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PREVALENCE OF MULTIDRUG-RESISTANCE PATHOGENS ISOLATED FROM WOUND INFECTION PATIENTS VISITING COMBINED MILITARY HOSPITAL (CMH) PESHAWAR, PAKISTAN

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ABSTRACT

The main goal and aim of this study was to find out the prevalence of different bacterial pathogens and their antibiotic susceptibility in different patients having different sorts of wound infections. Total 200 positive pus samples were collected from patients of all genders and ages in the duration of three months. These samples were examined to detect the antibiotic susceptibility which has significant growth of pus producing pyogenic bacteria. The samples which were collected from patient's wounds were then inoculated on Blood agar, MacConkey agar media and also Chocolate agar media for preliminary identification of pyogenic bacteria such as Pseudomonas spp, staphylococcus aureus, E. coli, Klebsiella specie, Enterococcus specie. After growth colonies were presumably identified according to colony formation, pigmentation, elevation and margins. After that the supposed isolates were then tested for further verification. The supposed isolates were then tested through biochemical tests for instance MIU Motility Indole Urea test, TSI Triple Sugar Iron test, Citrate utilization test, Coagulase test and Oxidase, the bacterial growth were then subjected to MHA media to detect the sensitivity/susceptibility of antibiotics using antibiotics discs. This study depicted that 64% men are more infected than women 36%. Among infectious agentsS.aureus (30%) was the most prevalent. E. coli 24% Pseudomonas24%, Klebsiellaspp.10%Streptococcus4%&Proteus spp 3%Acinetobacter spp. 3% and Enterococcus 2% were the least prevalent. And the minimum numbers of candida spp 0.83% were also detected. Mostly the Gram positive bacteria from our isolates were resistant against Cephalosporin group of antibiotics and were sensitive against Carbapenem group of antibiotics for instance Ceftazidime 94% and Cefixime 92% were extremely resistant through Staphylococcus aureus bacteria, against Enterococcus specie antibiotics Imipenem was 20% and Meropenem was 80% resistant. On the contrary the Gram-negative bacteria Pseudomonas specie Acinetobacter and E. coli depicted highly resistance towards the antibiotics. Prevalence of MDR to the antibiotics that were not resistant to pathogenic species decades ago was found to be emerging gradually to an alarming situation which is most likely due to the excessive usage, partial medication and self-medication along with the other factors.

INTRODUCTION

The infections that induced by multidrug resistance (MDR) bacteria are an emerging hazard to the world including Pakistan [1,2].The world health Organization has already declared antimicrobial resistance as a risk to public health and has encouraged extraordinary international locations to formulate a strategy to resist the upcoming disaster [3].

The bacterial species taken from wound infections have indicated more than one resistance mechanisms to major classes of antibiotics [4,5]. Yet wound gives the most favorable environment such as warm, moist and nutritious environment facultative to microbial, growth and infectious diseases [6,7]. The infectious wounds are represented by the microbial growth, severe inflammation, and weak immune system [8] microbes linked with wound infection comprise pathogens like *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, Proteus spp, *Streptococcus pyogenes*, Acinetobacter spp and fungus Candida albicans etc. [9]. In developing nations wound infections are major health issues and a vast amount of people die on daily basis from infections which are preventable and curable in developed nations. [10,11].

The range and spectrum of pyogenic bacteria inducing infections and their susceptibility pattern have been showed that their pattern of susceptibility to various antibiotics varies from person to person in same species [12]. Antibiotic Resistance evolves naturally over a period of time, because of the partial medication excessive usage, and self-medication along with the other factors.

The inhibition of specified antimicrobial pathways lead to antimicrobial resistance for instance cell wall synthesis inhibition, nucleic acid synthesis inhibition, ribosome function, protein synthesis, foliate metabolism inhibition, and cell membrane function [[13], [14], [15]]. The violation of laws and regulations of the purchases and sales of antibiotics are also the main factors in the misuse and access of antibiotics. In many countries, antibiotics can be purchased without a doctor prescription [16].

In Pakistan, it is a common practice that we can easily purchases antibiotics without a doctor prescription this result to mishandling of antibiotics by the public, thus, contributing to the spread and increase of antimicrobial resistance [17]. Researches and biologists have been performed experiments in Pakistan to see the multi-drug microbial resistance pattern of the different specimens. Still, a study targeting multi drug resistance wound infection is crucial. Thus this study conducted to explore the (Multi-drug resistance) MDR pattern of bacteria which isolated from patients.

Materials and methodology

All samples were collected from patients in combined military hospital (CMH) Peshawar having clinical symptoms of microbial infection.

Study Period

23th February-23th May 2022

Study Site

Combined Military Hospital (CMH) Peshawar.

Types of samples

The sample type was isolated from Pus (wound infection).

Quantity of samples

We examined total of 200 positive samples from patients.

Methodology and working procedure:

Sterilization

Media were sterilized by the help of autoclave. Also all the glass beakers were sterilized at 180 Celsius for 60 minutes in a hot air oven before using. Solutions which were used during my research were also sterilized.

Collection of samples

The pus sample was obtained from patient having wound infections. Pus samples were obtained by the help of swab stick and also through syringes.

Culturing of samples

All the samples were cultured on Blood agar media, chocolate and MacConkey agar media by streak plate technique. Hereafter the plates were then incubated for growth in incubator at 37°C for 1 to 2 days.

MacConkey agar

MacConkey agar media is used for the differentiation and isolation of GNRs. It is also used for the differentiation of lactose fermenting and non-lactose fermenting GNRs. The color which appears pink in this media indicates lactose fermenters bacteria.

E.g. Shigella, Salmonella (non-lactose fermenting) Escherichia coli, Klebsiella (lactose fermenting)

Working Procedure
The pus from infectious wound samples were cultured on the media with the sterilized inoculating loop in antiseptic condition by streak plate technique and then put the media in incubator for colony growth up to 1 to 2 days at 37°Celcius.

Blood agar
Blood agar media is a differential and enriched media used for the detection of hemolytic reactions consist of defibrinated mammalian blood (usually we use 5% sheep blood). Various kinds of hemolysis occur on blood agar for instance (alpha, beta, and gamma).
E.g. Streptococcus pyogenes, Staphylococcus aureus

Working Procedure
The infectious wound pus samples were cultured on the media by the help of sterilized inoculating loop by streak plate technique and then incubated for 1 to 2 days at 37°Celcius.

Chocolate agar
When the blood agar is heated to lyse the red blood cells in the blood so the medium becomes chocolate which is brown in color. Then it's referred as chocolate agar. It's used for the culturing of fastidious organisms.
E.g., Haemophilus influenza, Neisseria meningitidis

Working Procedure
The infectious wound pus samples were directly cultured on the media with the inoculating loop by streak plate technique and then incubated for 1 to 2 days at37°Celcius.

Biochemical tests performed for colony identification
Various biochemical tests were accomplished in this study for the identification of pathogenic bacteria in the wounds

Triple sugar iron (tsi) test
This TSI test enables us to differentiate the microbes among the family of Enterobacteriaceae depending upon its ability to utilize sugars i.e. sucrose, lactose, and glucose available in the agar media.

Working Procedure
The prepared TSI media was poured into various test tubes of 5ml to each test tube. Hereafter the tubes were positioned in inclined position to make slants. After that the bacterial samples were then cultured on these slants. These tubes were then incubated for a night at 37°Celcius.

Motility Indole Urease (MIU Test) for sample identification
These three various tests performed in a single tube infers the differentiation of microorganisms on the basis of motility, indole, urease.
These tests are done for the identification of gram negative bacilli.

Motility Test
It infers the movement of bacteria on the agar media. Very thinner agar media is used for this purpose to allow bacteria to move through it. Any kind of color change in media is considered motile bacteria.

Indole Test
Indole test indicates that type of bacteria having the enzyme "tryptophanase" which is used for hydrolyzing and de- ammoniate tryptophan amino acid by generating indole, pyruvic acid &ammonia. For this test indole paper is used if the color of paper changes it shows positive result for the test.

Urease Test
In urease test ammonia production will enhance the pH by increasing the basicity level of medium which alters the colorless phenolphthalein into pink color.

Urease test procedure
Pick up a small colony of bacteria from a plate with the help of sterilized inoculating loop.
Add the urease reagent into the test tube.
Dip the bacterial colony into the test tube.
If the bacteria contain an enzyme urease it will turn urea into ammonia in a solution which is alkaline in nature so the PH of medium increase which will turn into a pink color so the result is positive
If the color of medium changes to pink it will indicate positive result and no color changes shows negative result.

Simmons Citrate Test
A test which infers the utilization of carbon source of various bacteria for their growth. The medium is alkaline.

The dark blue indicates positive outcome and the dark green indicates negative outcome.

Bile esculin agar

Bile esculin agar is used for the identification of streptococci group D. Esculin is hydrolyzed to esculitin and dextrose in the medium. In this the esculitin provides the dark brown/black complex by reacting to ferric citrate.

Catalase Test

Biochemistry test that observers the catalase enzyme in the microorganism.

Catalase enzyme survives in oxygen and catalyzes the decomposition of hydrogen peroxide and release water and oxygen in living organisms

Catalase test procedure

1st take a drop of 1-2 ml of hydrogen peroxide solution into a test tube.

After that using a sterile loop for picking up of colony from a plate which contains bacterial growth, dip that colony into the hydrogen peroxide solution in the test tube.

Observe for immediate bubbling.

If bubble formation occurs result is positive which staphylococci specie.

If no bubble formation occurs result is negative which is streptococcus spp.

Coagulase test

Coagulase enzyme is produced by Staphylococcus aureus which Converts fibrinogen which is an inactive form to an active form called fibrin in plasma

If no clumping is occurred result is negative and the presence of clumping is positive.

Coagulase test procedure

1ST take a drop of human or rabbit plasma with the help of micropipette with the slide.

By using a sterile colony picker and pick the colony from the plate.

Add that colony into the slide which has plasma mix it.

Observe the clumps.

If clumping occurs result is positive result which is staphylococcus aureus specie.

If no clumping occurs result is negative which are staphylococcus saprophyticus and staphylococcus epidermidis species.

Oxidase test

It's the enzyme of bacterial electron transport chain the bacteria which contains oxidase enzyme will depict positive outcome and will provide purple color and enzyme absence provides no color.

Oxidase test procedure

1st add 0.2ml of 1% oxidase reagent in a normal saline in tube.

Pick up a colony with the help of sterile swab stick and dip the swab stick in the oxidase reagent.

Immediate observe the color change.

If color turns into purple result is positive

If no color change result is negative.

Antibiotic Susceptibility Test:

It's a microbiology laboratory test which shows how effective antibiotic therapy is towards bacteria. The aim antimicrobial susceptibility testing is to predict the in vivo success or failure of antimicrobial therapy. These Tests are conducted in vitro and measure the growth of an isolated organism against a particular drug.

Disc diffusion technique is used for the antibiotic susceptibility testing.

Disc Diffusion Method

In this technique discs soaked with known concentrations of antibiotics are placed on sensitivity plates which are inoculated with a culture of the bacterium to be tested. Hereafter the plate is incubated at 37°C for 24hours. The susceptibility of drug is determined from the zones of inhibition of bacterial growth surrounding the antibiotic discs. The diameters of the zone of inhibition are calculated with thin transparent millimeter scale.

Procedure

The antibiotic discs are putted with sterile forceps onto the surface of the medium streaked with test strains and the results are reported after incubating the plate for 24 hours at 37°Caerobically.

Results

This study was conducted in the microbiology section of Combined Military Hospital laboratory Peshawar where a total of 200 samples were analyzed to assess the current breadth of multidrug resistance present in patients. The overall rates of resistance for these 200 samples analyzed are provided according to age status, gender and MDR status.

Results of biochemical tests for isolated organisms
Table:1
Percentage of Gram positive & negative organisms of total positive samples

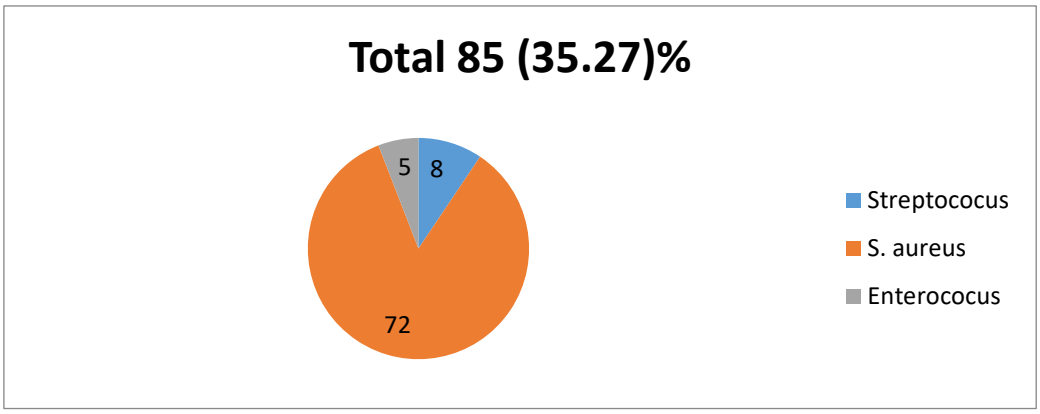
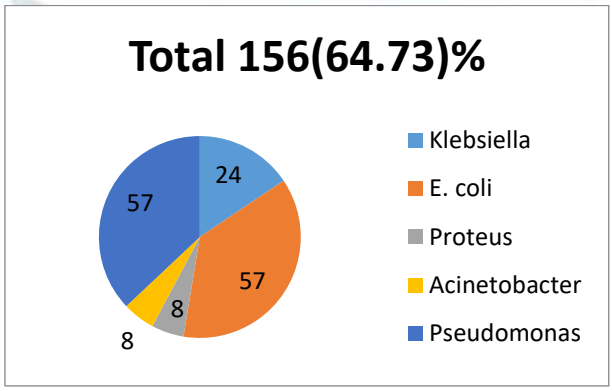


Figure:1

Organisms	Citrate test	Oxidase test	MIU Medium			TSI		
			Motility	Indole	Urea	Slant	Butt	H_2S
E .coli	-	-	+	+	-	A	A	+
Klebsiella spp	+	-	-	-	+	A	A	+
Pseudomonas spp.	+	+	+	-	-	A	A	+
Staphylococcus aureus	-	-	-	-	-	K	K	-
Acinetobacter spp.	+	-	-	+	+	A	A	-

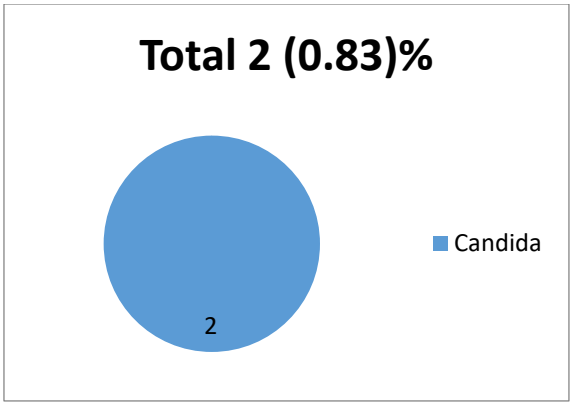
Throughout all the Gram positive organisms S.aureus is likely to have the most advantages on exhibiting positive growth results from the wound pus samples.

Figure:2



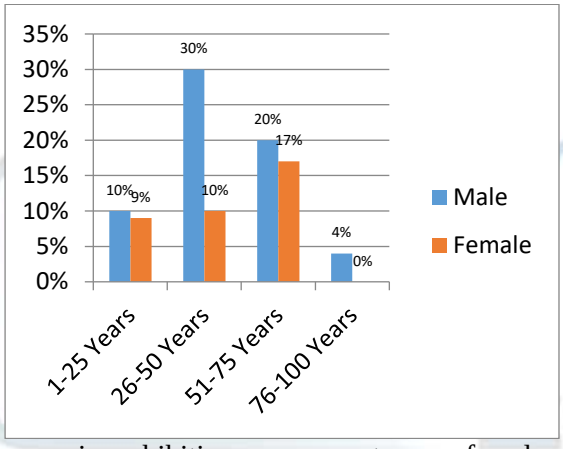
Throughout all the Gram negative organisms Escherichia. coli and Pseudomonas are advanced in number which is more than (20%) and other pathogens Klebsiella, Proteus, Acientobacter are mostly in (2-10%) in number which is very minimal.

Figure:3



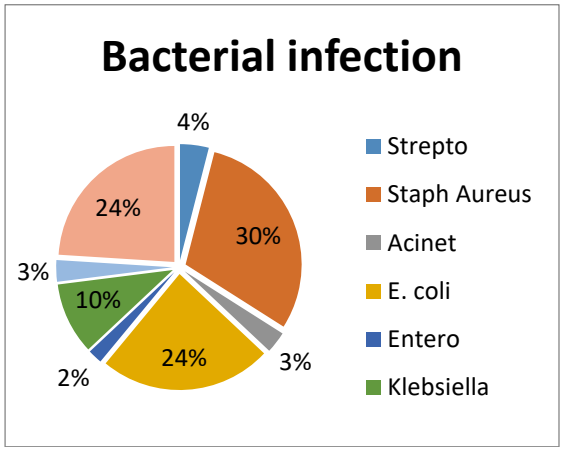
Besides Gram-positive and Gram-negative pathogens findings, there are small amount of Candida species (0.83%) were also detected. Invasive contamination because of Candida species is generally a condition related with clinical advancement, and is broadly known as a significant reason for morbidity and mortality in the health care sector.

Percentages of positive patients according to sex
Figure:4



Among (26-50) years of men is exhibiting predominance in positive patients which is likely to be (30%) and slowly (51-75) years is 20% and (76-100) years are 4%. On the contrary female patients are showing predominance in the age group of (51-75) years and steady reduces to (26-50) years in 10% and (1-25) years' in9%.

Percentages of etiological agents of bacterial infection
Figure:5



Percentages of etiological agents of Positive
This chart shows the pathogens all together in their specific percentage

Antibiotic resistance pattern of different organisms
Klebsiella spp.
In this research Linezolid, Vancomycin, Cloxacillin, Fusidic Acid, Azithromycin steady depict 100% sensitivity against Klebsiella spp. And with this outcome these antibiotics can be recommended as some right medicines to treat various infections with Klebsiella spp. There are various types of antibiotics which are moderately resistant and mostly sensitive starting with Amoxyclav 96%, Imipenem 79%, Colistin 83%, Amoxycillin 79%, and Tigecycline 87%. Antibiotics which are mostly resistant against this pathogen are Cefotaxime 75%, Cotrimoxazole 88%, Ceftazidime 88%, Cephalexin 83% and Cefuroxime 75%.

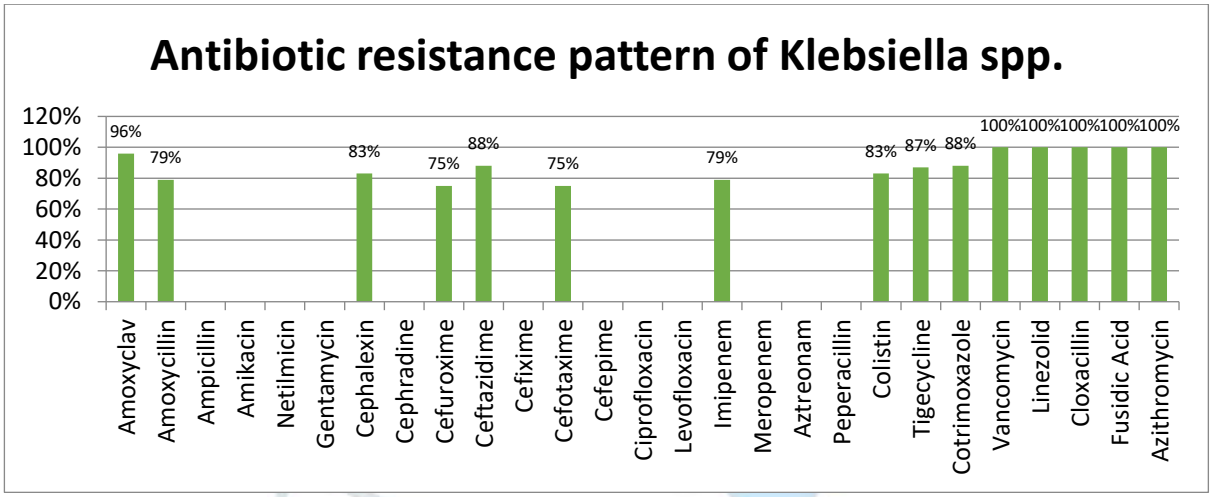


Figure 5: Antibiotic resistance pattern of Klebsiella spp.

Pseudomonas spp.
This chart indicates that the Cephalexin 95%, Cefuroxime 93%, Ceftazidime 81%, Cefotaxime 88%, Cotrimoxazole 89% are depicting the most resistance against Pseudomonas species. So the antibiotics mostly under Cephalosporin group will not be effective in treating diseases under this pathogen. Antibiotics which are moderately resistant are Amoxycillin 84%, Ampicillin 75%. Amikacin 68%, Imipenem 68%, Meropenem 41%. 100% sensitive towards this pathogen are Vancomycin, Linezolid, Cloxacillin, Fusidic Acid, Azithromycin, and Amoxyclav.

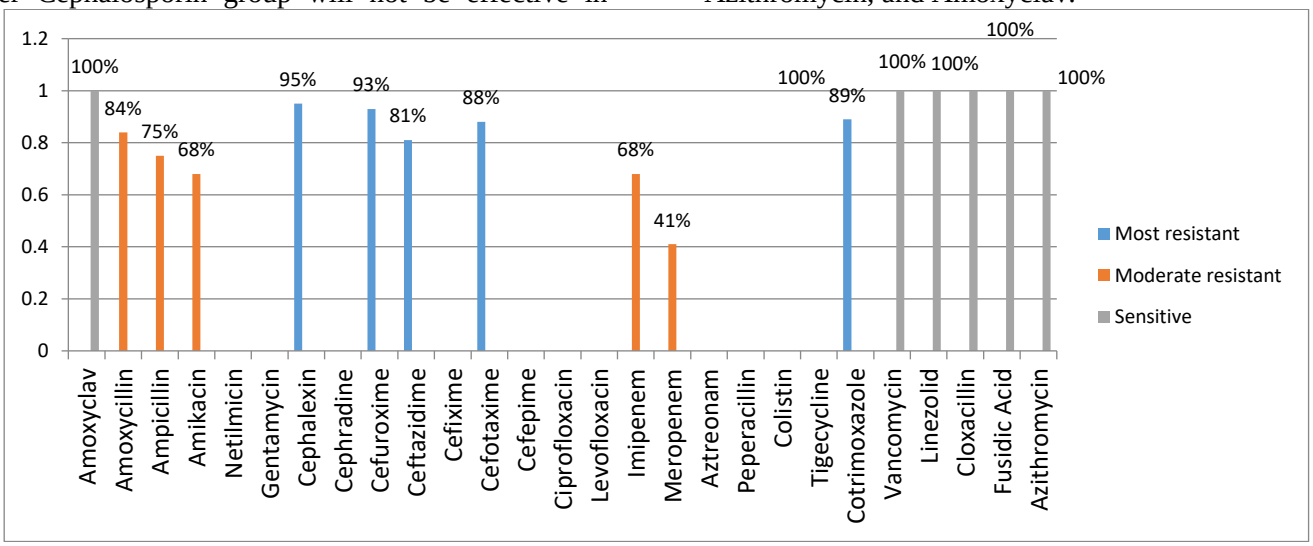


Figure 6: Antibiotic resistance pattern of Pseudomonas spp.

Proteus spp.

This chart indicates that the Amoxyclav, Vancomycin, Linezolid, Cloxacillin, Fusidic acid, Azithromycin show 100% sensitivity, that infers the possibility of proper medication against this bacterium. Cephalexin 88%, Cefuroxime 63%, Ceftazidime 75%, Collistin 88%, Cotrimoxazole 63% are respectively showing more resistance towards Proteus. Antibiotics which are moderately resistant are Amikacin 25%, Netilmicin 25%, Cephradine 38%, Cefixime 25%, Ceftriaxone 25% and Imipenem, Azteronam, Tigecycline are showing minimal resistance and mostly sensitivity.

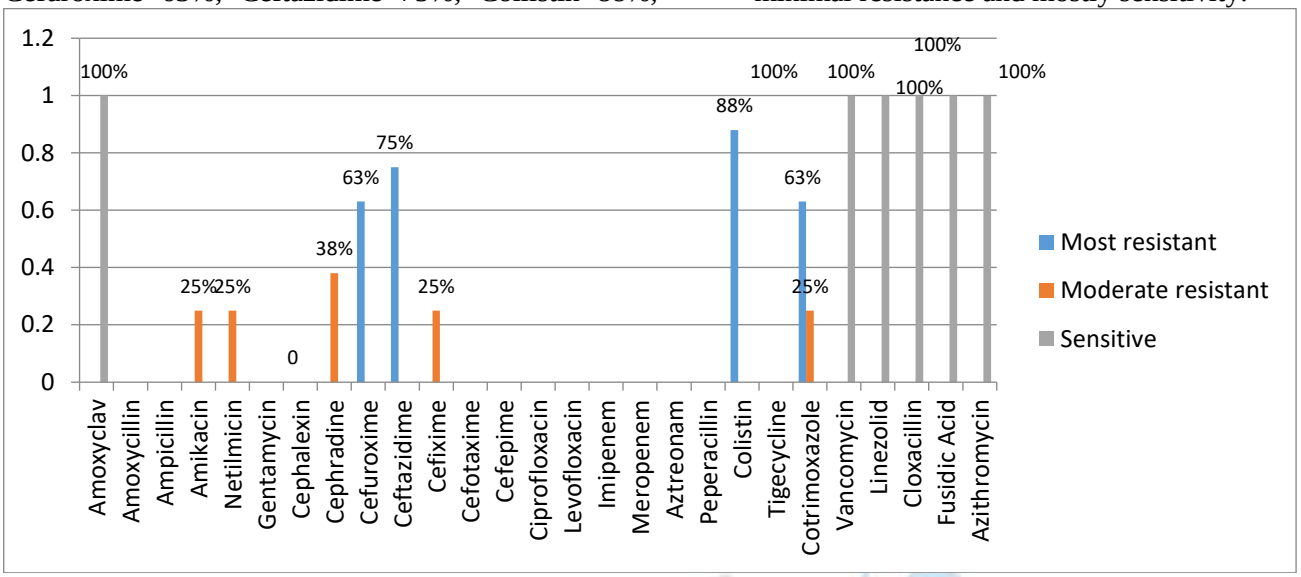


Figure 7: Antibiotic resistance pattern of Proteus spp.

Enterococcus spp.

This chart indicates the antibiotics Amoxyclav 60%, Ampicillin 80%, Gentamycin 80%, Cephalexin 80%, Cefuroxime80%, Ceftazidime 80%, Cefixime 80%, Cefotaxime80%, Meropenem (80) %, Azithromycin (80) % are respectively indicating most resistance against Enterococcus species. Nevertheless, Piperacillin-tazobactam, Levofloxain, Azteronam, Colistin, Tigecycline, Vancomycin, Linezolid, Fusidic acid are indicating 100% sensitivity against this organism

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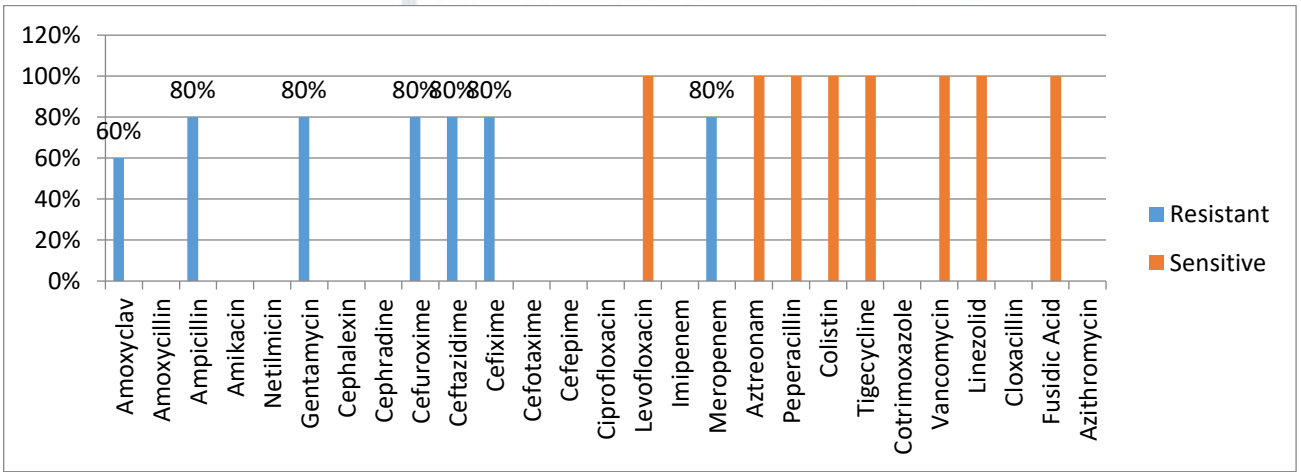


Figure 8: Antibiotic resistance pattern of Enterococus spp.

E. coli

Among E coli Meropenem, Piperacillin-tazobactamAmoxyclav, Imipenem, Colistin, Linezolid, Cloxacillin, Tigecycline, Vancomycin, Fusidic acid, Azithromycin indicating more than 80% of sensitivity. Antibiotics which are resistant against this organism are Cephalexin 93%, Cefuroxime 82%, Ceftazidime79%, Cefixime79%, Cotrimoxazole75%.

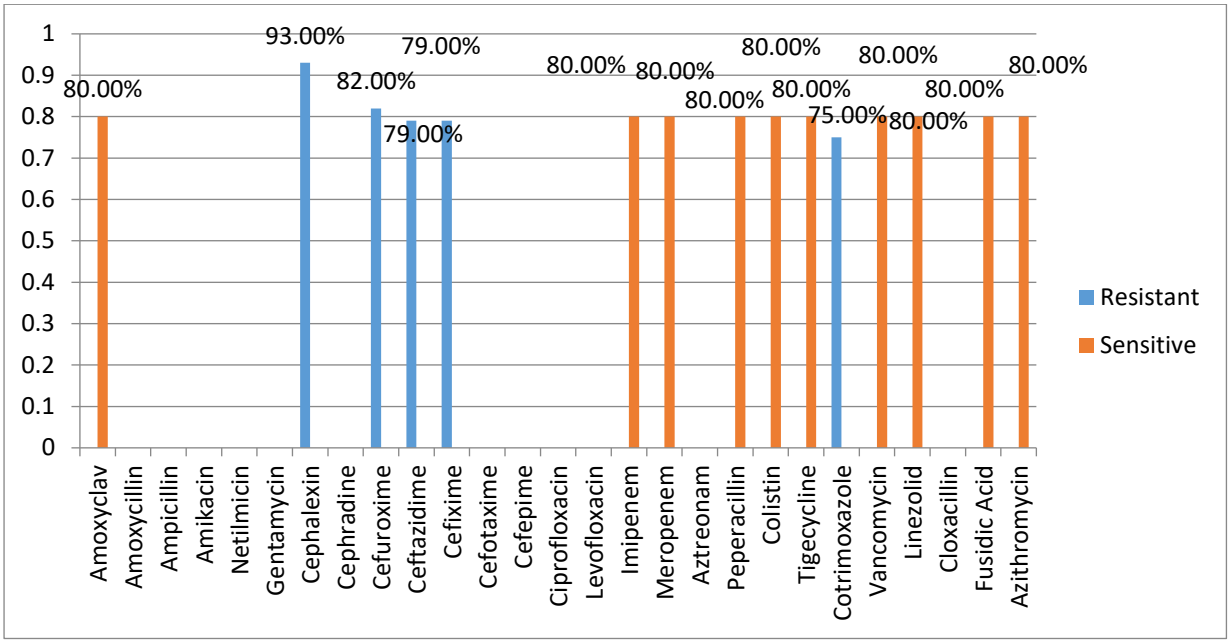


Figure 9: Antibiotic resistance pattern of E. coli

Acinetobacter

This chart shows Acinetobacter is highly resistance to a potential antibiotic group Cephalosporin, which are Ceftazidime Cefixime Ceftriaxone Cefotaxime accounted for 100% Cefepime 88% accordingly. Also Meropenem, Azteronam, Piperacillin-tazobactam are not showing resistance. On the contrary Amoxyclav, Vancomycin, Linezolid, Cloxacillin, Fusidic acid and Azithromycin are 100% sensitive against this bacterium.

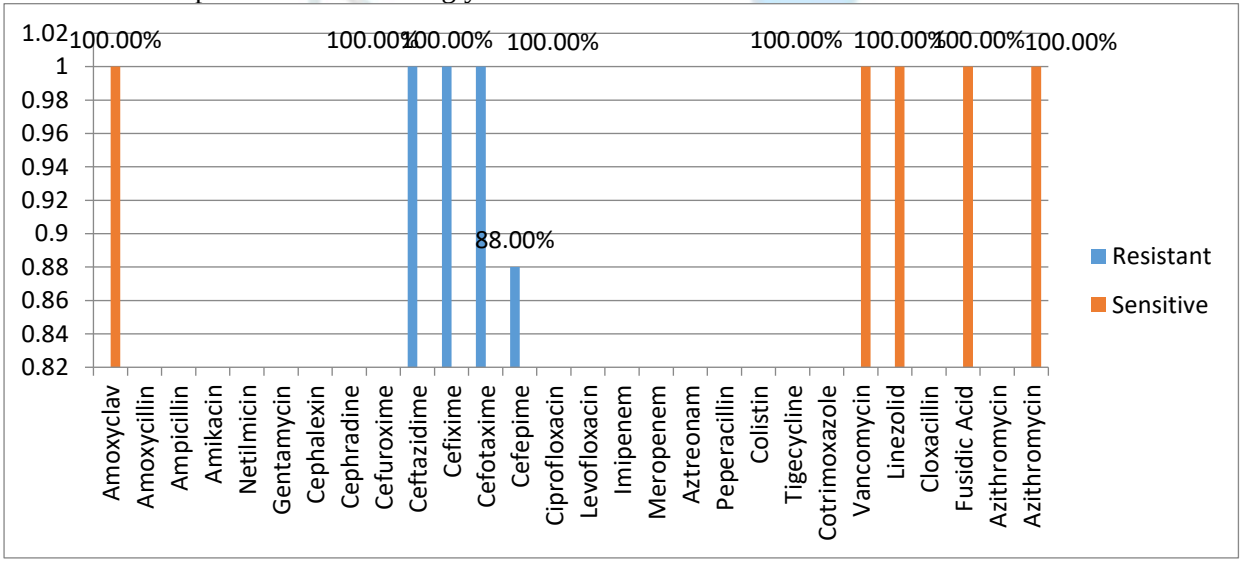
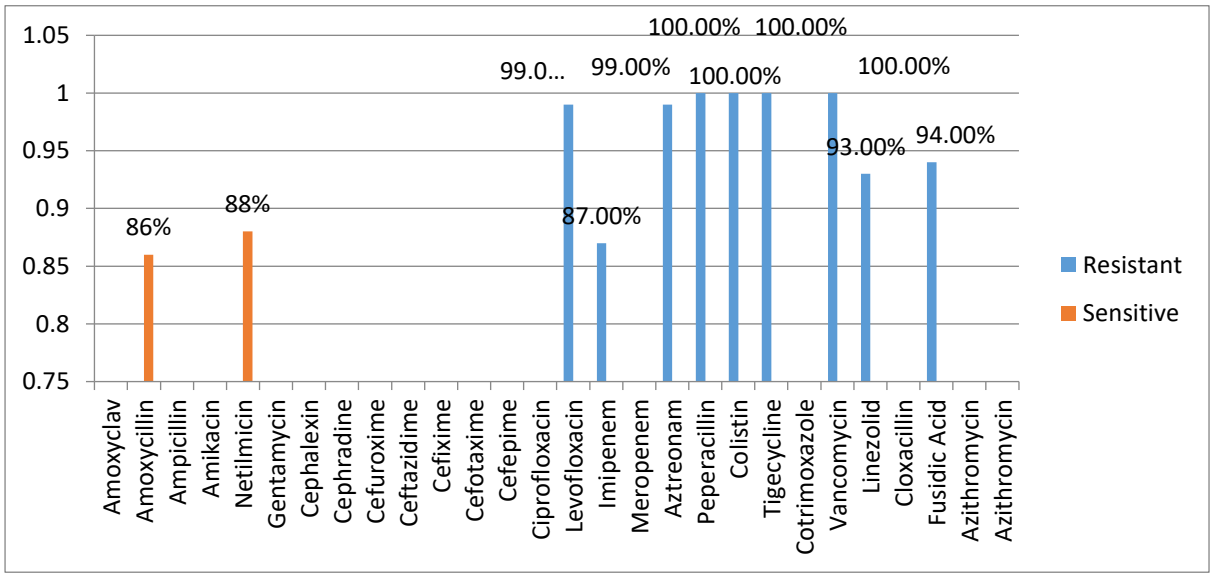


Figure 10: Antibiotic resistance pattern of Acinetobacter

Staphylococcus aureus:

S.aureus appears highly sensitive against Levofloxacin 99%, Imipenem 87%, Azteronam 99%, Piperacillin-tazobactam100%, Colistin 100%, Tigecycline 100%, Vancomycin 100%, Linezolid 93%, Fusidic acid 94%. Antibiotics which are depicting most resistance against this organism are Ampicillin 93%, Ceftazidime94%, Cefixime 92%. It was moderately sensitive Amoxycillin 86% and Netilmicin 88%.

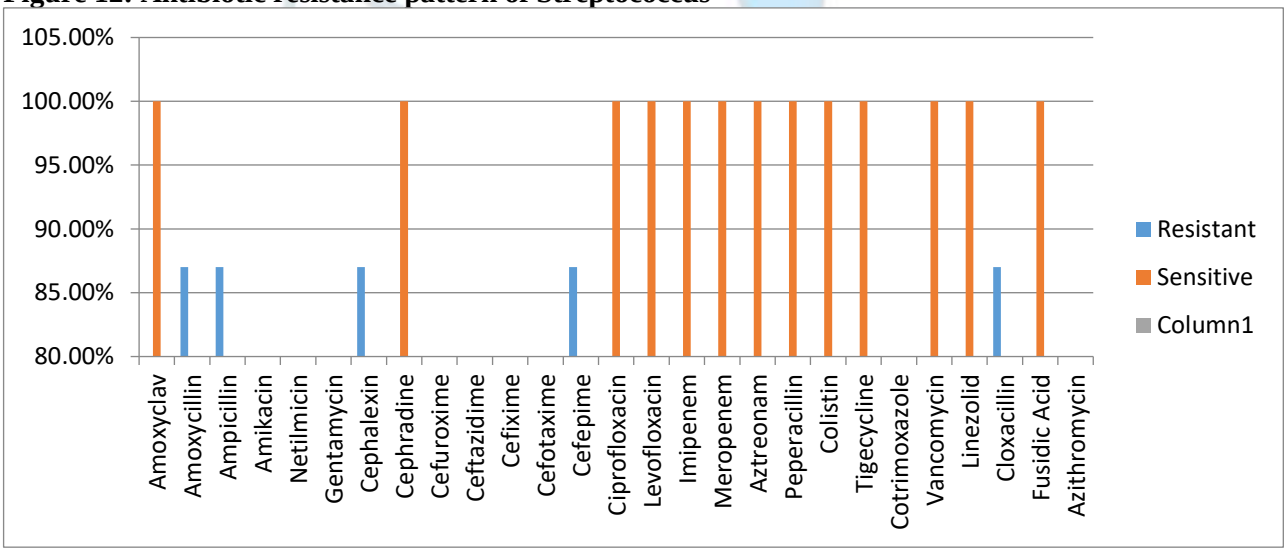
Figure 11: Antibiotic resistance pattern of S.aureus



Streptococcus:

This organism is depicting 100% sensitivity against various antibiotics which are Cephradine, Ciprofloxacin, Amoxyclav, Levofloxacin, Imipenem, Meropenem, Azteronam, Piperacillin-tazobactam, Colistin, Tigecycline, Vancomycin, Linezolid, Fusidic acid. It is moderately sensitive to AmpicillinAmoxycillin, Cephalexin, Cefepime, and Cloxacillin which is around87%.

Figure 12: Antibiotic resistance pattern of Streptococcus



DISCUSSION

Total 200 pus samples were collected from patients of all genders and ages in the duration of six months. These samples were examined to observe the antibiotic susceptibility having significant growth of pyogenic bacteria. Gram positive bacteria accounted for (35%) and Gram negative bacteria accounted for (64%) which is approximately double of total Gram positive isolates comparatively.

The samples were inoculated on MacConkey agar media, Blood agar and Chocolate agar media for primary identification of pyogenic bacteria such as Pseudomonas spp, S.aureus, E.coli, Klebsiella spp, Enterococcus spp. After growth colonies were presumably identified according to colony formation, pigmentation, elevation and margins. After that the presumed isolates were further tested for further confirmation. The isolates were then examined through biochemical tests for instance MIU (Motility Indole Urea) test, TSI (Triple Sugar Iron) test, Citrate utilization test, Coagulase test and Oxidase, the bacterial growth were then

subjected to MHA media to detect the sensitivity/susceptibility of antibiotics using antibiotics discs.

This study depicted that (64%) men are more infected than women (36%). Among infectious agents S.aureus (30%)was the most prevalent. E. coli (24%), Pseudomonas (24%), Klebsiellaspp. (10%), Streptococcus (4%), &Proteus spp (3%), Acinetobacter spp. (3%) and Enterococcus (2%) was the least prevalent. In this study, the Streptococcus has depicted maximum sensitivity towards the antibiotics among all the isolates. On the contrary Gram negative organism Staph. Aureus was extremely resistant against to some of the most prescribed antibiotics. Cephalosporin group was mostly active in this resistance pattern of this organism. It's clearly revealed that approximately (30%) of infection rate is only from Staph. Aureus itself. Gram negative organisms were extremely resistant against Penicillin and Cephalosporin. Pseudomonas spp (24) %, E. coli (24) % and Klebsiella spp (10) % accordingly were most found pathogens in the Gram negative group. In a study, it is also found that Eschericshia.coli is one of the major pathogen in the wound infection hereafter that Staph.aureus comes but in a different platform. Furthermore, Vancomycin, Linezolid, Fusidic acid, Tigecycline, were some most effective antibiotics as they were susceptible to most of the microorganisms. Besides this the pattern examined in this study has depicted that there were pathogens which were (MDR) multi drug resistant. Nevertheless, Fungus isolates were not much available in the findings which were only (0.83%). Antibiotic resistance is increased due to the overdose and misuse of the antibiotics. Proper cleaning and bandaging can stop most of the infections. Only prescribed antibiotics by physicians should be taken. The Incentives should be focused on antibiotic stewardship rather than concentrating on the antibiotic misuse and overdose.

Patients also required to be informed about the proper utilization of the antibiotics. Also sustainable antibiotic utilization requires being enlightened among health professionals, policy makers etc. Periodic studies are also required as evaluation measure of the level of infection control practices. Animal farm industry Food industry requires to obtained proper precautions to decrease the health risks. Assuring political commitment to meet the hazard of the antibiotic resistance is another crucial need.

Conclusion

This study underscores the high prevalence of antibiotic-resistant infections among pus samples, with Staphylococcus aureus being the most common and notably resistant pathogen. Gram-negative bacteria such as E. coli, Pseudomonas spp., and Klebsiella spp. also showed significant resistance, particularly against penicillin and cephalosporins. Effective antibiotics like Vancomycin, Linezolid, and Tigecycline were identified, though the emergence of multidrug-resistant strains highlights the urgent need for stringent antibiotic stewardship. To combat rising resistance, it is essential to promote responsible antibiotic use across healthcare, policy, and industries. Continuous monitoring and public health initiatives are critical to ensuring sustainable infection control and effective treatment options

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