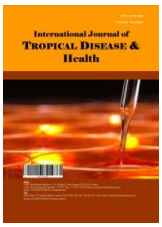

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Value Addition on Trend of Pneumonia Disease in India- The Current Update

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Authors' contributions

This work was carried out in collaboration with all authors. Author PKG designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors SC and SSM managed the analyses of the study. Author MHN managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Pneumonia continues to be the leading infectious cause of death among children under the age of five worldwide. Diagnosis of this disease is primarily dependent on physical examination, clinical history, and radiographic studies. Microbiological studies of the lower respiratory tract secretions have proven to be futile, however, sputum gram staining and culturing methods often aid in the diagnosis and management of these infections. Aspiration pneumonia often occurs in a community setting and primarily involves anaerobes like *Staphylococcus aureus* or gram-negative rods such as *Klebsiella pneumonia*, and other *Enterobacteriaceae* and *Pseudomonas* species. The total number of cases taken in the study of acute pneumonia was 22 (15 male subjects and 7 female subjects). Biochemical tests were conducted for identifying different organisms present in the samples

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collected from patients suffering from acute pneumonia. Distribution of bacteria in the case of acute pneumonia was as follows: *Staphylococcus aureus* was recorded to be the highest (36.36%) followed by *Streptococcus pneumonia* (18.18%) and *Klebsiella pneumonia* (18.18%), *Pseudomonas pneumonia* (13.63%), *Haemophilus influenza* (9.09%) and lastly *Chlamydia pneumonia* (4.45%). A maximum number of laboratories proven acute pneumonia cases (36.36%) belonged to 61-70 years. The distribution of cases was marginally more in urban areas (63.63%). By occupation largest group (36.36%) was of others in case of acute pneumonia were as farmers, housewives and others were the largest groups (22.73%) each. The microbial etiology derived from the present study found that *Klebsiella pneumonia* was an independent risk factor for mortality in severe community-acquired pneumonia. Moreover, two important findings were drawn from this study. *K. pneumonia* was identified as the causative pathogen in 22% of cases, second to *S. pneumonia.*

Keywords: Pneumonia; Streptococcus pneumonia; Staphylococcus aureus; Klebsiella pneumonia; community-acquired pneumonia; hospital-acquired pneumonia; public health; a trend of pneumonia.

1. INTRODUCTION

Pneumonia is defined as an acute respiratory illness associated with inflammation and the alveoli abnormally being filled with fluid. The recently developed radiological pulmonary shadowing has aided in more reliable diagnosis either in segmental fashion or multi-lobular. The current mortality rate recorded due to pneumonia is around 5 percent, among which the most susceptible group of people are women aged 70 years old [1]. Bacteria is the primary cause for more than fifty percent of the pneumonia cases recorded to date. *Streptococcus* bacteria, known as Pneumococcal, is the main cause of the most widespread form of pneumonia. Infection usually occurs when an individual breathes in the micro-organisms [2]. In some rare cases, pneumonia is contracted when bacterial colonies from infections in other places in the body - such as an infected bone - travel via blood circulation to the lungs and stay there [3]. The initial symptoms of classic bacterial pneumonia are sudden fits, fever, chest pain, and coughing. The cough is dry at first, but after a day or two, the person starts to cough up phlegm. The phlegm is usually yellow, bloodstained, or rusty in color. Breathing is typically fast and shallow and the area around the lips and nails may seem slightly bluish due to the lack of oxygen [3].

Pneumonia is classified as either community-acquired, hospital-acquired, those occurring in the immunocompromised host, or due to damaged lungs (including suppurative and aspirational pneumonia). To this day, community-acquired pneumonia remains a major cause of mortality. The etiology of community-acquired pneumonia has rarely been identified as a mortality risk factor [4]. A prospective study was conducted to assess the prognostic factors of community-acquired pneumonia patients admitted to the intensive care unit (Centre Hospitalize Departmental Felix Guyon, St Denis de la Reunion, France), with a special emphasis on microbial etiology. All variables for assessing the severity were collected, with a special emphasis on microbial investigations. Among 112 immunocompetent patients (with a mean standard age of 54.7 to 15.1 years), 84% were male. The severity of community-acquired pneumonia was demonstrated by mortality rate (43%), shock (48%), mechanical ventilation support (82%) along with a simplified acute physiology score of 46.4 to 21.6 and a mean risk factor score of 2.2 to 1.2. Microbiological identification was obtained in 78.6% of the cases, with positive blood culture being observed in 33% of these. Among the assessed samples, the most frequent microbial agents identified were *Streptococcus pneumonia* and *Klebsiella pneumonia* (42% and 22%, respectively) [5].

The above-mentioned studies give a clear idea about the causative agents for community-acquired pneumonia and aid in the present study. The present study aims at creating an antibiotic susceptibility profile of such causative agents for their possible eradication. In the case of agents of community-acquired pneumonia vary with age and state of health of the patient. Neonates may acquire lower respiratory tract infection with Chlamydia trachomatis. Children suffer less commonly from bacterial pneumonia usually caused by *H. inflenzae, Staphylococcus aureus, Pneumonococci*, a common causative agent of Pneumonia in children are also

associated with such superlative infection as meningitis, and arthritis **(**Vienne, Pascale, et al. 2003**)**. The most common bacterial agent of lower respiratory tract among adults younger than 30 years old are *Mycoplasma pneumonia* and *Streptococcus pneumonia* [6].

Pneumonia remains the sixth leading cause of death in the United States. Diagnosis of this disease is primarily dependent on clinical history, physical examination, and radiographic studies. The role and value of microbiological studies of lower respiratory tract secretions are uncertain, sputum gram staining and culture are often used as an aid to the diagnosis and management of these infections, however, numerous studies have disputed their usefulness, especially in providing information helpful in establishing a diagnosis of bronchopulmonary infection [7]. Aspiration pneumonia occurs in the community setting and involves primarily and anaerobes and *Staphylococcus aureus* or gram-negative rods such as *Klebsiella pneumonia*, other *Enterobacteriaceae* and *Pseudomonas* species, particularly in a patient with the recent hospital or nursing home experience [8]. Infection of the lower respiratory tract is of common concern in terms of complications they bear. These infections become severe with time, if control measures are lacking, some pathogenic bacteria are the common cause of these infections. The aim of the present study the antibiotic susceptibility profile of such causative agents for their possible eradication.

2. MATERIALS AND METHODS

The present study was conducted in Microbiological Laboratory of Department of Microbiology, Motilal Nehru Medical College, and associated hospital Allahabad. Samples were collected from patients of different age groups and sex having an acute and chronic infection. Twenty-two patients with acute and chronic lower respiratory tract infection were selected for the study. Sample of the respiratory specimen (Sputum, Bronchial aspirates, Bronchial-alveolar lavage, Pleural fluid, Lung aspirate or fluid, Pus from intercostals drainage, Pus from empyema thoracic) were collected from the patients visiting the Microbiological lab of Motilal Nehru Medical College of Allahabad and a private microbiological clinic. Specimens from the respiratory tract were transferred to the laboratory onto a sterile container maintained under aseptic conditions and streaked directly on the blood agar plates and MacConkey agar plates within 2 hours for primary isolation of pathogens. These plates were then incubated at 37°C. After growth bacterial culture was aseptically inoculated into nutrient agar plate from the original plate for further identification and other investigation.

Table 1. Biochemical tests for identifying different organisms present in the samples collected from patients of acute pneumonia [9,10]

Biochemical test	Organism identified
Gelatin Hydrolysis	*Pseudomonas* and *Vibrio cholerae*
Citrate Utilization Test (Simmons citrate agar slants)	*Enterobacteria*
Indole Production (Peptone Broth)	*Pseudomonas, E.coli* etc
Methyl Red test (MR-VP broth)	*Enterobacteria*
Voges – Proskaur (MR-VP broth)	*Enterobacteria and Klebsiella pneumonia*
H2S Production test (Triple sugar iron agar slants)	differentiate *Klebsiella* from *Enterobacter*
Urease test (Urease slants)	differentiate *Salmonellae* and *Shigellae* from other bacterial species
Carbohydrate Fermentation(Fermentation Broth)	differentiate *Pseudomonas aeruginosa* from other species of bacteria
Hugh and Leifson's test	Species with deletion of fermentation of Glucose
Coagulase test	Differentiate *Staphylococcus aureus* from other species of Staphylococci
Catalase Test (Trypticase soy agar slants)	Differentiate staphylococci from streptococci

Further investigation was carried out by identification of different bacteria based on whether they were gram-positive or gram-negative Cocci or bacilli and whether they were in chains or present individually. This was done by gram staining and observing under 100 X objective. To identify the various bacteria accurately further, cultures were prepared with appropriate nutrients, pH, and osmotic pressure, these cultures were used for performing biochemical tests to identify the different organisms present (Table 1).

Other than the above-mentioned tests, an antibiotic sensitivity test was performed using the agar disc diffusion method [11,12], which was designed to determine the inhibitory effect of antibiotic discs used. The antibiotic sensitivity test was done for using various antibiotics as mentioned in Apart from the biochemical tests few laboratory techniques such as direct smear examination and Petroff's method (concentration method) were performed (see Table 2).

3. RESULTS AND DISCUSSION

In the present study, 22 patients were observed for the case of pneumonia which is being considered in lower respiratory tract infection. Out of these 15 (68.17%) were males and 7 (31.81%) were females. This demarcation was done since sex is a significant epidemiological factor for several diseases. However, not many studies have carried out to support this claim. Relevant studies suggest that females are more commonly affected by upper respiratory tract infections whereas men are more commonly affected by lower respiratory tract infections like pneumonia.

Fig. 1. Shows the age and sex distribution of the cases. The sample size was 22 cases. Maximum number of cases (36.36% ~ 8 cases) were seen in the age group 61-70 (for both males and females) followed by 51-60 years of age group (27.27% ~ 6 cases). The minimum number of cases (4.54% ~ 1 case) were observed in the age group of the range of 31-40 years. The preponderance of males over females was evident with a rough estimate of a 2:1 ratio. This observation led to a conclusion of males being more susceptible to community-acquired pneumonia, the reason for which could be anatomic, lifestyle, behavioral, or socioeconomic differences between males and females. The role of sex hormones in the regulation of the immune system may also contribute to the reported sex differences in the incidence and severity of the various types of respiratory tract infections, especially in adolescents and adults [13].

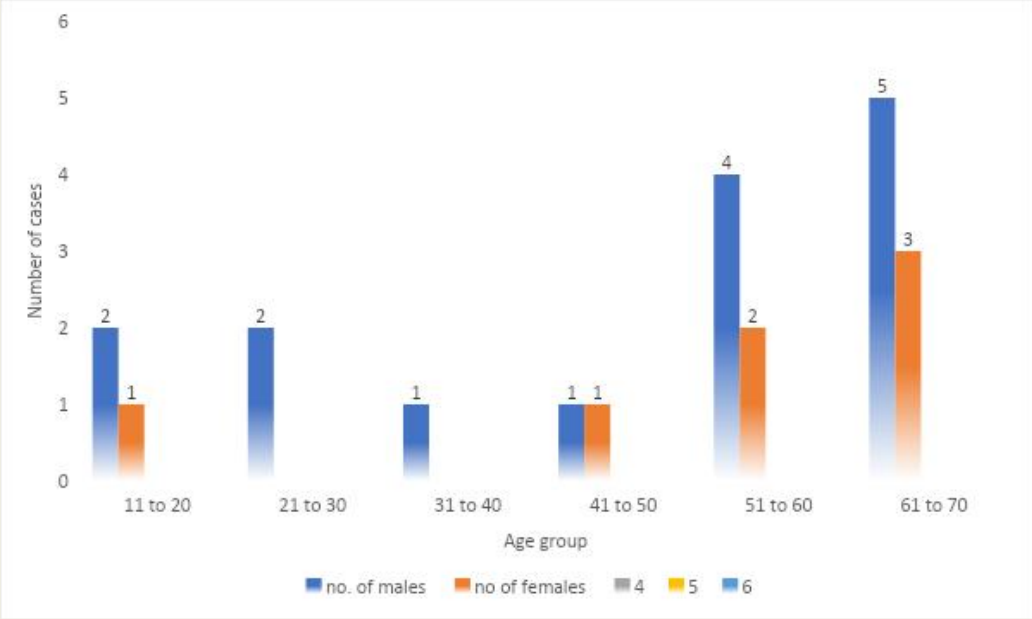

Fig. 1. Age and Sex distribution of cases(out of 22 cases)

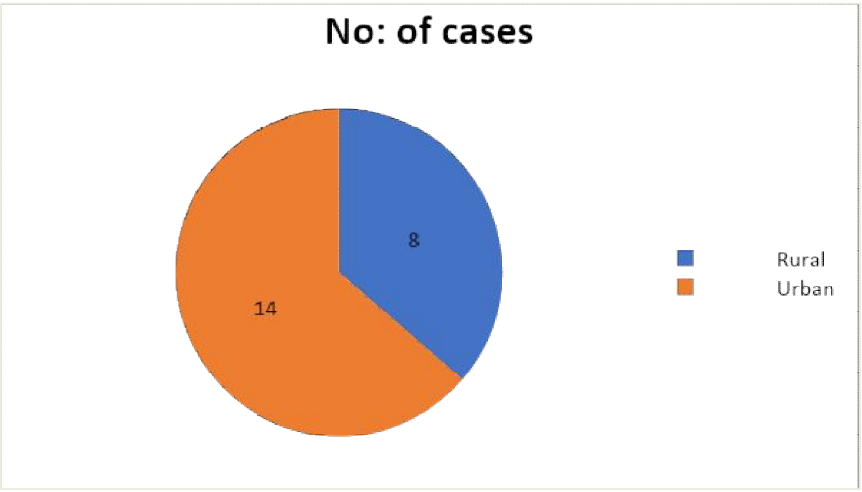

Fig. 2. Distribution of cases according to Rural-Urban (sample size 22)

Another factor used for comparison among patients was the socioeconomic setting and background of an individual i.e., rural or urban areas. There was a distinct difference present between rural and urban pneumonia patients, here Fig. 2 shows that the former had a lesser number (36.36%) of patients than later 14 (63.63%). In a similar study conducted in China, even though they were a clear difference between the number of pneumonia occurrences in urban and rural areas, the X-ray reports did not show much of a difference suggesting that other than the number of incidences there was no difference between the severity of the disease among individuals from rural and urban settings [11,12].

Occupation wise 36.36% of the patients had miscellaneous jobs which included working people, children, shopkeepers, etc. Farmers and housewives were of equal percentage with 22.72% each, followed by laborers and students with 9.09% each. Unlike occupational asthma and various other occupational lung diseases, there are not many documented cases of occupational pneumonia. Few epidemiological studies suggest that exposure to metal fumes is a risk factor for infectious pneumonia [12,14]. Whether occupational exposure to other agents, such as inorganic dust or chemicals, also increases the risk for infectious pneumonia is not clear. But in the set of individuals under examination for the current study, not many were exposed any sort of harmful metal fumes, and these were cases of community-acquired pneumonia, this suggests that people who had to spend more time with another individual due to their occupation were more susceptible to the disease, but this also depends on an individual's immunity.

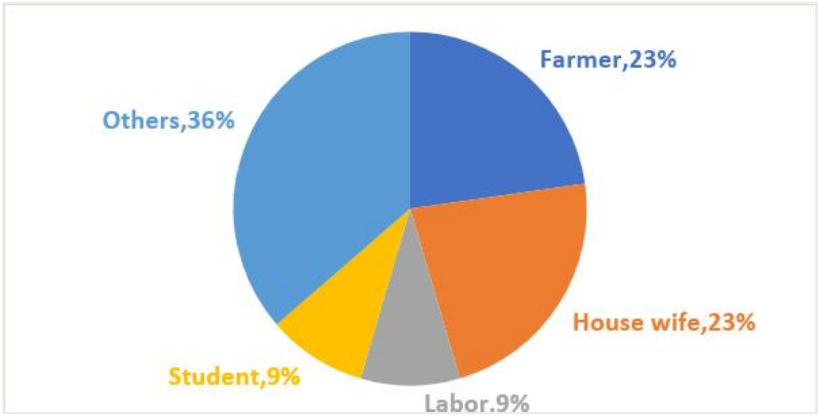

Fig. 3. Distribution of cases according to the occupation (sample – size 22)

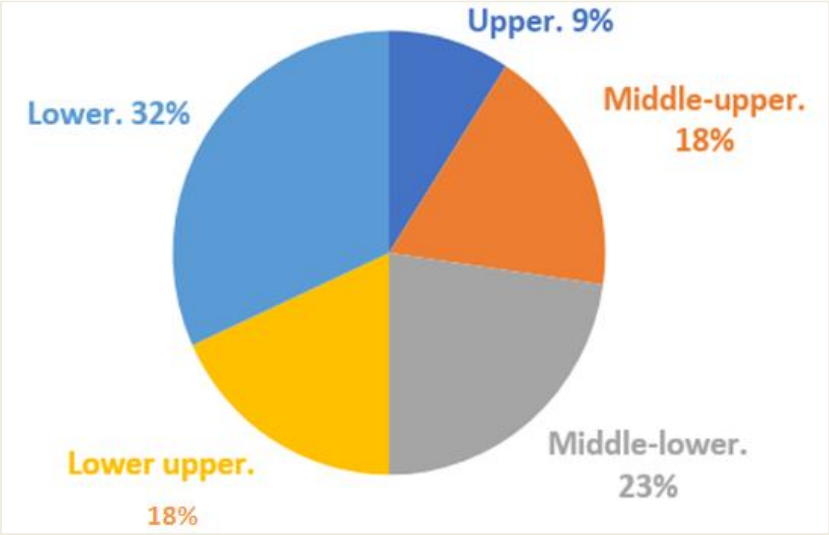

Fig. 4. Socioeconomic status of cases (sample cases-22)

Fig. 4. Shows that the maximum number of cases 7 (31.81%) were from lower socio-economic status followed by middle-lower with 5 (22.72%) and in middle-upper and lower-upper with 4 (18.18%) each. The upper class having the least number of cases in pneumonia with 2 (9.09%). The above classification is based on Kuppuswammy's Socioeconomic Status [12].

Fig. 5. Shows distribution of cases according to their smoking habits in which 12 (54.54%) were smokers and all were males. All females were non-smokers. Tobacco use may also favor diseases that are also known risk factors for community-acquired pneumonia, such as periodontal disease and upper respiratory viral infections. Usually one of the preventive steps taken to avoid pneumonia or any respiratory infections is to give up smoking, since it increases the susceptibility for such bacterial lung infections, even in case of passive smokers. The relationship between the susceptibility to infection and tobacco usage also seems to show a dose-response effect, since the risk reduces spectacularly 10 years after giving up smoking, returning to the level of non-smokers.

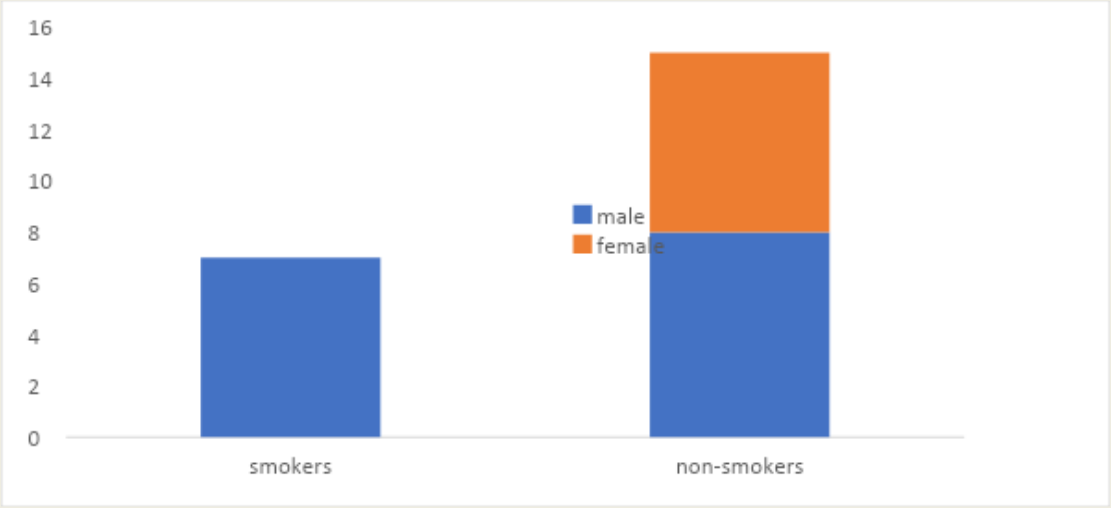

Fig. 5. Distribution of cases according to smoking habits (sample size- 22, male(15), female(7)

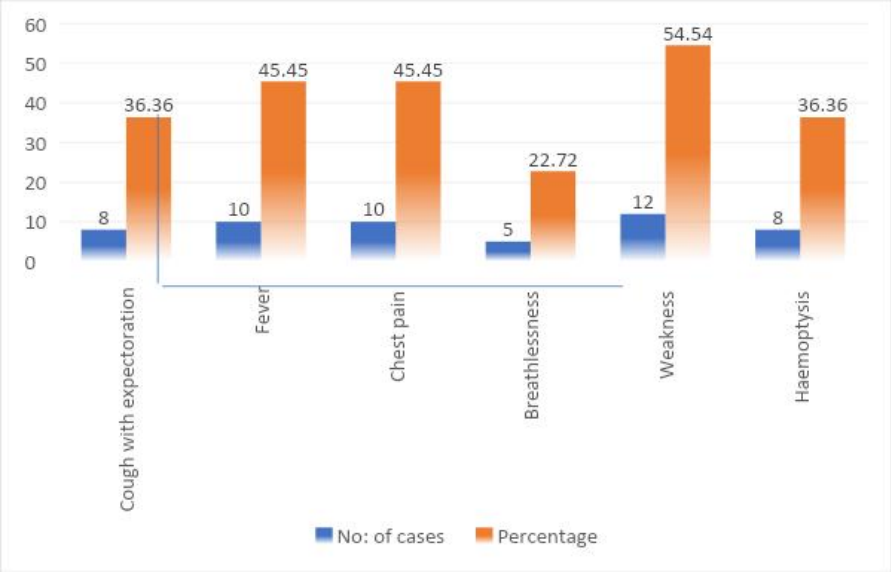

Fig. 6. Distribution of cases according to symptoms present (n=22)

Observing the spectrum among 22 patients, weakness was found in the maximum number of cases 12 (54.54%), followed by fever with and chest pain both having an equal number of cases with 10 (45.45%) each. Other spectrums such as cough with expectoration, hemoptysis, and breathlessness have 8 (36.36%), 8 (36.36%), and 5 (22.72%) cases respectively. Symptoms of pneumonia become evident at a slower rate compared to that of flu, but it's faster than cold. Sometimes pneumonia manifests as a complication of cold and flu. But more than thirty symptoms have been observed for pneumonia, these can vary from mild to severe, depending on the type of pneumonia acquired, and other factors like age and health may be contributing factors. In case of coughs associated with the infection the expectorate is usually greenish or yellow mucus, sometimes in severe cases, the patient might cough up bloody mucus also. Fevers might shoot up suddenly, might develop into shivering in some cases. In some cases, the span of breath is reduced by a great degree and the patient might find it difficult to perform simple physical activities as simple as climbing up the stairs. The reduced capacity of lungs to retain oxygen from the environment may cause weakness and the patient's lips and nailbeds may have a bluish color due to the same. All the above-mentioned symptoms may not necessarily manifest at once or together, so to confirm the presence of the infection is better to get microbial tests done.

So, to test for microbes present in the sputum of a pneumonia patient etiological studies are carried out, and the most common approach to do so is to conduct a Sputum Gram stain or Gram's staining by direct smear. Fig. 7. Shows that out of 22 patients observed, 12(54.54%) were positive for Gram's staining by direct smear and 10 (45.45%) were negative.

Fig. 8. shows the distribution of cases in different bacteria of pneumonia according to their infectious availability in India, here *Staphylococcus aureus* was the predominant organism present in 8 (36.36%) cases in 22 patients of pneumonia. *Streptococcus pneumonia* and *Klebsiella pneumonia* were the second most predominant bacteria, having 4 (18.18%) each in 22 pneumonia, pneumonic patients, followed by Pseudomonas pneumonia with 3 (13.63%) cases. In several studies, *Streptococcus pneumonia* is the causative microorganism responsible for community-acquired pneumonia most frequently associated with smoking particularly in invasive pneumococcal disease and septic shock. It is not clear how it acts on the progress of pneumonia, but there is evidence to suggest that the prognosis for pneumococcal pneumonia is worse [14]. Chlamydia pneumonia bacteria have 1 (4.45%) case whereas *Chlamydia psittaci*, *Actinomyces Israeli*, *Legionella pneumonia,* and *Coxiella burnetti* showed no infection in any 22 pneumonia patients. However, their availability in India is quite considerable. In community-

acquired pneumonia caused by *Legionella pneumonia,* it has also been observed that smoking is the most important risk factor, with the risk rising 121% for each pack of cigarettes smoked a day.

Table 2 shows antibiotic susceptibility test for pathogens which were isolated from 22 pneumonia patients, in which *Streptococcus pneumoniae* showed sensitivity for Amikacin, Amoxicillin – clavulanic acid, Erythromycin, Vancomycin, and Sulpha-trimethoprim. For Gentamycin and Cefotaxime, it showed sensitivity for two patients out of four patients each. Other antibiotics were resistant to culture and sensitivity tests. *Klebsiella pneumonia* showed sensitivity for Amikacin, Amoxicillin-clavulanic acid, and Gentamycin. Cefotaxime and ciprofloxacin showed sensitivity for two patients out of four, whereas Levofloxacine showed sensitivity for one out of four patients. *Staphylococcus aureus* showed sensitivity for Erythromycin, Vancomycin, Cefotaxime, Ofloxacin, Cefazolin, Cefotaxime, Ciprofloxacin. For Ampicillin and Levofloxacine, it showed sensitivity for 5 patients out of 8 patients.*Pseudomonas aeruginosa* showed sensitivity for only two antibiotics Meropenen and Piperacillin. Other's antibiotics are resistant for pseudomonas aeruginosa. No antibiotic susceptibility test was done for *Haemophilus influenzae* and *Chlamydia pneumonia* patients.

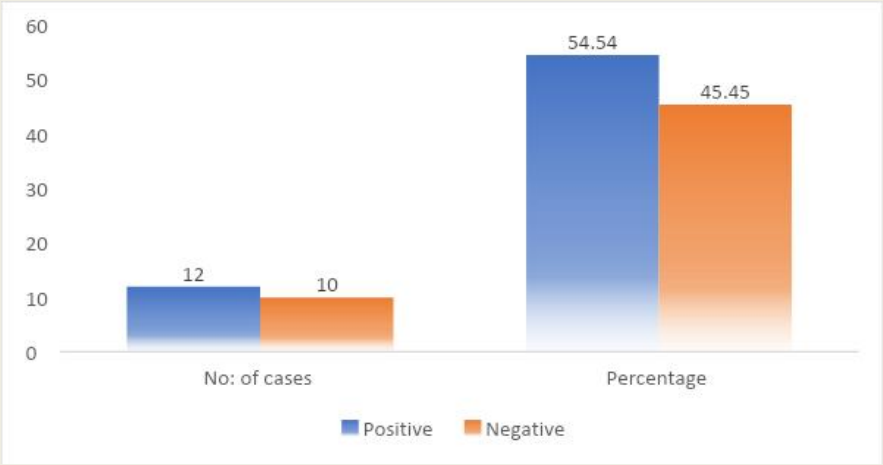

Fig. 7. Quantitative evaluation of Gram's Staining positivity by direct smear (total cases – 22)

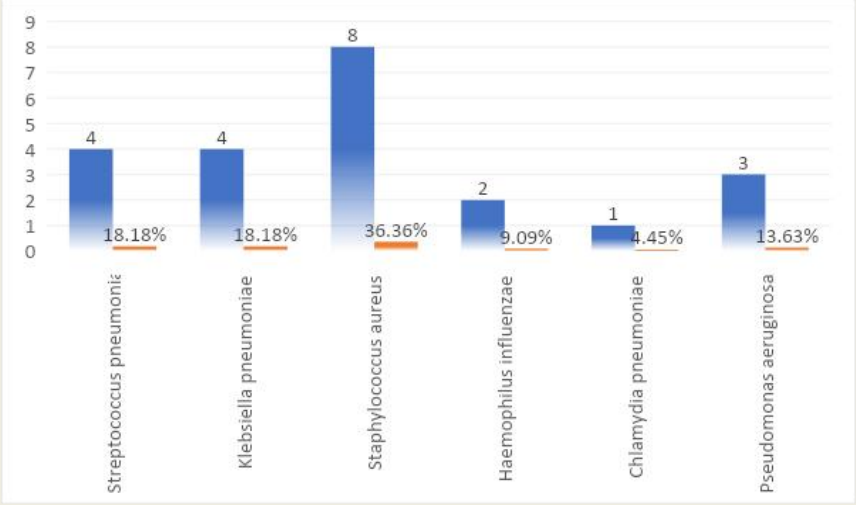

Fig. 8. Distribution of cases according to different bacteria of Pneumonia (out of 22 patients)

Table 2. Antibiotic susceptibility test for pathogens which are found in all pneumonia patients (n=22) (R-resistant, S-sensitive)

Antibiotics	Conc	Susceptible zone diameter			*Streptococcus us pneumonia e N=4*	*Klebsiella pneumonia N=4*	*Staphyloc coccus aureus N=8*	*Pseudomonas pneumonia e N=3*
		R (mm)	Inter mediates	S (mm)				
Amikacin	30µg	14	15-16	17	S	S	-	R
Amoxycillin-clavulanic acid	20 + 10µg	19	-	20	S	S	-	-
Ampicillin/AmoxillIlin	10 µg	18	19-21	22	R	R (3/4)	S (5/8)	R
Cefotaxime	30 µg	25	26-27	28	S (2/4)	S	S	R
Chloramphenicol	30 µg	12	13-17	18	R	R	-	R
Ciprofloxacin	5 µg	15	16-20	21	-	S (2/4)	S	R
Cephalexin/Cefazo Lin	30 µg	14	15-17	18	R	-	S	R
Erythromycin	15 µg	13	14-22	23	S	R	S	R
Gentamycin	10 µg	12	13-14	15	S (2/4)	S	-	R
Levofloxacin/Lom ofloxacin	5 µg	13	14-16	17	-	S (3/4)	S (5/8)	R
Linezolid	30 µg	20	21-22	23	-	-	S	-
Meropenen	10 µg	13	14-15	16	-	-	-	S
Norfloxacin	10 µg	12	13-16	17	R	-	-	-
Ofloxacin	5 µg	12	13-15	16	R	-	R	-
Oxacillin	10 µg	14	15-18	19	R	-	R	-
Piperacillin-tazobatam	100+10µg	17	-	18	-	-	-	S
Roxithromycin	30 µg	9	10-20	21	-	R	-	-
Sulpha-trimethoprim	30 µg	15	16-18	19	S	-	R	-
Vancomycin	30 µg	-	-	17	S	-	S	-

4. CONCLUSION

Distribution of bacteria in case of acute pneumonia, *Staphylococcus aureus* was recorded highest (36.36%) followed by *Streptococcus pneumonia* and *Klebsiella pneumonia* (18.18%) each, *Pseudomonas pneumonia* (13.63%), *Haemophilus influenza* (9.09%) and in last *Chlamydia pneumonia* (4.45%). The total cases taken in the study of acute pneumonia, were 22. Out of the, males were 15 and the females were 7 in acute pneumonia. A maximum number of laboratory proven acute pneumonia cases (36.36%) belonged to 61-70 years whereas chronic pneumonia cases (38.63%) belonged to the age group 21-30 years. Distribution of cases was marginally more in an urban area in acute pneumonia which was around (63.63%). It may be because of more health check-up facilities and easy to access health services. However, in urban and rural area cases discrepancies in our study may be due to selection bias. Most of the cases belonged to lower socio-economic in both acute. By occupation, the largest group (36.36%) was of others in the case of acute pneumonia. The most common symptoms were weakness and chest pain, in case of chronic pneumonia. Gram's staining positivity was observed (54.54%) in acute pneumonia. Acute pneumonia showed, most of the isolated pathogens were tested highly resistance against Chloramphenicol as compared to other antibiotics used. Based on the present finding, it may be recommended that other antibiotics used against acute are effective as well, but it appears due to the injudicious use of antibiotics, pathogens are gaining resistance. Therefore, it is recommended that appropriate and full courses of antibiotics should be prescribed.

CONSENT

As per international standard or university standard, the patient's written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

The research study was done in the Department of Microbiology, Motilal Nehru Medical College (MNRC) Allahabad (Now known as Prayagraj), U.P India. I would like to acknowledge Dr. Aundita Bhargava Prof and Head of Microbiology Department MNRC Allahabad for allowing me permission to perform my research during my M. Tech Project course in 2006 and 2007 and to analyze OPD (Outdoor Patients) data during that time. Apart from I would like to mention that this research study was performed to make more people aware of the trends of some deadly diseases such as Pneumonia hence this detail cannot be used to generate some kind of funds or any other benefits. Besides, I would like to mention that the name of patients and their specific locations cannot be revealed to maintain the confidentiality of medical practices.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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