ORIGINAL ARTICLE

# Pathogens Causing Pneumonia Among Cancer Patients

**Rabia Jabbar[1], Muhammad Saeed[2], Farhan Rasheed[3], Shagufta Iram[4], Ambereen Anwar Imran[5], Sara Saeed[6] Maqsood Ahmad[7]**

**Author`s Affiliation**

*[1,] Medical Lab Technologist Pathology Department Allama Iqbal Medial College, Lahore, Pakistan*
*[2]Infection Control Officer (ICO) & Medical Lab Technologist Microbiology Lab, Umar Hospital & Cardiac Centre Lahore Pakistan*
*[3,4,] Assistant Professor Pathology Pathology Department Allama Iqbal Medial College, Lahore, Pakistan*
*[5]Head and Professor of Pathology Pathology Department Allama Iqbal Medial College, Lahore, Pakistan*
*[6]Assistant Professor Oncology Department of Oncology Allama Iqbal Medial College/Jinnah Hospital, Lahore Pakistan*
*[7]Medical Lab Technologist Chemical Pathology Department University of Health sciences Lahore*

**Author`s Contribution**

*[1]Lab work, Data collection*
*[2,3] Drafted the manuscript, Statistical Analysis, Study design, results in interpretation*
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***Address of Correspondence***

*Farhan Rasheed*
*dr.farhanrasheed@gmail.com*

**ABSTRACT**

**Objective:** The aim of this study was to determine the pathogens causing lower respiratory tract infections (RTI) among immunocompromised patients and their antimicrobial susceptibility pattern.

**Materials and Methods:** It was a cross-sectional study conducted at Pathology Department, Allama Iqbal Medical College, Lahore, from July 2015 to December 2015. Early morning deeply coughed out sputum samples from patients having productive cough and fever admitted in the oncology ward of Jinnah Hospital, Lahore, belonging to any age group, any gender, and on chemotherapy were included. Salivary specimens and specimens from the same patient during the same episode of illness were excluded from the study. These sputum samples were cultured on Blood agar, MacConkey agar and Chocolate agar using standard microbiological techniques & antibiotic susceptibility pattern were determined using Modified Kirby Baur disc diffusion method following CLSI guidelines 2015.

**Results:** During study duration, a total of 100 sputum specimens from immunocompromised cancer patients were received. Out of total 100 samples, 70% were culture positive, 30% samples yielded normal throat flora. Out of 70 culture positive, 55(79%) were Gram negatives and 15(21%) were Gram positives. Among Gram positives, Streptococcus species were yielded from 11(73%) specimens. Among Gram negatives, Klebsiella species were yielded from 20(36%) specimens. All Gram-positive isolates were susceptible to linezolid and vancomycin. All Gram-negative isolates were susceptible to amikacin and 88% Gram-negative isolates were susceptible to imipenem.

**Conclusion:** Gram-negative rods usually don't cause respiratory tract infections in normal healthy individuals. But in immunocompromised patients like cancer patients, they become a serious concern. As in our study, Gram-negative rods were responsible for around 79% of the respiratory tract infections.

**Keywords:** Respiratory Tract Infections (RTI), Immunocompromised, Opportunistic Pathogens.

## Introduction

Opportunistic infections are common among hospitalized immunocompromised patients. The lungs are one of the most often involved organs in a diversity of opportunistic infections. Pulmonary infections being one of the most

common ones and they account for about 75% of the pulmonary complications and are associated with high morbidity and mortality.[1]

In 2013, 2.7 million deaths reported, down from 3.4 million death in 1990 by lower respiratory tract infections (LRTI). This was 4.8% of all deaths in 2013 and upper respiratory infections caused about 3,000 deaths in 1990.[2] Mortality has been reported to be higher than 40% to 50%, especially in patients who develop diffuse infiltrate.[3] Pneumonia of bacterial, viral, or fungal origin is the most frequent complication as a consequence of altered immunological status of the host. Experience has shown that a particular clinical setting is also a major source of infection by particular pathogens. The setting comprises (i) the particular environmental exposure, (ii) underlying immune defect, (iii) the period and severity of the immune defect and (iv) the headway rate and pattern of the abnormality .[3]

From the past few years, the population of immunocompromised patients has risen extremely in Pakistan and also around the globe. Immunity can be suppressed due to many reasons like cancer patients taking anticancer chemotherapy, patients taking steroids for a long duration, solid organ transplant patients on immunosuppressive therapy. Opportunistic pathogen which usually doesn't cause infections in a healthy individual becomes a nightmare for such immunocompromised patients. Moreover, it becomes more difficult to treat such opportunistic pathogens. Chest radiography and computed tomography (CT) are vital diagnostic tools, but still, radiologists repeatedly have difficulty in establishing the precise diagnosis on the basis of radiologic findings alone. The reasons are that the immunocompromised patients are potentially susceptible to infection from many different pathogens and those radiologic findings are seldom specific for the detection of a particular organism.[4]

Infections of the specific areas of the upper respiratory tract can be named specifically. Examples of these may include rhinitis, sinusitis, nasopharyngitis, pharyngitis, epiglottitis, laryngitis, laryngotracheitis and tracheitis. Bacterial pathogens responsible for these pulmonary infections are *Streptococcus pneumonia*, *Haemophilus influenza, Corynebacterium diphtheria, Bordetella pertussis* and *Bacillus anthracis*. [4]

Bacterial pathogens causing lower respiratory tract infections among immunocompromised patients are *Streptococcus pneumonia*, *Haemophilus influenza,* Streptococcus *pyrogens, Staphylococcus aureus, Nocardia species, Moraxella catarrhal, Klebsiella pneumonia, Escherichia coli, Pseudomonas aeruginosa, Acinetobacter baumannii, Burkholderia pseudomallei.*[5]

Sputum is mucus that is coughed up from the lower airways. This process is known as expectoration.[6-7] Sputum expectoration is not a normal phenomenon, there is always some underlying pathological cause. Sputum colour varies like yellow-green sputum indicates some bacterial infection, orange to brown shows presence of blood in mucus, bloody sputum from lungs indicates some serious illness.[8]

Sputum bacterial culture is used to diagnose lower respiratory tract infections. Bacterial infections are also responsible for pleural effusions so pleural fluids can also be taken for diagnosis. Lower Respiratory Tract Infection (LRTI), a synonym for pneumonia. This study was designed to identify bacterial pathogens causing lower respiratory tract infections among immunocompromised cancer patients from a tertiary care hospital and their antimicrobial susceptibility pattern.

## Methodology

This cross-sectional study was conducted at Pathology Department, Allama Iqbal Medical College, Lahore, Pakistan, from July 2015 to December 2015. Random sampling technique was used. Deeply coughed out sputum samples from patients having productive cough and fever admitted in the oncology ward of Jinnah Hospital, Lahore, belonging to any age group, any gender, and on chemotherapy were included. Salivary specimens and specimens from the same patient during the same episode of illness were excluded from the study.

Early morning, expectorated sputum samples were collected from all the patients in separate, sterile, wide-mouthed, screw-capped and disposable plastic containers. The samples were processed immediately in Microbiology laboratory. The quality of the expectorated sputum was assessed both by macroscopic and microscopic examination. Specimens which were clear, thin and watery, with no purulent material, were rejected. Microscopically, Bartlett's scoring method 3 was used to assess the quality of the sputum. Smears were prepared and subjected to Gram's staining and Ziehl Neelsen staining [20% $H_2SO_4$ ][11]

The specimens were cultured on 5% Sheep blood agar, MacConkey agar, and chocolate agar according to standard laboratory methods.[10,11] Bacterial isolates were identified on the basis of colonial morphology, Gram

staining, catalase test, coagulase test, oxidase test. API 20E and API 20NE (BioMerieux) were used to identify Gram-negative rods. Antimicrobial susceptibility pattern was determined using Modified Kirby Baur disc diffusion method and zone sizes were interpreted according to CLSI guidelines 2015.[12]

## Results

During study duration, a total of 100 sputum samples from oncology patients were included in this study. Out of which 70% yielded positive cultures, 30% samples yielded normal throat flora. Out of positive cultures 79% (n=55) were Gram-negative and 21% (n=15) were Gram-positive bacteria (Figure:1).

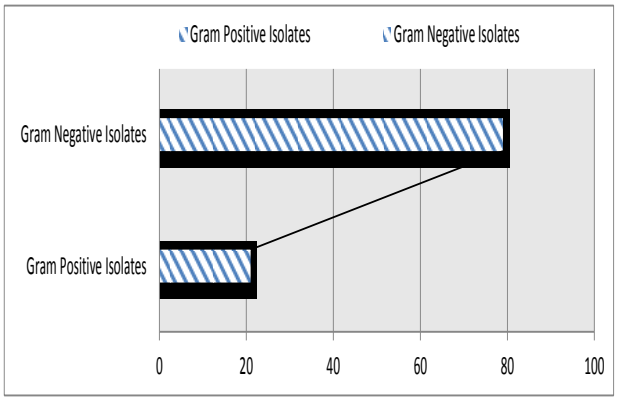


**Figure:1 Frequency distribution of gram positive and negative isolates**

Among 15 Gram positives, *Streptococcus pyogenes* was yielded from 73% (11) specimens, *Streptococcus pneumonia* was yielded from 2.86% (2) specimens, *Staphylococcus aureus* was yielded from 2.86% (2) specimens. Among 55 Gram negatives, *Klebsiella pneumonia* was yielded from 28% (20) specimens, *Escherichia Coli* was yielded from 24.29% (17) specimens, *Pseudomonas aeruginosa* was yielded from 14.29% (10) specimens, *Acinetobacter species* were yielded from 7.14% (5) specimens, *Haemophilus influenza* was yielded from 2.86% (2) specimens, *Proteus mirabilis* was yielded from 1.42% (1). (Table:1).

**Table:1 Frequency distribution Gram positive and Gram negative isolates**

| Isolated organisms | Number of isolates | Percentage % |
|---|---|---|
| Klebsiella pneumoniae | 20 | 28.57% |
| Escherchia coli | 17 | 24.29% |
| Streptococcus pyogenes | 11 | 15.71% |
| Pseudomonas aeruginosa | 10 | 14.29% |
| Acinetobacter species | 5 | 7.14% |
| Haemophilus influenza | 2 | 2.86% |
| Staphylococcus aureus | 2 | 2.86% |
| Streptococcus pneumoniae | 2 | 2.86% |
| Proteus mirabilis | 1 | 1.42% |
| Total | 70 | 100% |

Among Gram-negative rods, 25% (14) isolates were resistant to amikacin, 65% (36) isolates were resistant to co-amoxiclav except for *Pseudomonas aeruginosa*, 76% (34) isolates were resistant to ceftriaxone except for *Pseudomonas aeruginosa*, 50% (5) of *Pseudomonas aeruginosa* isolates were resistant to Cefoperazone, 43% (24) Gram-negative isolates were resistant to cefoperazone-sulbactam, 49% (27) isolates were resistant to ciprofloxacin, 20% (11) isolates were resistant to Imipenem, 32% (18) isolates were resistant to gentamicin. All the Gram-negative isolates were susceptible to Polymyxin except *Proteus mirabilis* which is intrinsically resistant to Polymyxin. (Table:II, Figure:2) Among Gram positives, 100% (15) isolates were susceptible to linezolid and vancomycin, 6% (1) isolates were resistant to penicillin and 80% (12) isolates were resistant to erythromycin. Among *Staphylococcus aureus*, 50% (1) isolate was resistant to cefoxitin i.e; MRSA. (Table, Figure:3)

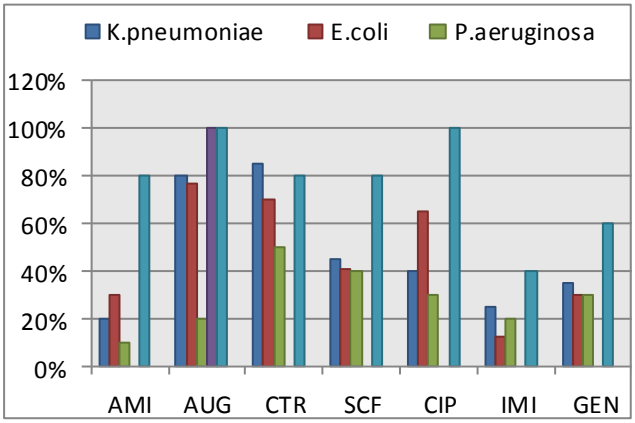


**Figure:2 Antimicrobial resistance trends among Gram negative isolates**

**Table:2 Percentage resistance among Gram negative bacterial isolates**

| Bacterial isolates | AK | AMC | CRO | SCF | CIP | IPM | PB | CN |
|---|---|---|---|---|---|---|---|---|
| K. pneumonia | 20 | 80 | 85 | 45 | 40 | 25 | 0 | 35 |
| E. coli | 29 | 76 | 70 | 41 | 64 | 11 | 0 | 29 |
| P. aeruginosa | 10 | - | - | 40 | 30 | 20 | 0 | 30 |
| P. mirabilis | 0 | 0 | 100 | 0 | 0 | 0 | 100 | 0 |
| Acinetobacter spp. | 80 | 100 | 80 | 80 | 100 | 40 | 0 | 60 |
| Haemophilus influenzae | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

AK=Amikain / AMC= Co-Amoxiclave / CRO=Ceftriaxone / SCF=Cefoperazone-sulbactam / CIP=Ciprofloxacin /IPM= Imipenem / PB= Polymyxin –B /CN= Gentamicin

**Table: 3 Percentage resistance among Gram positive isolates**

| Bacterial isolates | | P | FOX | E | DA | CRO | LZD | VA |
|---|---|---|---|---|---|---|---|---|
| *S.aureus* | R% | 50 | 50 | 100 | 0 | - | 0 | 0 |
| *S. pyogenes* | R% | 0 | - | 50 | 50 | 0 | 0 | 0 |
| *S. pneumoniae* | R% | 0 | - | 81 | 91 | 0 | 0 | 0 |

P=Penicillin / FOX=Cefoxitin / E=Erythromycin / CRO=Ceftriaxone / DA=Clindamycin / LZD= Linezolid, VA=Vancomycin
R=Resistant

## Discussion

Rate of occurrence of opportunistic pathogens is increasing day by day and immuno-compromised patients are at higher risk of getting respiratory tract infections as compared to normal healthy individuals. Pneumonia is the most common infectious disease among immunocompromised patients because respiratory tract could be the portal entry for a wide range of pathogens through airways. [9]

Among immunocompromised pneumonia patients the identification of causative microorganism is a difficult task. Unfortunately, the gain in years of useful life through the successful management and treatment of diseases is offset by serious effects on the immune system. As a result, secondary infections, rather than the primary illness, become the leading cause of death in immunocompromised patients. In our study sputum from the immunocompromised patients yielded Gram negative rods predominantly *Klebsiella pneumoniae.* Its antimicrobial resistance is on rise day by day.

A study was conducted by Ashour, H.M.,*et al*[13] in 2009 in Egypt. It included 772 clinical samples of all types, out of which 201 were sputum samples while in our study 100 sputum samples were included. In that study predominant isolate among the Gram negative rods was *Klebsiella pneumoniae* 31% followed by *Escherchia coli* 22% while in our study it is 28% and 24% respectively. (Table:I)

In that study, among Gram negative rods, 38% isolates were resistant to amikacin while in our study 25% isolates were resistant to amikacin, 55% isolates were resistant to gentamicin but in our study 32% isolates were resistant to gentamicin, 43% isolates were resistant to ciprofloxacin but in our study 49% isolates were resistant to ciprofloxacin, 69% isolates were resistant to ceftriaxone while in our study 76% isolates were resistant to ceftriaxone . (Table:II) Both of studies showed that most commonly occurring isolate in the sputum of immunocompromised patients is *Klebsiella pneumoniae* followed by *Escherchia coli.*

Another study conducted by Mythri *et al*[7] in 2013 in India, included 72 sputum specimens from pneumonia patients but our study included 100 sputum samples of immunocompromised cancer patients. Out of 72 sputum samples, 34 (47%) yielded normal commensals while in our study it is 30 (30%). Among the Gram negative isolates, *Klebsiella species* 55% was the most predominantly occurring pathogen followed by *Pseudomonas species* 10% and *Streptococcus pneumoniae* 26%, while in our study it is 28%, 14% and 2% respectively. (Table:I)

A study conducted by Oberoi *et al*[14] in 2006 in India, included 233 clinical samples out of which 67 were sputum samples. Among the Gram negative isolate, *Pseudomonas aeruginosa* was the most predominant 31% followed by *Escherchia coli* 12%, while in our study it is 14% and 24% respectively. Among the Gram Positive *Streptococcus pneumonia* was common with 32% isolates while in our study it is 2%. (Table:I) Among Gram negative rods, 18% isolates were resistant to ciprofloxacin while in our study it is 49%, 14% isolates were resistant to gentamicin while in our study 32%, 11% isolates were resistant to co-amoxyclav but in our study it is 65%, 23% isolates were resistant to ceftriaxone but in our study it is 76%. (Table:II) Among Gram positive isolates both the studies gives 100% susceptibility for linezolid and vancomycin,11% isolates were resistant to erythromycin while in our study 80% isolates were

resistant to erythromycin.(Table:III)

A study was conducted by Shah *et al*[15] in 2016, included 257 clinical samples out of which, 152(59%) samples yielded positive cultures, while in our study out of 100 samples only 70% yielded positive cultures.(Figure:1) In that study *Pseudomonas aeruginosa* was the most predominant pathogen (42%) followed by *Streptococcus pneumoniae* (26%). While in our study it is (14%) and (2%). (Table:1) In that study penicillin was resistant to 84% of Gram positive isolates while in our study it is resistant to 6% of Gram positive isolates. (Table:III)

# Conclusion

Among immunocompromised cancer patients Gram negative rods become a big threat by causing lower respiratory tract infections. In normal circumstances Gram negative rods are not among the major pathogens causing lower respiratory tract infections.

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