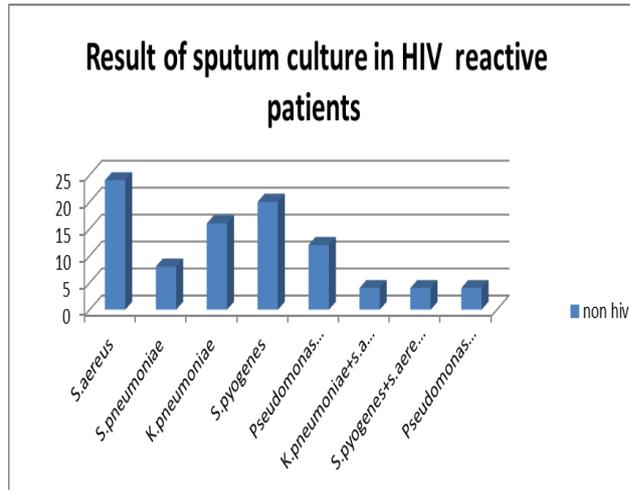


Figure 8b: Bar-diagram showing comparison of sputum culture specific bacteria in HIV-R patients.

H) Radiological Findings

Table10a: Showing comparison of Radiological Parameters in HIV-R and HIV-NR patients.

Chest radiograph	No of HIV-R patients	No of HIV-NR patients
Normal	3(12%)	3(12%)
Patchy consolidation	17(68%)	16(64%)
Pleural effusion	2(8%)	3(12%)
Calcification	0(0%)	1(4%)
Mediastinal lymphadenopathy	0(0%)	0(0%)
Bilobar patchy consolidation	0(0%)	1(4%)
Hilar lymphadenopathy	2(8%)	2(8%)

Table 10b: Correlation of CD4 count with Chest X ray Findings (n=25)

	<200(% out of n)	200-350 (% out of n)	>350 (% out of n)
Patchy consolidation	9(36%)	4(16%)	4(16%)
Pleural effusion	2(8%)	0	0
Hilar L.N.	2(8%)	0	0
Normal	1(4%)	0	2(8%)

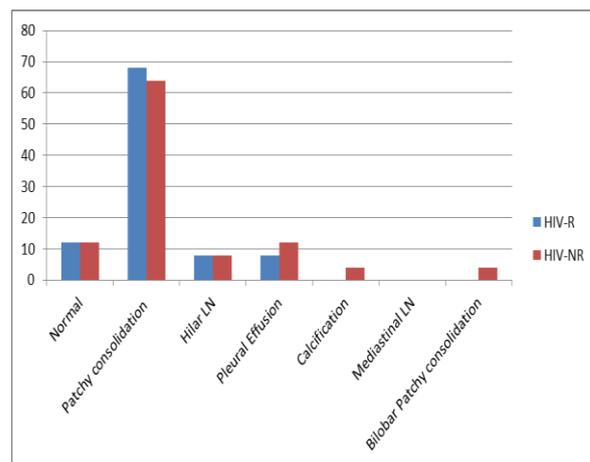
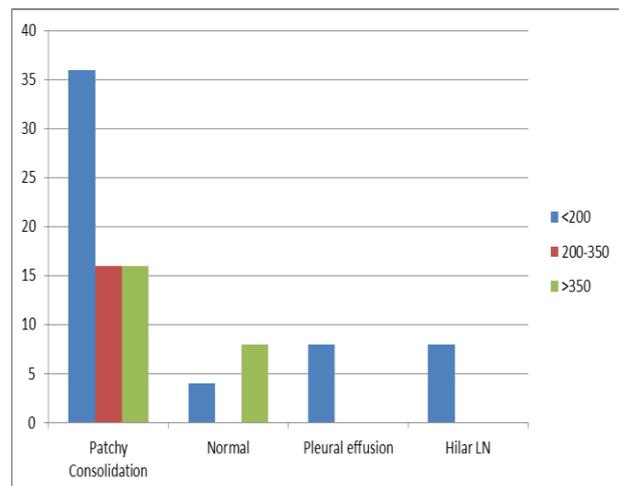
Table 10c: Growth of different micro organisms in different Radiological findings.

Radiological findings	HIV-R / Growth of organism	HIV-NR / Growth of organism
Patchy Consolidation	S.aureus, S.pyogenes, S.pneumoniae, K.pneumoniae, Pseudomonas	S.aureus, S.pyogenes, S.pneumoniae, K.pneumoniae, E.coli, Pseudomonas, K.oxytoca
Hilar lymphadenopathy	Pseudomonas, K.pneumoniae, S.pyogenes	K.pneumoniae, S.pneumoniae
Pleural effusion	K.pneumoniae, S.pneumoniae, S.aureus	K.pneumoniae, S.pneumoniae, Pseudomonas
Calcification	None	Pseudomonas
Bilobar patchy Consolidation	S.aureus, S.pyogenes, K.pneumoniae, Pseudomonas	S.pyogenes, S.aureus
Normal x-ray	K.pneumoniae, S.pyogenes	K.oxytoca, K.pneumoniae, S.aureus

A chest radiograph was undertaken routinely in all patients. The commonest chest x-ray finding in HIV-R was patchy consolidation (68%). Pleural effusion was seen in 8% and also hilar lymphadenopathy was 8%. Pleural tap was done in 3 patients. There was no calcification, no mediastinal lymphadenopathy or bilobar patchy consolidation in HIV-R patients. The patients showing patchy consolidation ultimately found to be culture positive. Normal chest x-ray finding was seen in 3 patients which were also sputum culture positive.

Patchy consolidation in chest X ray was observed in 36, 16 and 16% of patients in CD4 range of less than 200, 200 to 350 and more than 350 cells respectively.

In our 25 HIV-NR patients the commonest chest x-ray finding was also patchy consolidation (64%). Among them, parapneumonic pleural effusion was seen in 12% of the patients. Hilar lymphadenopathy was seen in only 2 patients. Calcification was seen in only 1 patient. Bilobar patchy consolidation was seen in only 4% of the patients. No mediastinal lymphadenopathy was seen in HIV-NR patients. Normal chest x-ray finding was seen in 12% of the patients but they were also sputum culture positive showing growth of organism.

**Figure 9a: Bar-diagram showing comparison of Radiological Parameters in HIV-R and HIV-NR patients.****Figure 9a: Bar-diagram showing CD4 count relationship with Chest X ray in HIV-R patient.**

I) Anti-microbial susceptibility pattern of isolated micro-organisms

a) Klebsiella pneumoniae in HIV-R (n=6)

Klebsiella pneumoniae	Car	Flu	Ami	B-Lac	Cepha
HIV-R (out of n)	100%	83.33%	16.66%	16.66%	33.33%

b) *Klebsiella pneumoniae* in HIV-NR (n=10).

Klebsiella Pneumoniae	Car	Col/Poly	Flu	Ami	B-Lac	Cepha	Tig
HIV-NR (out of n)	50%	30%	40%	40%	40%	50%	10%

c) *Staphylococcus aureus* in HIV-R (n=8).

Stap. aureus	Van	Lin	Flu	B-Lac	Cepha	Mac
HIV-R (out of n)	100%	100%	25%	25%	12.5%	0%

d) *Staphylococcus aureus* in HIV-NR (n=5).

Stap. aureus	Van	Lin	Flu	B-Lac	Mac
HIV-NR (out of n)	60%	60%	60%	40%	0%

Abbreviations: Car- carbapenem, Col/Poly- colistin/polymixin, Flu- Fluoroquinolone, Ami- aminoglycoside, B-Lac- Beta-lactum, Cepha- Cephalosporins, Cot- Cotrimoxazole, Tig- tigecycline, Van- Vancomycin, Lin- Linezolid, Mac- Macrolides.

j) *Outcome*

Table 11: Showing outcome after treatment received in HIV-R and HIV-NR group.

	HIV-R	HIV-NR
Cured	24	25
Expired	1	0

Our study had only one HIV patient who died due to multiorgan failure.

DISCUSSION

There were 50 patients who fulfilled our inclusion criteria and were able to cough out acceptable sputum. Every third patients having the inclusion criteria attending OPD were selected. The presence of more than 10 squamous epithelial cells in direct smear of sputum per low power of field (100x magnification) indicates contamination and discarded for further study. A specimen with few or no squamous cells and more than 25 polymorphonuclear white blood cells per low power field is ideal for staining and culture. Even after sputum induction many patients were unable to produce deeply coughed out sputum. They were excluded from our study. So the exact number of patients with similar clinical features was much more than our enrolment.

SEX, AGE AND OTHER DEMOGRAPHIC FACTORS

Lower respiratory tract infection is known to occur in all part of society.

In our study, 68% of HIV-R patients are male and 32% are female and in case of HIV-NR group males are 56% and females are 44%.

In a study by Almirall J et al^[1], in Europe has shown that CAP incidence is more in males with ratio of 1.4 : 1. The incidence is shown to be increased with age.

From the overall enrolment of patients at Tropical Medicine OPD and admission register of our hospital we can suggest that number of male patients with LRTI is more than female. Number of male patients with LRTI are more as compared to females in HIV group. In HIV-NR group LRTI is more or less equal in both males and females.

In our study, HIV infection was found more in younger age group and they are prone to suffer from LRTI. LRTI incidence increases with age more than 50 years in HIV-NR patients. The most commonly visited age group in HIV-R patients is 18 to 30 years with mean age 37.48 and the incidence of LRTI was high in this age group. The mean age was 53.48 in HIV-NR group.

In a study on LRTI by the Microbiology Department of Christian Medical College and Hospital, Ludhiana the mean age of presentation was 40 years.^[2]

In a study by S. Bansal et al^[3], mean age was of 52.77 ± 18.1 years (range 17-93 years). There were 50 males. Thirty of the 70 patients were in the sixth and seventh decades of life. Patients older than 40 years were more predisposed to the development of CAP ($t=24.441$; $p<0.01$).

In our study, HIV-R with LRTI was more common in rural population as compared to urban. HIV-NR with LRTI was more common in urban as compared to rural population. Admission requirement was higher than other community based study on LRTI possibly because our hospital is a tertiary referral centre.

In our study 60% of the patients were inpatients.

PERSONAL HABITS

In our study, information regarding smoking and alcohol was taken. These two addictions seemed to occur simultaneously in some patients. In female these

addictions were found to be less. In HIV-R patients 15(60%) smoker, 15(60%) are alcoholic and 13(52%) are smoker and alcoholic. Cigarette smoking was clearly associated with high incidence of LRTI which was also observed by

In a study by Almirall J et al^[4], there is epidemiological evidence to show that tobacco smoking is a risk for CAP. In a population-based, case-control study, the relationship was observed between tobacco smoking and CAP.

In a study by S. Bansal et al^[3], smoking was the most common predisposing risk factor observed in 50 (71%) patients with CAP ($\chi^2=12.857$; d.f. <0.01).

In a study by de Roux A et al^[5], streptococcus pneumoniae is more frequently isolated from alcoholic patients than others. Multivariate analysis showed an independent association between pneumococcal CAP and alcoholism.

In our study, comorbidities like COPD, hypertension, diabetes were common in elderly people. Some features of severity like hypothermia, mental confusion, high respiratory rate were common in elderly people. So as per the BTS guideline(CURB-65) old age is an important factor guiding the LRTI management.^[6,7] Similar data was observed in a South African study.^[8]

In a study by K V Ramana et al^[9], nosocomial and community acquired LRTI's have been on the rise as is the case with other debilitated conditions that include compromised respiratory tract (Asthma, COPD), diabetes, chronic kidney disease CKD).

In a study by S. Bansal et al^[3], co-morbid conditions were noticed in 49 (70%) of the patients. Six patients had more than one co-morbid conditions. Chronic obstructive pulmonary disease (COPD) was the most common underlying co-morbid condition observed in 40 cases (57%) and this association was significant ($t=9.592$; $p<0.01$).

PRIOR ANTIBIOTIC THERAPY

In our study, more than half of population took some antibiotic before coming to us.60% of rural and urban patients took prior antibiotic.

In a study by Ezgi Ozilmaz et al^[10], calculated the incidence of prior antibiotic therapy in their country Turkey which was 36%.So it is much higher in our study (overall 60%).This data might also suggest that over use of antibiotics is more common in both rural and urban areas.

CLINICAL FEATURE

In our study, almost all patients had cough as presenting symptom. 60% of HIV-R patients and 68% of HIV-NR

patients had given history of cough with expectoration. Fever was present in 100% of population in HIV-R group and 92% in HIV-NR group. The presence of fever is not a must in the diagnosis of LRTI. Fever may be absent in very severe LRTI. It may also be present in many systemic illness. It can divert clinician's attention from respiratory tract infection. So it is better to put more emphasis on clinical features related to lower respiratory system.

In a study by Shrestha R et al^[11], cough (76%) was the commonest presenting feature followed by fever (64%); dyspnea (43%) and chest pain (31%).

In our study, pallor and cervical lymphadenopathy was present in 88% and 68% of HIV-R patients respectively. Clubbing (20%) and cyanosis (8%) is present in HIV-R group. A respiratory rate >30 /min and tachycardia found in 68% and 80% in HIV-R group and in HIV-NR group it is 76% and 88% respectively. Apart from the illness tachycardia could be due to beta 2 agonist drugs.

In a study by S. Bansal et al^[3], out of 70 patients the most common presenting clinical signs included cyanosis in 19 (27%), tachypnoea in 17 (24%) and pallor in eight (11%).

In HIV-R group, 5 patients had hepatosplenomegaly of which 4 patients was diagnosed as disseminated TB and 1 had a past history of visceral Leishmaniasis.1 patient had splenomegaly,who also was sputum positive for AFB and diagnosed as a case of disseminated tuberculosis.

On the other hand in HIV-NR group,1 patient had hepatomegaly with liver abscess and 1 patient had splenomegaly with portal hypertension.Both of them are chronic alcoholic.

4 patients in HIV-R group had hepatosplenomegaly with presence of anaemia and palpable cervical lymphadenopathy with low CD4 count. Out of which 2 patients had low platelets (less than 1.5 lacs) and leucopenia (less than 4000 cu/mm) which can be explained by chronic bone marrow suppression mediated by advanced HIV infection.Other 2 patients had normal leucocyte and platelet count.

Laboratory evaluation

19 patients in HIV-R group had a haemoglobin level less than 10 gm/dl and 16 patients in HIV-NR group had Hb level less than 10gm/dl.

9 HIV-R patients and 14 HIV-NR patients had a high leukocyte count with predominance of neutrophils.

In a study by S. Bansal et al^[3], in total 70 patients-haematological and biochemical abnormalities were observed in 23 (33%) patients. These included anaemia (n=12), leucocytosis (n=8), leucopenia (n=1), abnormal

liver function (n=13) and abnormal renal function (n=7) tests. Eleven patients had more than one abnormality.

LRTI produces neutrophilic leukocytosis (TLC more than 10,000). 84% of the patients had leukocytosis in HIV-NR group and 32% in HIV-R group. Out of the 20 patients with wheeze, 7 patients had high eosinophil count (more than 4) in HIV-R group and out of 18 patients with wheeze in HIV-NR group 12 patients had high eosinophil count. Leucopenia was found in 32% of the patients in HIV-R patients and 8% of HIV-NR group. Rest of the patients had lymphocytic leucocytosis.

Growth of mixed organisms in the sputum with low CD4 count in HIV-R group are usually sensitive to cephalosporin, glycopeptides (vancomycin), polypeptide antibiotics (colistin, polymyxin-B), fluoroquinolones (levofloxacin, ciprofloxacin) and oxazolidinone (linezolid).

Sputum culture showed growth of bacteria in all the 25 patients in HIV-NR group and 23 patients in HIV-R group.

Sputum culture showed growth of microorganism in almost all the patients and blood culture was positive in one patient of HIV-R group only (*Staph. aureus*). So bacteremia is not common in LRTI patients.

Both of the group showed growth of microorganism in sputum culture. On Gram staining in HIV-R group 13 patients had Gram positive bacteria and 7 patients had Gram negative bacteria. In HIV-NR group it was 9 and 15 respectively. Growth was detected in 92% of the patient's sputum on conventional sputum culture in HIV-R group and 100% in HIV-NR group.

Single organism was found in 80% in HIV-R group and 84% in HIV-NR group. Mixed organism was detected in 12% in each group. Detection of multiple organisms is important. Patients with mixed flora had a severe course of illness. The assumed clinical diagnosis of resistant bacteria could be due to infection caused by mixed organisms. In this way finding of a mixed flora can reduce the use of unnecessary broad spectrum antibiotics and the cost of treatment.

In a study by Ezgi Ozilmaz *et al*^[10] percentage of multiple organism was around 10%.

The most commonly detected single organism is *Staphylococcus aureus* (24%) in HIV -R patients. *Klebsiella pneumoniae* (28%) is the most common single organism in HIV-NR patients.

In a study by Mustaq Ahmed *et al*^[12], Egbe *et al*^[13] and Akingbade^[14] have also reported the same.

Klebsiella pneumoniae to be the most common isolate recovered from patients with LRTIs. This was the

findings in all groups like diabetics, smokers, alcoholics, patients with COPD, etc. All the patients having *Staphylococcus aureus* (24%) required admission.

In a study by Baik I *et al*^[15], among the bacteria *Staphylococcus aureus* (24%) and *Streptococcus pyogenes* (20%) was commonly cultured organism in HIV-R patients.

In a study by Hirschtick *et al*^[16], atypical pyogenic bacteria may also be the causative agent, particularly in patients with advanced HIV disease. For example, *Klebsiella pneumoniae*, other members of the Enterobacteriaceae family and *Pseudomonas aeruginosa* were present in 13, 10 and 8% of cases, respectively, of confirmed pneumonia in this US cohort study.

In a study by Bekele Afessa *et al*^[17], *P. aeruginosa*, the Enterobacteriaceae family and *Staphylococcus aureus* were the cause of 25, 9 and 10% of community-acquired pneumonia, respectively.

One HIV-R patients with very low CD4 count (base line=34 cells/ μ l) with right sided encysted empyema had sputum growth of *Klebsiella pneumoniae*. His direct smear of sputum also showed plenty of pseudohyphae (*Candida*) and pus cells. Sputum for acid fast bacilli was negative.

In our study it has been found that in very low CD4 count we usually found sputum growth of Gram negative bacteria like *Klebsiella*, *Pseudomonas*, *E. coli*, *Acinetobacter* etc. All these patients were severely ill.

In a study by Bekele Afessa *et al*^[17], pseudomonal pneumonia is becoming a common pulmonary complication, especially in patients with low leukocyte and CD4 lymphocyte counts. Compared with pneumococcal pneumonia, pseudomonal pneumonia is associated with a lower incidence of bacteremia and a longer hospital stay. Despite the low CD4 lymphocyte and leukocyte counts associated with pseudomonal pneumonia, the mortality rate is only 19%.

In a study by C Feldman *et al*^[18], pneumonia is most common when the CD4+ count falls below 200 cells/ μ l. The organisms responsible for CAP in HIV-seropositive patients are the same as in HIV-seronegative cases. The most common bacterial causes of pneumonia are *S. pneumoniae* and *H. influenzae*.

In our study, pleural tap was done in 3 patients in each group of which all showed bacterial growth in the culture of pleural fluid. It indicates that empyema fluid, when present is a better bacteriological sample than sputum.

In a study by S. Bansal *et al*^[3], by pleural fluid specimens were available from seven (10%) patients. Pleural fluid from two patients grew *Staphylococcus aureus*.

12% of patients in each group had normal finding in chest X ray. Patchy consolidation was found in 60% of HIV-R patients and 64% of HIV-NR patients. In both the groups presenting with consolidation sputum showed growth of bacteria or fungus. Sputum culture detected growth in 92% in HIV-R group and 100% in HIV-NR group. So chance of getting organism in sputum is high in patients showing consolidation in chest x-ray.

One patient in the HIV-R group had a very low CD4 count (base line CD4 27 cells/ μ l) showed ill defined non homogeneous opacity in right mid and lower zone in chest X ray. Her sputum showed growth of mixed organism- Pseudomonas, Acinetobacter and Aspergillus fumigatus. She was anaemic, icteric, had bilateral pedal edema with hepatomegaly with high serum ferritin and triglyceride level. Her CMV DNA PCR was also positive. She was diagnosed as a case of Hemophagocytic syndrome.

One HIV-R COPD patient presenting with high fever, cough with expectoration, anemia (Hb-7.1 g/dl) with low CD4 count (CD4 86 cells/ μ l) showed growth of Klebsiella pneumoniae in sputum sensitive to beta lactum, quinolones, and third generation cephalosporin. Chest X ray showed bilateral non homogenous opacity in lower lung fields with increased broncho vascular markings in upper and mid zones of both lungs. USG showed bilateral renal parenchymal disease (Creatinine- 2.88 mg/dl).

One HIV-R patient came to us with low CD4 count with history of cough with expectoration and fever suggestive of LRTI showed growth of mixed organism -Klebsiella pneumoniae, Streptococcus pyogenes and Staphylococcus aureus. Patient was chronic alcoholic, smoker with past history of treatment for EPTB. His Chest x-ray showed left sided pleuropericardial effusion and USG showed mild hepatomegaly with presence of significant retro peritoneal lymph node. The patient needed inpatient treatment and was cured by giving inj. Meropenem and inj. Linezolid.

One HIV-R patient showed growth of Streptococcus pneumoniae in sputum but Staphylococcus aureus in blood culture. Chest x-ray showed right mid and lower zone consolidation.

2 HIV-R patients did not show growth of any organism in sputum. The cause could be prior antibiotic therapy, viral pneumonia, infections by anaerobes or atypical organisms that were difficult to grow by conventional aerobic bacteriological culture like Mycoplasma, Chlamydia, Legionella etc.

In the study of CMC, Ludhiana in 2006 used serology for Mycoplasma and Chlamydia for all patients. They detected the occurrence of atypical pneumoniae around 34%.

Dey AB et al from AIIMS, New Delhi in 2000 suggested that the prevalence of Mycoplasma was around 35%.^[19]

In HIV-R groups 4 patients had fungal growth in sputum. Among them Aspergillus fumigatus was detected in 2 patients. 1 patient had candida spp. 1 patient presented with high grade fever, cough with expectoration with growth of Aspergillus niger and pseudomonas in sputum culture. The patient was admitted and treated successfully with inj. Piperacillin tazobactam intravenously.

In a study by VV Shailaja et al^[20], among the 27 fungal isolates from HIV reactive patients, 9 were pathogenic (12.83%), 6/9 were *Candida albicans*, 2/9 were *Cryptococcus neoformans* and one was *Aspergillus niger*. The rest of the 18 isolates were non albicans *Candida* spp. that were considered as colonizers of the oropharynx.

In our study, klebsiella pneumonia in HIV-NR group is usually sensitive to carbapenems, Colistin, polymyxin-B & fluoroquinolones/aminoglycosides in some cases but resistant to beta-lactams and third generation cephalosporins. Klebsiella pneumonia in HIV-R group is usually sensitive to carbapenems and fluoroquinolones and resistant to third generation cephalosporins, beta lactams, cotrimoxazole and in some cases to aminoglycosides also.

In our study, staphylococcus aureus in HIV-R and HIV-NR group is usually sensitive to vancomycin and linezolid and resistant to aminoglycosides, beta-lactam, third generation cephalosporin, macrolides, cotrimoxazole and fluoroquinolones but was found to be sensitive to levofloxacin in HIV-NR group.

In a study by K V Ramana et al^[9], imipenem and amikacin was found to show greater activity against gram negative bacteria isolates whereas linezolid, amikacin, ciprofloxacin, ofloxacin and cotrimoxazole were effective against gram positive bacteria isolates.

In our study only one patient in HIV-R group expired even after taking full treatment for LRTI. This patient was on treatment for sputum positive DTB with Cat-1 ATD. He was also undergoing treatment for COPD and DM. He also developed skin rash and oro-genital ulcer during treatment. Rest of the patients got cured in both HIV-R and HIV-NR group.

In a study by S. Bansal et al^[3], out of the 21 patients hospitalised 8 patients died. 2 patients out of 8 had COPD and one had pulmonary embolism.

None of the patients in my study were vaccinated with pneumococcal or influenza vaccine.

CONCLUSIONS

At the end of my study of clinical, radiological and laboratory parameters of HIV infected and HIV non infected adults, it is concluded that following points should be considered while dealing with a case of LRTI

- A reasonable number of LRTI patients require in-patient treatment.
- Increased age is a significant risk factor for morbidity in LRTI.
- LRTI in HIV-R group is more common in younger age group as compared to HIV-NR group in which it is more common after 50 years of age.
- Males are more commonly affected with LRTI in both groups.
- LRTI is common among diabetics, smokers and alcoholics in both groups.
- COPD is an important association for LRTI in both groups, more commonly in HIV-NR group and a risk factor for mortality in HIV-R group.
- Past history of tuberculosis is also an important association for LRTI in both groups.
- Use of antibiotic before coming to hospital is a very common practice in both rural and urban population. Cough and fever are the most common presentations in both groups.
- Chest pain and shortness of breath is more common in HIV-R group.
- High BP associated with LRTI is more common in HIV-NR group.
- The severity criteria given by BTS guideline i.e. CURB-65 is pretty useful in a set up like us. It helps to recognize the severely ill patients early.
- Crepitations are commonly present in both the groups.
- Anemia and cervical lymphadenopathy are more common in HIV-R group.
- Clubbing is more common in HIV-NR group.
- Pleural effusion is a common finding in both groups.
- Leucopenia was more common in HIV-R group whereas, leucocytosis was more common in HIV-NR group.
- Most of the HIV-R patients had CD4 count less than 350 cells/ μ l.
- Gram negative bacteria is more commonly found in CD4 less than 150 cells/ μ l.
- Gram positive bacteria is more commonly found in CD4 more than 150 cells/ μ l.
- Single or mixed organism causing LRTI does not depend on immune status of the patient.
- The most common single organism found in sputum culture of patients of LRTI in HIV-R group is *Staphylococcus aureus* and in HIV-NR group is *Klebsiella pneumoniae*.
- *Klebsiella pneumoniae* in HIV-NR group is usually sensitive to carbapenems, Colistin, polymyxin-B & fluoroquinolones/aminoglycosides in some cases but resistant to beta-lactams and third generation cephalosporins.
- *Klebsiella pneumoniae* in HIV-R group is usually sensitive to carbapenems and fluoroquinolones and

resistant to third generation cephalosporins, beta lactams, cotrimoxazole and in some cases to aminoglycosides also.

- *Staphylococcus aureus* in HIV-R and HIV-NR group is usually sensitive to vancomycin and linezolid and resistant to aminoglycosides, beta-lactam, third generation cephalosporin, macrolides, cotrimoxazole and fluoroquinolones but was found to be sensitive to levofloxacin in HIV-NR group.
- Fungal respiratory infections are more common in HIV-R group as compared to HIV-NR group.
- Patchy consolidation is the commonest radiological finding in both the groups.
- Pleural effusion is more common in HIV-NR group.
- Normal radiological finding is found equally in both groups.
- Hilar lymphadenopathy was more common in HIV-R group.
- Consolidation is more common in CD4 count <200 cells/ μ l.
- Gram negative bacteria like *Pseudomonas*, *Klebsiella pneumoniae*, *E. coli*, *Klebsiella oxytoca*, *Acinetobacter* are usually found in HIV- Infected patients with CD4 Count <150 cells/ μ l.
- Gram positive bacteria like *Staphylococcus aureus*, *S. Pyogenes*, *S. pneumoniae* are usually found in sputum of HIV-Infected patients with CD4 count >150 cells/ μ l.
- The demerit of our study was small number of patients included in the study, sensitivity pattern was not done against all available antibiotics and minimum inhibitory concentration of the tested antibiotics could not be performed due to lack of facilities.

Conflicts of interest

All contributing authors declare no conflicts of interest.

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