
Original Article

Ventilator associated pneumonias and its antibiogram

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Abstract:

Background: Various studies show *Pseudomonas* species, *Acinetobacter* species, *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus* were identified as common VAP pathogens with varying prevalence. Due to increasing incidence of MDR in ICU, early and correct diagnosis of VAP is a challenge for an optimal antibiotic treatment.

Objective: To know the Bacteriological Profile of Ventilator associated pneumonias, their prevalence and also their susceptibility pattern

Methods: The study was conducted in Intensive Care units in Osmania General Hospital Hyderabad among 300 patients both male and female age group ranging from 15- 60 years admitted in ICU's. Specimen collection was done by anesthetists, ETA was collected using 8 F suction catheter which was guided through the lumen of Endotracheal tube for approximately 24 cm. Gentle aspiration was then performed without instilling saline and catheter was withdrawn from endotracheal tube. After catheter was withdrawn approximately 2.5 – 5 ml of saline was injected into it with a sterile syringe to flush the exudate into a sterile container.

Results: The total no. of patients on mechanical ventilation included in the study during one year period was 300. Out of these 138 patients developed Ventilator Associated Pneumonia (VAP). The most common isolated pathogen was *Klebsiella pneumoniae* in (40.63%) cases followed by *Pseudomonas aeruginosa* (15.63%), *Acinetobacter* species (12.50%) and *Staphylococcus aureus* (9.38%). *Klebsiella pneumoniae* was the commonest pathogen isolated in both early onset and late onset.

Conclusion: The most common isolated pathogen was *Klebsiella pneumoniae* in (40.63%) cases followed by *Pseudomonas aeruginosa* (15.63%), *Acinetobacter* species (12.50%) and *Staphylococcus aureus* (9.38%).

Key words: Ventilator, pneumonia, antibiogram

Introduction:

Pneumonia is the second most common (86%) nosocomial infection in critically ill patients, associated with mechanical ventilation and are termed as Ventilator Associated Pneumonias. Nosocomial pneumonia (NP) is defined as an infection of the lung parenchyma that was neither present nor incubating at the time of hospital admission and which develops after 48 hrs of hospital admission. Ventilator associated pneumonia is defined as pneumonia occurring after 48 hrs of endotracheal intubation and initiation of mechanical ventilation. The onset of VAP can be divided into 2 types: early and late.¹

Early onset VAP: occurs 48 to 96 hours after intubation and is associated with antibiotic susceptible organisms. Late-onset VAP: occurs more than 96 hours after intubation and is associated with antibiotic resistant organisms.^{2, 3, 4}

Several risk factors reported are duration of mechanical ventilation, presence of chronic pulmonary diseases, sepsis, Acute Respiratory Distress Syndrome (ARDS), neurological diseases, trauma, prior use of antibiotics and red cell transfusions.^{5, 6}

Mortality rates range from 20-70% when infection is caused by multi resistant and invasive pathogens. Beyond mortality, VAP includes increased length of stay in ICU and its

incremental cost. Delayed or incorrect diagnosis may lead to unnecessary treatment and subsequent complications related to therapy. Diagnosis of VAP requires a high clinical suspicion combined with bedside examination, radiographic examination and microbiological analysis of respiratory secretions.⁷

3. Center for Disease control and Prevention

Radiology signs: two or more serial chest radiographs with at least one of the following: New or Progressive persistent infiltrate, Consolidation, Cavitation

Clinical signs: At least 1 of the following

1. Fever ($> 38^{\circ}C$)
2. Leucopenia ($< 4000\text{ mm}^3$) or Leucocytosis ($> 12000\text{ mm}^3$)
3. Altered mental status, for adults 70 years or older with no other recognized cause

Microbiological criteria:⁷

At least one of the following:

Positive growth in blood culture not related to another source of infection

Positive growth in culture of pleural fluid

Positive quantitative culture from broncho-alveolar lavage ($>10^4$) or PSB ($>10^3$)

5% or more of cells with intracellular bacteria on direct microscopic examination of Gram stained bronchoalveolar lavage fluid

Histopathological evidence of Pneumonia

Plus at least 2 of the following:

New onset of purulent sputum, or change in character of sputum

Increased respiratory secretions or increase suctioning requirements

New onset or worsening cough, or Dyspnoea or tachypnoea

Rales or bronchial sounds

Worsening gas exchange

Increased oxygen requirements

Microbiological diagnosis:

Methods to obtain culture material from the lower respiratory tracts:-

Non-invasive: Endotracheal aspirate-(standard): Simplest method

Non bronchoscopic techniques

Plugged telescoping catheter (PTC)

Protected bronchoalveolar mini-lavage (mini-PBAL),

"Blind" Protected specimen brushing

Invasive; Bronchoscopic techniques

1. Protected specimen brushing (PSB)
2. BAL (Bronchoalveolar Lavage),
3. Open lung biopsy

Various studies show Pseudomonas species, Acinetobacter species, Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus were identified as common VAP pathogens with varying prevalence. Due to increasing incidence of MDR in ICU, early and correct diagnosis of VAP is a challenge for an optimal antibiotic treatment.⁸

In view of the above facts, the present study on Bacteriological Profile of VAP was undertaken and aimed at isolating and identifying the causative organisms of VAP and their antibiogram in patients admitted in Respiratory Intensive Care Unit at a tertiary care hospital, Hyderabad

Methods:

The study was conducted in Intensive Care units in Osmania General Hospital Hyderabad, a tertiary care centre from 9/9/10-11/9/12

Study group: 300 patients both male and female age group ranging from 15- 60 years admitted in ICU's

Specimen: endotracheal aspirate

Specimen collection: Specimen collection is done by Anesthetists, ETA was collected using 8 F suction catheter which was guided through the lumen of Endotracheal tube for approximately 24 cm. Gentle aspiration was then performed without instilling saline and catheter was withdrawn from endotracheal tube. After catheter was withdrawn approximately 2.5 – 5 ml of saline was injected into it with a sterile syringe to flush the exudate into a sterile container.

Specimen processing:⁹ Specimen was immediately processed. Gram stain was done to consider it as an appropriate sample more than 10 PMN neutrophils/HPF, 1 bacteria/ oil immersion field, Squamous epithelial cells < 1 bacteria/ oil immersion field, Squamous epithelial cells $< 1\%$. Sample was mechanically liquefied and homogenized by overtaxing for 2-3 min with sterile glass beads. Samples were then serially diluted using 0.9% sterile saline solution with final dilution of 1 in 100 and 1 in 1000.

Dilutions are plated using 4 mm Nichrome wire loop (Himedia) which holds 0.01 ml sample on to Blood agar, Chocolate agar, MacConkey agar, Sabourad's Dextrose agar with antibiotics, without antibiotics. Inoculated plates were incubated at 37 °C for overnight. Chocolate agar was incubated at 37 °C under 5-10% CO₂ tension in a candle jar. SDA slants were incubated for 1 week in BOD incubator. All plates were checked for growth overnight and then after 24-48 hr of incubation. SDA slants were checked for up to 1 week. Colony count of 10⁵ cfu/ml is considered significant. Colony morphology was noted followed by Gram stain and identification of the isolate was done by conventional methods.¹⁰ Antibiogram of the isolate was done were determined by Kirby-Bauer's Disk Diffusion method using Mueller-Hilton Agar and the Zone Diameters were interpreted as per NCCLS guidelines.

Results:

The total no. of patients on mechanical ventilation included in the study during one year period was 300. Out of these 138 patients developed Ventilator Associated Pneumonia (VAP). Patients who developed VAP within four days of Mechanical Ventilation were categorized as early onset VAP and no. of cases who developed early onset VAP were 60 (43.48%) out of 138 patients. And those who developed after 4 days were categorized as late onset VAP and patients under this category were 78 (56.52%).

The maximum rate of isolated pathogens was in the age group of 31-45 years (32.61%) followed by those in the age group of 46-60 years (30.43%). There was also male preponderance showing 78 (56.52%) male cases (56.52%) and 60 (43.48%) female cases. Out of 138 samples which were processed 18 (13.04%) were sterile while bacterial pathogens were isolated in 96 (69.57%) samples and *Candida albicans* was isolated in 6 (4.35%) samples. Poly-microbial growth was reported in 18 (13.04%) samples. Among 96 bacterial pathogens obtained majority of them were Gram negative bacteria (90.62%). The most common isolated pathogen was *Klebsiella pneumoniae* in (40.63%) cases followed by *Pseudomonas aeruginosa* (15.63%), *Acinetobacter* species (12.50%) and *Staphylococcus aureus* (9.38%). *Klebsiella pneumoniae* was the commonest pathogen isolated in both early onset and late onset. *Pseudomonas aeruginosa* and *Acinetobacter* species were isolated only in late onset cases.

Discussion:

Hospital acquired or Nosocomial infection continues to be an important cause of mortality and morbidity. Critically ill patients are at particular risk of developing ICU acquired infection. Nosocomial bacterial pneumonia occurring after 2 days of mechanical ventilation is associated with 7 fold to 21 fold increase in the incidence of Pneumonia and 28% of patients receiving mechanical ventilation will develop this complication. Its development is associated with an attributable increase in mortality and morbidity. The establishment of an accurate diagnosis of VAP remains

problematic and as yet there is still no accepted gold standard test for the diagnosis. The responsible pathogen vary according to case mix, local resistance patterns and methodology of sampling. Keeping in view the above facts, this study was undertaken to determine the prevalence of VAP, the common pathogens responsible for VAP and their resistance pattern in patients admitted in Intensive Care Unit in a tertiary care centre. The study group comprised 300 patients who were on mechanical ventilation for more than 48 hrs. out of these 300 patients, 138 patients are clinically diagnosed to have developed VAP (46%), out of which 43.48% (60) had an early onset and 56.52% (78) had late onset. Studies by Dey A et al⁸ 2007 reported an incidence of 45.4% among mechanically ventilated patients with 47.7% developing early onset and 52.3% developing late onset VAP. Chawla R¹¹ (2008) in his comparative study of epidemiology of VAP among various Asian countries reported an incidence of 33% early onset and 67% late onset, Set R¹² et al 2011 in her study reported a higher incidence of late onset VAP (68%) compared to early onset (32%). These studies showed correlation with the present study.

In the present study out of the 138 patients 56.52% (78) were males 43.48% (60) were females, showing higher preponderance in males which is correlating with studies by Rakshit P et al¹³ in 2005 and Manoel J et al¹⁴ 2007, Bennani B⁷ et al 2008 reported high incidence of VAP among young adults which correlates with our study where 32.61% of patients were of 31-45 years age group.

Bacteria were established as the most common etiologic agents of VAP in many of studies conducted worldwide. In the present study also bacterial isolates were more predominant (69.57%). Among all isolates Gram negative bacteria the most common pathogen responsible for VAP. Set R et al¹²

in 2011 in their study reported *Klebsiella Pneumoniae* (33.33%) as the commonest isolate followed by *Pseudomonas aeruginosa* (31.25%). In the present study, among Gram negative bacteria *Klebsiella Pneumoniae* (40.63%) was the most common pathogen followed by *Pseudomonas aeruginosa* (15.63%) as the second most common isolate. Heyland DK et al¹⁵ in 1999 reported 3.5% occurrence rate of *Acinetobacter* species. A study by Dey A et al⁸ 2007 reported *Acinetobacter* as the commonest agent of VAP in their ICU setting with a very high incidence rate of 48.94%. However in the present study 12.50% of the isolates were *Acinetobacter* species and it was isolated in late onset cases only which was also the same in study by Rakshit P et al¹³ in 2005

Staphylococcus aureus was the most common Gram positive cocci isolated in studies by Wu CL et al¹⁶ in 2002 (24%), Wahid F et al⁴ in 2005 (20%), Rakshit P et al¹³ in 2005, Gacouin A et al¹⁰ in 2009 (21%), In the present study also *Staphylococcus aureus* was the commonest and the only Gram-positive cocci isolated (9.38%). Wu CL et al¹⁶ 2002 observed a single isolate each of

Enterobacter and Escherichia coli in his study. In the present study also a single isolates of Enterobacter and Escherichia coli were obtained. Other Organisms isolated in our study were citrobacter (9.38%) and Proteus mirabilis (3.23%) which were also reported in studies by Heyland DK et al¹⁵ in 1999 and George P et al¹⁷ 2010. Pseudomonas putida was isolated in one case which was suspected as Acinetobacter species. It was later confirmed as Pseudomonas putida by Vitek method and was reported in an elderly patient who is diabetic. The incidence of polymicrobial flora in our study was 15.55%. Hortal J et al¹⁸ 2009 reported 25% incidence. Rakshit P et al¹³ in their study found that incidence of Polymicrobial flora was higher in tracheal aspirate culture .They reported it as 54%. The incidence was found to be varying in different studies probably due to different methods of sample collection in different studies . Wahid F et al⁴ reported 9% incidence of polymicrobial flora in BAL samples. Singhal R et al¹⁹ 2005 reported incidence of 12.3% from BAL samples. Samples showing polymicrobial flora mostly compromised of mixed oropharyngeal growth with a few colonies of pathogenic flora and were not processed further as the patients were either responding well to routine antimicrobials or were shifted from RICU to their respective wards.

The antibiogram of Klebsiella pneumoniae in our study showed 100 % sensitivity to imipenem which correlated well with studies Chita L Nazal Matunog et al²⁰ 1993, George P et al¹⁷ 2010, Manoel J et al¹⁴ in 2007, Seth R et al¹² 2011, Japoni A et al²¹ 2011. The isolates showed resistance to most of the cephalosporin including ceftriaxone (100%) with moderate susceptibility to ceftazidime (38.47%) and cefepime(53.84%) . This pattern was in concordance with studies by Maria N et al²² 2010 and George P et al¹⁷ 2010 .

Pseudomonas aeruginosa was isolated in 5 samples showed maximum sensitivity to imipenem ,Piperacillin+Tazobactam(80%) and fairly sensitive to ceftazidime and cefepime (80%) whereas it was resistant to Gentamicin(100%) , Ciprofloxacin(60%) . This was correlating with resistance pattern of Pseudomonas aeruginosa isolates of other studies. Nazal- Matunog CL et al²⁰ in 1993 reported 17% resistance to imipenem. Seth R et al¹² 2011 reported 10% resistance to Imipenem and 23.33% resistance to ceftazidime and 20% resistance to cefepime. George P et al¹⁷ 2010 found that Pseudomonas were sensitive to Imipenem, Piperacillin and cefepime.

All the isolates of Acinetobacter species in this study were 100 % sensitive to Imipenem. Seth R et al¹² 2011 also reported 100% sensitivity to Imipenem. The isolates were showing 100% resistance to Gentamicin which correlated with studies by Maria N et al²² 2010. In the same study 33% resistance was reported against Piperacillin+ tazobactam .However in the present study 50% resistance was observed .

Among all Staphylococcus aureus isolates one isolate was resistant to ceftazidime (30 mcg) and was reported as MRSA . MRSA was reported in VAP cases in studies by

Chawla R et al¹¹ in 2008 (20%), Hortal J et al¹⁸ (10%) and Japoni A et al²¹ (17.2%).

Cefoxitin disc was used as studies by Anand KB et al 23 2009 and Mathews AA et al 24 2010 on comparison of different screening methods for MRSA detection stated that results with ceftazidime disc were in concordance with PCR results for mec A gene. All the three isolates showed excellent sensitivity to Vancomycin. Very few studies reported fungal isolates. Candida albicans was the only fungal isolate seen in our study which correlates with studies by Maria N et al²² 2010 where they reported Candida spp.

Conclusion:

The most common isolated pathogen was Klebsiella pneumoniae in (40.63%) cases followed by Pseudomonas aeruginosa (15.63%), Acinetobacter species (12.50%) and Staphylococcus aureus (9.38%).

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Figure 1: Overall result of the cases

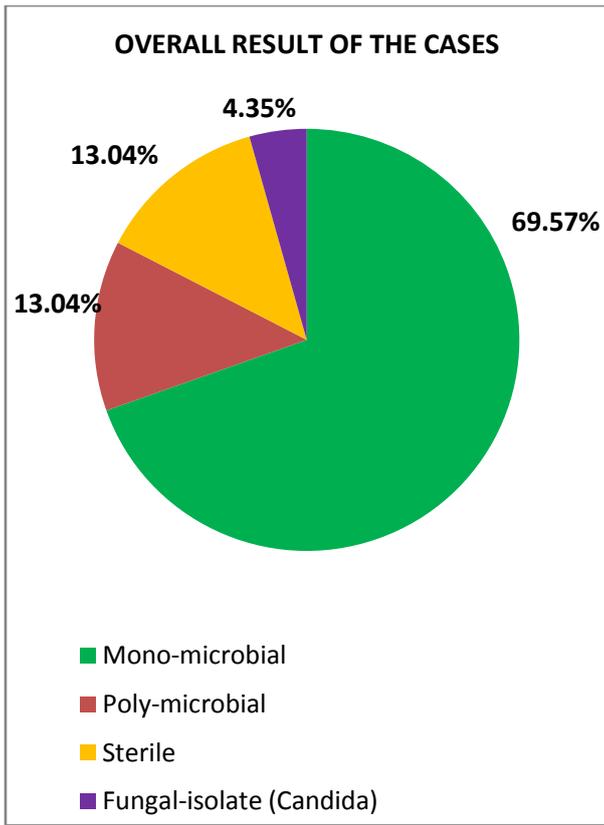


Figure 2: Age distribution of cases

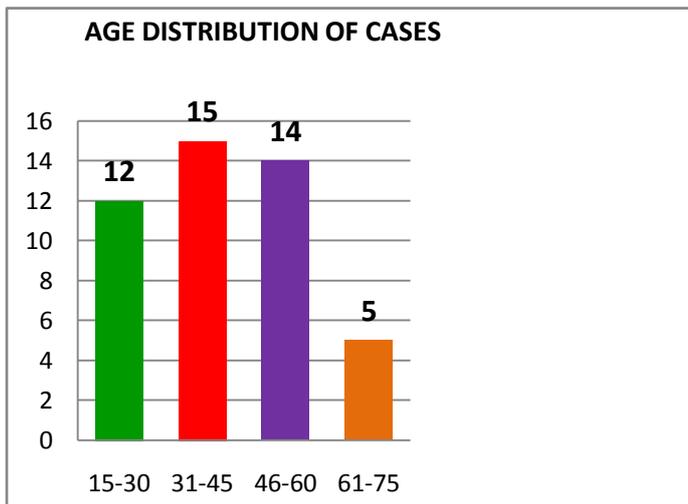


Figure 3: Antibiotic susceptibility pattern of *K. pneumoniae*

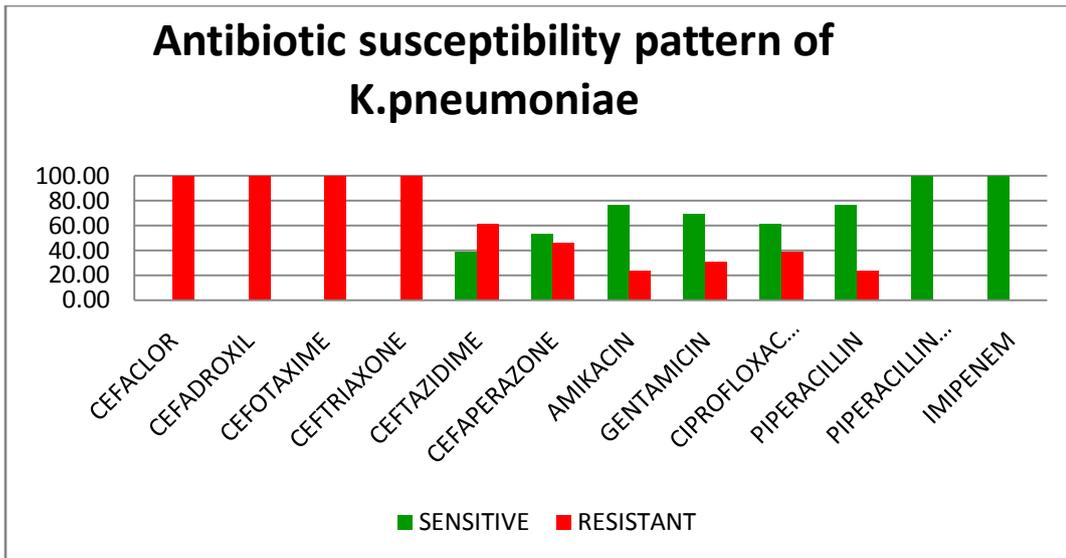


Figure 4: Antibiotic susceptibility pattern of *P. aeruginosa*

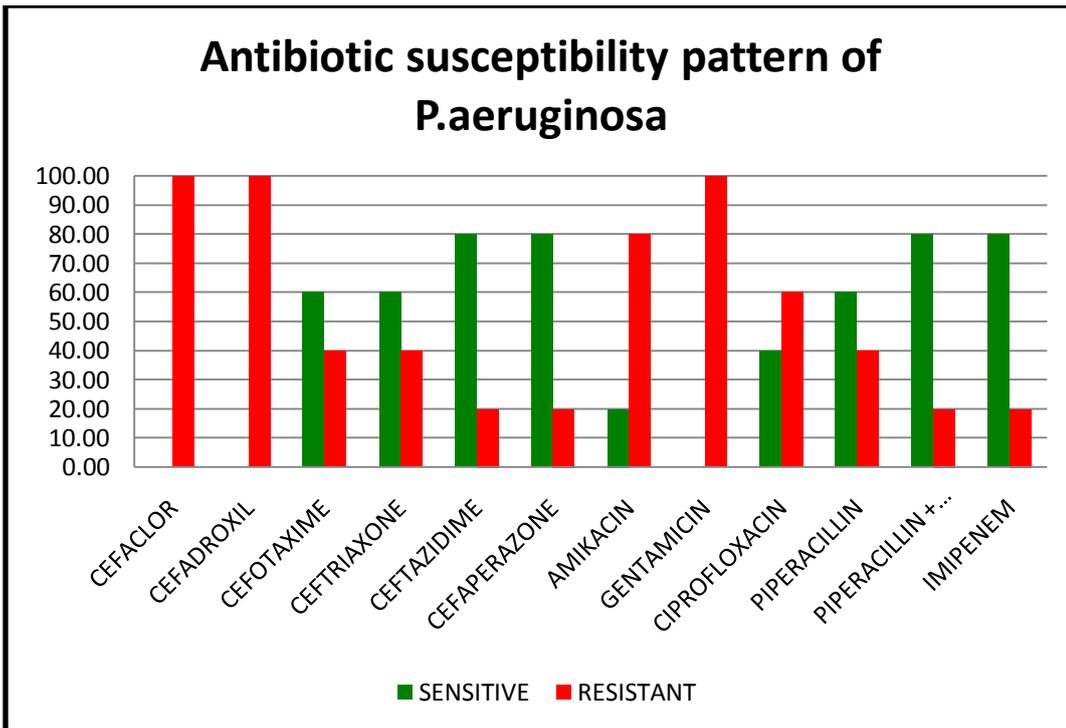


Figure 5: Antibiotic susceptibility pattern of Acinetobacter

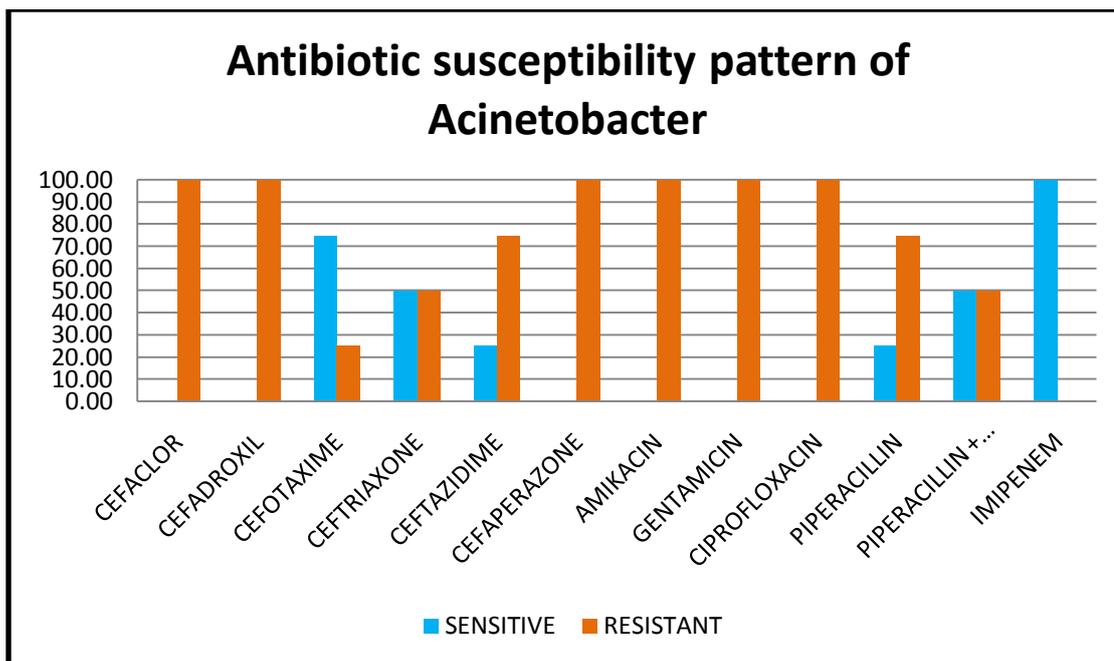
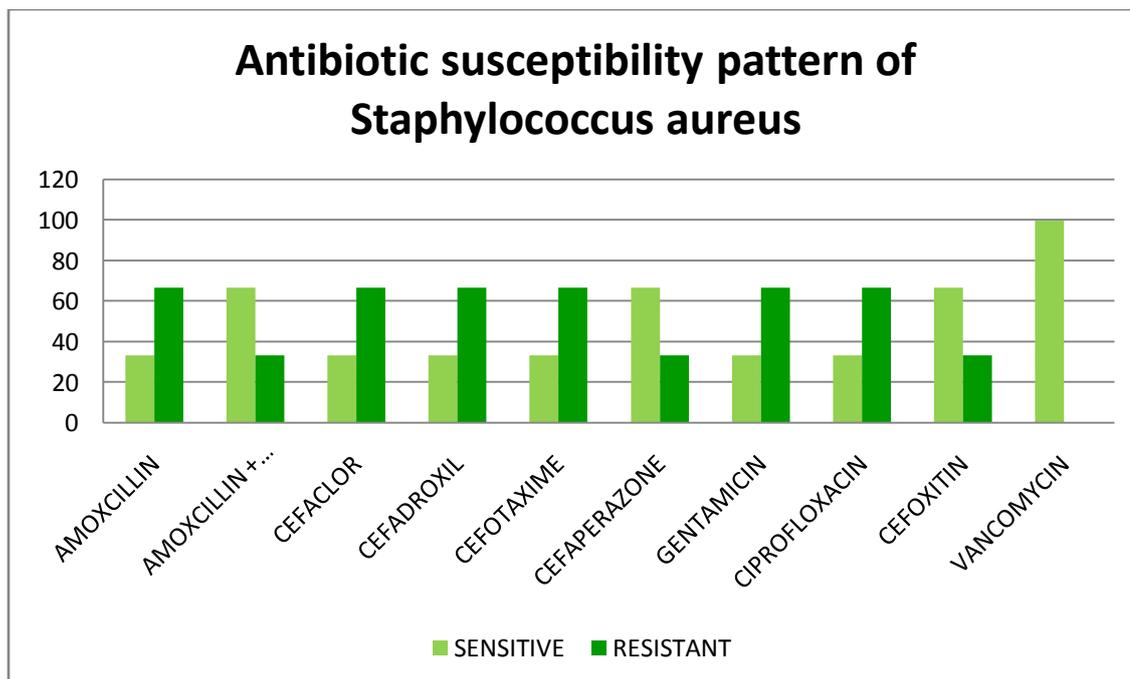


Figure 6: Antibiotic susceptibility pattern of Staphylococcus aureus



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