



## Original Research Article

# Bacteriological Profile of Lower Respiratory Tract Infection (LRTI) among HIV Seropositive Cases in Central Terai of Nepal

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## ABSTRACT

### Keywords

Human Immuno deficiency Virus (HIV), Lower Respiratory Tract Infection (LRTI), CD4+ cell count, Anti-retroviral therapy, Acid Fast Bacilli (AFB)

Patients with HIV infections frequently present with spectrum of pulmonary complications from opportunistic infections and neoplasm that may be associated to high mortality rates. Disease of respiratory tract accounts for half of death from AIDS. This present study evaluates the presence of respiratory tract pathogens in HIV/AIDS patients and thus requiring the awareness among clinicians regarding the occurrence of these pathogens in HIV/AIDS patients. A total of 121 sputum samples were collected from confirmed HIV/AIDS patients, with/without respiratory symptoms. Patients were requested to cough deeply to produce purulent sputum specimen free from salivary contamination in a clean, dry, wide-necked, leak proof container. Standard protocol was followed to isolate and identify organism which was followed by disc diffusion antibiotic susceptibility tests. Among 121 sputum samples, 39.7% were growth positive whereas 60.3% growth negative. The study showed females had more LRTI (54.3%) than male (51.2%). *K. pneumoniae* (27.0%) was the most prevalent Gram negative bacteria whereas *S. aureus* (20.8%) was the most predominant Gram positive bacteria. In addition 15.7% of cases had infection with Acid Fast Bacilli (AFB). Among the tested antibiotics, all bacterial isolates was found highly resistant towards amoxicillin (79.3%) followed by other antibiotics. Female had more LRTI than male. The older age group, smoking habit and lower CD4+cell count are the risk factors for LRTI allied with HIV/AIDS. Similarly, patients under ART had lower LRTI.

## Introduction

AIDS, the acquired immunodeficiency syndrome sometimes called as 'slim disease' is a fatal illness caused by retrovirus known as the human immunodeficiency virus (HIV) which breaks down the body's immune system, parting the victim vulnerable to a host of life threatening opportunistic infections, neurological disorders, or

unusual malignancies. The term AIDS refers only to the last stage of the HIV infection (Park, 2007).

HIV infection is solely dependent on the interaction between the viral load and host factors. HIV brings about the destruction of CD4+ T-lymphocytes, which are crucial

cells in forming immune response to foreign antigens and it is also the primary target cells of HIV (Pattanapanyasat and Thakur, 2005; Paranjape, 2005). The progressive loss of these lymphocytes ultimately results in the loss of an ability to mount desirable immune response to any pathogen (Pattanapanyasat and Thakur, 2005) and death of the patients in the terminal stage of HIV infection occurs (Paranjape, 2005).

Lower Respiratory Tract Infection (LRTI) is one of the leading causes of the morbidity and mortality in the world (Murray and Lopez, 1997). LRTI is not a single disease but a group of specific infection each with a different epidemiology, pathogenesis, clinical presentation and outcome. The etiology and symptomatology of respiratory diseases vary with age, gender, season, the type of population at risk and other factors. These are frequently the first infection to occur after birth and pneumonia is too often the final illness to occur before death (Dawadi *et al.*, 2005).

Patients with HIV infections frequently present with spectrum of pulmonary complications from opportunistic infections and neoplasm that may be associated to high mortality rates. Disease of respiratory tract accounts for half of death from AIDS. Bacterial pneumonia and AIDS can lead to significant morbidity and mortality and are second to *Pneumocystis carinii* pneumonia (PCP) (Oreinstein *et al.*, 1985). Since the initial AIDS cases were associated with opportunistic infection such as PCP, the importance of bacterial infection, including bacterial pneumonia, was not recognized at the beginning of the epidemic. However, studies have shown that bacterial infections occur more frequently than other opportunistic infection in patients with HIV (Selwyn *et al.*, 1988; Wallace *et al.*, 1997).

*Streptococcus pneumoniae* is the commonest cause of community-acquired pneumonia with the second most common being *Haemophilus influenzae* (Janoff *et al.*, 1992; Moreno *et al.*, 1991). In comparison, nosocomial pneumonia occurs primarily in patient with AIDS and is usually due to *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and other gram negative bacilli (Hirschtick *et al.*, 1995; Polsky *et al.*, 1986). Nosocomial infection has high fatality rates.

*Mycobacterium tuberculosis* (MTB) co-infection with HIV increases thirty times the risk of developing active tuberculosis, extra pulmonary tuberculosis (lymphadenopathy, pericardial disease, pleural effusion, and meningitis) and military tuberculosis. Active tuberculosis accelerates the progress of HIV disease. HIV-related tuberculosis is the cause of one third or more of death in those with HIV/AIDS (Cheesebrough, 2009). The incidence of TB among person infected with HIV is increased with CD4 lymphocytes count less than 200 per cubic millimeter.

Resistance of numerous bacterial pathogens to many antibiotics continues to increase globally. Frequencies, pattern, and distributions of resistant bacteria vary significantly with geographic regions and often reflect the usage patterns of antibiotics. Factor that increase in resource-poor and resource-rich nation include total antibiotic consumption as well as under use through lack of access, inadequate dosing, poor adherence, and substandard antimicrobial usage (Spector *et al.*, 1994).

Ever since its discovery, the HIV has emerged as a global disaster. People in productive age groups are predominantly affected by AIDS and hence in same countries the impact of AIDS has led to major decrease in Gross National Product (GNP) (WHO, 2009). The progression and

outcome of HIV depends on the factors like baseline health, nutritional status, environment, endemic disease and access to therapy. It is important to understand the presentation of HIV disease in the local context to minimize the HIV-related mortality (Kumarasamy *et al.*, 2005). The type of pathogen responsible for Opportunistic Infections (OIs) varies from region to region. Therefore, identification of the specific pathogens is important for management of such cases (Ayyagari *et al.*, 1999). On this perspective it seems important that the causative agent of the endogenous source should be evaluated i.e. their occurrence, prevalence and their responsiveness to the available antibiotics either symptomatic or carrier by using enriched technique.

This present study evaluates the presence of respiratory tract pathogens in HIV/AIDS patients and thus requiring the awareness among clinicians regarding the occurrence of these pathogens in HIV/AIDS patients. The spectrum of bacterial infections and their respective antibiotic susceptibility pattern would be important inference regarding the empirical choice of antibiotics in the management of LRTI among the study population in areas with a high prevalence of HIV infection.

## **Materials and Methods**

The laboratory investigation of this study was carried out at Clinical Pathology Department, Janaki Medical College and Teaching Hospital (JMCTH) Janakpur, Nepal from April 2014 to July 2015. This study included the HIV/AIDS patients attending to Janaki Medical College, Janakpur, Janakpur Zonal Hospital, Janakpur, Janakpur City hospital, Janakpur and Janaki Health Care and Research Center, Janakpur, Nepal. All the cases were

confirmed HIV/AIDS, with/without respiratory symptoms.

All together 121 individuals were ready for voluntary participation in this study. Verbal as well as written consent were taken from all the study population. Patient's name/code, age, sex, marital status, smoking habit, CD4+ cell count and status of ART taken were recorded, either by interviewing with them or their care takers, or from their case files. All the information was filled in the questionnaire form. The data were analyzed using Chi-square test.

## **Specimen collection and processing**

Patients were requested to cough deeply to produce purulent sputum specimen free from salivary contamination in a clean, dry, wide-necked, leak proof container. Patients were advised to collect 2ml of early morning sputum specimen. The purulent part of sputum was then smeared and processed for Grams and Ziehl-Neelsen staining technique for Direct Microscopic examination.

Media were prepared as instructed by the manufacturer company (Hi-media). A sterilized loopful of specimen was streaked into Blood agar, MacConkey agar and Chocolate agar. Blood agar and Chocolate agar were incubated at 37°C for 24 hours in a candle jar. MacConkey agar was aerobically incubated at 37°C for 24 hours. After that, colony morphology of predominant aerobic and facultatively anaerobic bacteria was reported. This was followed by Gram's staining and appropriate biochemical tests were performed according to Gram's staining results for identification. Identification of significant isolates was done by using standard microbiological techniques as described in the Bergy's manual.

Antibiotic sensitivity test for the isolated organism were done by using Kirby Bauer Disc Diffusion Method. Bacterial inoculums were prepared by suspending the freshly-grown bacteria in 25 ml sterile Nutrient broth and compared with turbidity equivalent to 0.5 Mc Farland standard and was streaked on entire Muller-Hinton agar plate for those organism that were not fastidious, for fastidious organisms like *Haemophilus* spp it was streaked onto chocolate agar and for *Streptococcus* spp it was streaked onto blood agar. Six antibiotic discs were placed around the outer edge of the plate and incubated overnight at 37°C. Diameter of zone of inhibition was measured and CLSI zone diameter criterion was used to interpret the level of susceptibility to each antibiotic.

## Results and Discussion

The study was conducted among 121 HIV/AIDS patients. Among all patients, only 48 (39.7%) were culture positive whereas the remaining 73 (60.3%) were culture negative as shown in figure 1.

Among all cases, culture positive rate was found to be slightly higher in female (42.9%) than in males (38.3%). This was found to be statistically insignificant ( $P=0.65$ ). Similarly, AFB positive rate in female (17.1%) was also found to be higher than in males (15.1%). This was too statistically insignificant ( $P=0.78$ ) as shown in table 1.

Among age groups, higher prevalence rate of LRTI was observed in age group greater than or equal to 45 years (75.0%) followed by 15–45 years (51.4%). The occurrence of LRTI rate among age group below 15 years was found to be 0 (0%). This was found to be statistically significant ( $P=0.02$ ). However, higher prevalence was found in 15–45 years age group, 54 (85.7%),

followed by age group above or equal to 45, 9 (14.3%), and age group below 15, 0 (0%) as shown in table 2.

## Pattern of total microbial isolates

Altogether 9 different types of bacterial isolates were isolated. Of the total 48 isolates, 19 (39.6%) were Gram positive bacteria and 29 (60.4%) were Gram negative bacteria. Of all the isolates *Klebsiella pneumoniae* was most frequently encountered at 27.0%, followed by *Staphylococcus aureus* 20.8%, *S. pneumoniae* 18.8%, *E. coli* 8.3%, *H. influenzae*, *Klebsiella oxytoca*, *P. aeruginosa*, 4.2% each, *Enterobacter* spp 2.1% and unidentified gram negative bacteria 10.4%. Among 63 positive cases, 4 AFB positive sputum specimens showed growth of other bacteria. Among 4 polymicrobial infection case, AFB was associated with 4 different types of bacteria.

Among 38 current smokers, 42.9% had a LRTI, among whom 77.8% were male and 22.2% were female. Similarly, among 34 previous smokers, 31.7% had LRTI, among whom 75% were male and 25% were female. Additionally, among 49 non-smokers, 25.4% had LRTI, among them 50% were male and 50% were female. The data was found to be statistically significant ( $P=0.01$  as shown in table 3).

Among different CD4 cell count categories, rate of LRTI was found significantly higher among cases having CD4 cell below 200 (63.4%), followed by those within 200-500 range categories (53.1%) and those within range above 500 (18.7%). This result was found to be statistically significant ( $P=0.00$ ) as shown in table 4.

Of total cases, 67 cases (55.4%) were under ART whereas 54 cases (44.6%) were not under ART. Prevalence of LRTI was higher

among cases not under ART (64.8%) compared those under ART (41.8%). This was found to be statistically significant ( $P=0.01$ ) as shown in table 5.

Among the antibiotics used, Gram positive bacteria were found to be most resistant to co-trimoxazole and penicillin, 68.4% each, followed by amoxicillin (47.4%), chloramphenicol (42.1%), ciprofloxacin (36.8%), oxacillin (36.8%) and azithromycin (31.6%). Similarly, Gram-negative bacteria were found to be most resistant to amoxicillin (79.3%), followed by co-trimoxazole (62.1%), ciprofloxacin (55.2%), ceftriaxone (51.7%), azithromycin (48.3%), ofloxacin (51.7%) and gentamycin (62.1%) as shown in table 6.

The present study showed the rate of occurrence of lower respiratory tract infection in female (54.3%) was found to be slightly higher than in males (51.2%). Similarly, culture positive rate in female (42.9%) was also found to be higher than male (38.3%). Prescott *et al.* (1999) [18] reported that although women generally do not hold jobs, with major exposure to dusts and fumes that potentially cause respiratory disease.

In our study, occurrence of LRTI was observed relatively higher in elderly population (45 years and above) of 75.0% of total elderly cases than younger age groups i.e. below 15 years and 15–45 years. The higher incidence of LRTI in elderly can be attributed to weakening of immune system with age which renders them vulnerable to infection. In a study conducted by MacFarlane *et al.* (1993), confirmed that pneumococcal infection is common in patients over the age of 55, who also have an increasing incidence of LRTI as they get older.

The present study shows greater numbers of

isolates were Gram negative bacteria of 60.4% whereas the contribution of Gram positive bacteria in lower respiratory tract infection was 39.6%. The rate of Gram negative bacterial infection to Gram positive bacterial infection was found higher. Similar type of results was obtained in a study conducted by Rasheed and Thajuddin (2011) in which 37.5 % of bacterial isolates were Gram-positive and 62.5% of isolates were Gram-negative.

In our study out of all the pathogens isolated, *K pneumoniae* was the most common 13 (27.0%). This was followed by *S. aureus* in 10 (20.8%) and *S. pneumoniae* in 9 (18.8%). The rest were followed by *E. coli* 4 (8.3%), *H. influenzae* 2 (4.2%), *Pseudomonas* spp 2 (4.2%), *Klebsiella oxytoca* 2 (4.2%), *Enterobacter* spp 1 (2.1%) and unidentified gram negative bacteria 5 (10.4%). Sailaja *et al.* (2004), found 32.26% cases of *K. pneumoniae*, 25.81% of *S. pneumoniae* and 12.90% of *S. aureus*. Similarly, in a study conducted by Okesola and Ige (2008), *Klebsiella* spp and *Pseudomonas aeruginosa* were the most prevalent (38% and 16.7% respectively) among the Gram-negative pathogens. *S. pneumoniae* was the most prevalent among the Gram-positive organisms (14%) followed by *S. pyogenes* (3.3%) and *S. aureus* (2.7%). All these findings were in accord with our study. *K. pneumoniae* is the major gram negative isolates in our study. *K. pneumoniae* causes disease in normal population. However, pneumonia due to *K. pneumoniae* is classically thought of as community acquired and occurring in elderly and debilitated population with underlying alcoholism, chronic lung disease or diabetes.

In a French clinical epidemiology database, *S. pneumoniae* and *H. influenzae* were the cause of 52% and 16% of bacteriologically confirmed pneumonias respectively.

Bacterial pneumonia due to *H. influenzae* occurred less frequently than that due to *S. pneumoniae* and was particularly observed in patients with <100 CD4 T-lymphocyte count per cubic millimeter (Cordero *et al.*, 2000). *P. aeruginosa* infection in patients with HIV is often community acquired and is associated with substantial mortality. In a study carried by Sailaja *et al.* (2004) found 9.68% of the isolates were *P. aeruginosa*. Immunosuppressed hosts, including neutropenic patients and HIV-infected individuals, especially those with low CD4 cell counts, are at particular risk (Manfredi *et al.*, 2001).

The present study also reported that 3.3% patients had polymicrobial bacterial etiology was also associated with HIV cases. Okesola and Ige (2008), found 4.7 % of polymicrobial bacterial etiology. Pulmonary polymicrobial infections mostly have been found in HIV infected patients by various studies indicates the severity of the infection in the HIV positive patients (Yoshimine *et al.*, 2001; Eza *et al.*, 2006).

In the present study, 42.9% had a LRTI among 38 current smokers and 31.7% had LRTI among 34 previous smokers. In Nepal, tobacco smoking has been identified as one of the most important risk factors contributing to a high prevalence of chronic bronchitis and chronic obstructive lung disease. In addition, a higher prevalence of tobacco use and wide spread use of unventilated indoor fires for cooking and heating combine to produce high rates of lung diseases in Nepal (Pande *et al.*, 2001).

In our study LRTI was observed significantly higher among cases with CD4 T-lymphocyte count less than 200 per cubic millimeter (63.4%), followed by 200-500 range groups (53.1%). It was found lowest among cases with CD4 T-lymphocyte count more than 500 per cubic millimeter (18.7%).

A similar relationship between a decreased CD4 T-lymphocyte count and increased risk of bacterial pneumonia has been found in European studies (Boschini *et al.*, 1996; Tumbarello *et al.*, 1998). This data is in accord with our result. The most important risk factor for bacterial pneumonia is the degree of immunosuppression, as reflected by the CD4+ T-lymphocyte count (Mayaud *et al.*, 2002).

In our study, LRTI was found distinctively higher in cases not receiving ART (64.8%), than those receiving ART (41.8)%. The incidence of opportunistic LRTI is decreased during the current era of HAART, bacterial pneumonia remains (Mayaud *et al.*, 2002). Thus, pneumococcal vaccination might be given to the patient on highly active antiretroviral therapy with a CD4 cell count reaching 200 cells per millimeter (Mayaud *et al.*, 2002).

The increasing rate of human immunodeficiency virus (HIV) infection in many countries has an impact on tuberculosis (TB) epidemiology. While TB prevalence has remained stable, TB incidence continues to rise, especially in countries most severely affected by HIV epidemics as well as those facing political turmoil, migration, poverty and unemployment and where intravenous drug abuse is rampant (Swaminathan and Narendran, 2008). In this study, among 121 HIV/AIDS, 19 (15.7%) were found to be infected with PTB and 5 (4.1%) were extra PTB cases. PTB was confirmed with sputum microscopy and extra PTB with clinical findings. Among the large numbers of reports available, pulmonary tuberculosis is reported more than any other clinical forms in HIV/AIDS patients. HIV infection remains, in global terms, the largest risk factor for the development of tuberculosis (Boyton, 2005). This suggest that incidence

of TB is rapidly increasing among HIV/AIDS patients in Nepal indicating the threat of transmission to whole population.

In our study, *Pseudomonas* spp was the most resistant whereas *H. influenzae* was found to be the sensitive to nearly all of the antibiotics used, followed by *S. pneumonia* and *S. aureus*. *Pseudomonas* has been reported to develop resistance during prolonged therapy with all antibiotics. Majority of isolates were susceptible to ceftriaxone whereas *H. influenzae* showed 100% resistance followed by *E. coli* (75%) followed unidentified gram-negative bacteria (60.0%). *K. pneumonia*, the most prevalent isolate, showed high resistance to most of the antibiotics except ceftriaxone and azithromycin.

The emergence of strains of *S. pneumonia* that are resistant to penicillin is of great concern. Antimicrobial resistance is increasing globally, although patterns and degree of resistance vary by geographic

region (Jacobs, 2003; Jacobs *et al.*, 2003; Kaplan, 2004). The resistance to Amoxicillin in *S. pneumoniae* (33.3%) observed in this study is not as high as that observed in other countries such as in South Africa (Nascimento-Carvalho, 2001). This difference in antibiotic resistance pattern may be due to variations in the antibiotic prescribing habits in different geographical regions (Okesola and Ige, 2008).

For most non susceptible strains, cefuroxime or cefotaxime or ceftriaxone is somewhat more effective than either ampicillin or penicillin, although a high dose of amoxicillin is the preferred treatment for pneumonia in outpatients. The addition of  $\beta$ -lactamase inhibitor conveys no advantage, since the mechanism of resistance in this organism does not involve this enzyme. Vancomycin is rarely needed to treat pneumococcal pneumonia, even in severe cases (McIntosh, 2002).

**Table.1** Sputum culture positivity among genders

Sex	Total	Culture positive (%)	Statistics	AFB (%)	Statistics
Male	86	33 (38.3%)	P=0.65	13 (15.1%)	P=0.78
Female	35	15 (42.9%)		6 (17.1%)	
<b>Total</b>	<b>121</b>	<b>48 (39.6%)</b>		<b>19 (15.7%)</b>	

**Table.2** Agewise distribution of LRTI among patients

Age (Yrs)	Cases involved	Total Positive cases	Total %	Statistics
<15	4 (3.3%)	0 (0%)	0	P=0.025
15-45	105 (86.8%)	54 (51.4%)	85.7	
≥45	12 (9.9%)	9 (75.0%)	14.3	
<b>Total</b>	<b>121 (100%)</b>	<b>63 (52.0%)</b>	<b>100.0</b>	

**Table.3** Distribution of pathogens in smoking habit

Smoking habit	Cases involved			Positive cases			Statistics
	Male	Female	Total	Male	Female	Total	
Current smokers	29 (76.3%)	9 (23.7%)	38 (31.4%)	21 (77.8%)	6 (22.2%)	27 (42.9%)	P=0.01
Previous smokers	26 (76.5%)	8 (23.5%)	34 (28.1%)	15 (75.0%)	5 (25.0%)	20 (31.7%)	
Non-smokers	31 (63.3%)	18 (36.7%)	49 (40.5%)	8 (50.0%)	8 (50.0%)	16 (25.4%)	
<b>Total</b>	<b>86</b> <b>(71.0%)</b>	<b>35</b> <b>(29.0%)</b>	<b>121</b> <b>(100%)</b>	<b>44</b> <b>(69.8%)</b>	<b>19</b> <b>(30.2%)</b>	<b>63</b> <b>(100%)</b>	

**Table.4** Distribution of LRTI by CD4 cell count

CD4 cell count/ $\mu$ l	Cases involved	Positive cases	Statistics
>500	16 (13.2%)	3 (18.7%)	P=0.00
200-500	64 (52.9%)	34 (53.1%)	
$\leq$ 200	41 (33.9%)	26 (63.4%)	
<b>Total</b>	<b>121 (100%)</b>	<b>63 (52.0%)</b>	

**Table.5** Distribution of LRTI by Antiretroviral therapy (ART) status

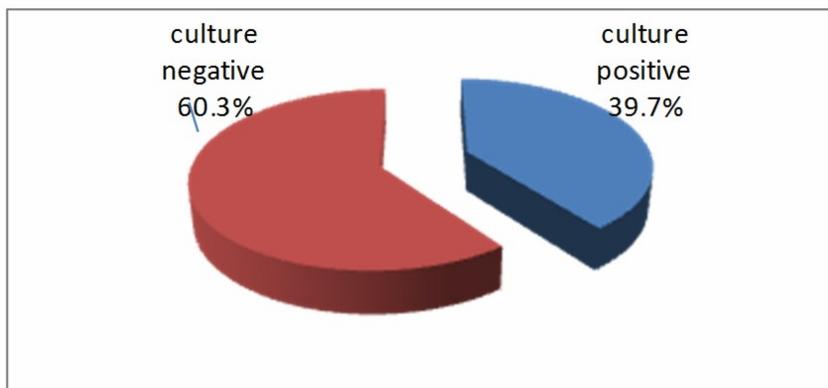
ART status	Cases involved	Positive cases	Statistics
ART taken	67 (55.4%)	28 (41.8%)	P=0.01
ART not-taken	54 (44.6%)	35 (64.8%)	
<b>Total</b>	<b>121 (100%)</b>	<b>63 (52.0%)</b>	

**Table.6** Antibiotic resistance percentage pattern of all bacterial isolates

Bacterial isolates	Pen	Oxa	Amox	Cip	Cot	Chlo	Azi	Cef	Ofi	Gen
<i>S. aureus</i>	70.0	30.0	60.0	50.0	70.0	30.0	30.0	0	0	0
<i>S. pneumoniae</i>	66.7	40.0	33.3	22.2	66.7	55.5	33.3	0	0	0
<b>Total</b>	<b>68.4</b>	<b>36.8</b>	<b>47.4</b>	<b>36.8</b>	<b>68.4</b>	<b>42.1</b>	<b>31.6</b>	<b>0</b>	<b>0</b>	<b>0</b>
<i>K. pneumoniae</i>	0	0	69.2	53.8	69.2	0	38.5	30.8	53.8	61.5
<i>E. coli</i>	0	0	100	75.0	75.0	0	75.0	75.0	50.0	75.0
<i>H. influenzae</i>	0	0	0.0	0.0	50.0	0	0.0	100	0.0	0.0
<i>Pseudomonas spp</i>	0	0	100	50.0	100	0	100	50.0	50.0	100.0
<i>K. oxytoca</i>	0	0	100	0.0	100	0	50.0	50.0	50.0	50.0
<i>Enterobacter spp</i>	0	0	100	100	0.0	0	0.0	0.0	100.0	100.0
<b>Other GNB</b>	0	0	100	80.0	20.0	0	60.0	60.0	60.0	60.0
<b>Total</b>	<b>0</b>	<b>0</b>	<b>79.3</b>	<b>55.2</b>	<b>62.1</b>	<b>0</b>	<b>48.3</b>	<b>48.3</b>	<b>51.7</b>	<b>62.1</b>

Pen-Penicillin, Oxa-Oxacillin, Amox-Amoxicillin, Cip-Ciprofloxacin, Cot-Cotrimoxazole, Chlo-Chloramphenicol, Azi-Azithromycin, Cef-Ceftriaxone, Ofi- Ofloxacin, Gen-Gentamycin

**Figure.1** Microbial culture status among study population



The key factor influencing the emergence of resistant pneumococci is unnecessary antibiotic use for viral respiratory infections in humans. It is also due to overuse of antibiotics in humans. In some developing countries antibiotics are available without prescription and this potentially facilitates overuse, although the expenses of antibiotics often deter indiscriminate use in these settings. Use of closely related drugs for other condition also plays a role in the spread of resistance (Schrag *et al.*, 2001). Other factors such as reduced drug quality and suboptimal regimen may also play a role in the emergence of pneumococcal resistance. Suboptimal and long-duration regimens increase the opportunity for acquisition and/or amplification of resistant *S. pneumoniae* (Schrag *et al.*, 2001).

After the discovery and unlimited use of penicillin for Staphylococcal infection, resistance emerged and rapidly spread possibly due to penicillinase enzyme. Today almost 90% of *S. aureus* are resistant to penicillin. Simultaneously methicillin resistant *S. aureus* (MRSA) were also discovered. MRSA infection in both the hospital and community setting are commonly treated with non  $\beta$ -lactamase antibiotics such as clindamycin and cotrimoxazole. In the present study, a substantial resistance was observed to a

number of commonly used antibiotics. This may be due to the indiscriminate and inappropriate use of antibiotics that is rampant in Nepal. Hence, it is important to periodically monitor the antibiotic resistance pattern in different regions.

In conclusion, the present study indicated that there have not been any significant changes in the bacterial involvement in causing LRTI. Smoking habits and CD4 cell count below 200 per  $\mu$ l has remained as the major risk factors. Similarly, the age groups at risk have remained more or less same over a period of time. In contrast, increasing number of drug resistant pathogens in the vicinity truly sets the alarm for an immediate action to be undertaken towards judicious use of antibiotics. Higher prevalence of TB among females observed in this study emphasizes the need of a gender based study in finding TB cases among the study population.

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