STUDY OF ANTIBIOTIC-RESISTANCE AND SENSITIVITY PATTERN IN A TERTIARY CARE TEACHING HOSPITAL

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Introduction: Antibiotics are helpful in bacterial infection control and management. Irrational antibiotic use leads to resistance, which puts modern medicine’s achievements at risk. This study aims to know antibiotic resistance and sensitivity patterns and to assess possible factors that favor the development of antibiotic resistance.

Methods: It is a retrospective observational study. Data collected from June 2019 to May 2020 from the culture & sensitivity records of various clinical isolates at the Microbiology department of SMC, Vijayawada, and analyzed by descriptive statistics.

Results: Total samples collected 2905. Only 746 samples showed significant growth. Most commonly, isolated organisms were from Pus and Body fluids: Staphylococcus aureus (31.16%), Klebsiella (23.02%). From blood samples: Staphylococcus aureus (44%), Klebsiella (32%). From urine samples: Escherichia coli (27.31%), Staphylococcus aureus (16.66%). Bacteria isolated from Blood and Pus & body fluid samples showed more resistance to Amoxicillin + Clavulanic acid, 60% & 58.60%, and urine samples showed more resistance to Norfloxacin 69.44%.

Conclusion: In this study, bacteria isolated from blood, pus, and body fluid samples showed more resistance to Amoxicillin + Clavulanic acid, from urine samples showed more resistance to Norfloxacin. Parenterally used drugs like aminoglycosides and vancomycin have retained their sensitivity but bacteria also showed resistance to Imipenem, Vancomycin, new combinations like Cefoperazone + Sulbactam. A culture & sensitivity test and following antibiotic stewardship guidelines before prescribing antibiotics will give good results to prevent antibiotic resistance.

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Introduction: Antimicrobial agents were viewed as a miracle cure when first introduced into the clinical practice but the development of resistance dims the luster of a miracle. Inappropriate use of antibiotics favors the emergence and spread of antibiotic resistance which is putting the advancements of modern medicine at risk. Antibiotic resistance refers to the ability of microorganisms to withstand the effect of the antibiotic. Antibiotic-resistant leads to longer hospital stays, higher medical costs, and increased mortality. Many infections such as pneumonia, tuberculosis,
gonorrhea, and foodborne diseases are becoming difficult and sometimes impossible because of antibiotic resistance. World Health Organization (WHO) has declared AMR a public health threat and has urged different countries to develop an action plan to combat the problem.

The major factors associated with the emergence of antibiotic resistance:

**Evolution & clinical/environmental practices**

**Intrinsic factors:**
- Reduced entry of antibiotic into a pathogen.
- Enhanced export of antibiotics by efflux pumps.
- Release of microbial enzymes that alter or destroy the antibiotic.
- Alteration of target proteins.
- Development of alternative pathways to those inhibited by the antibiotic.

**Social factors:**
- Demographic changes.
- Deficient hygienic practices.
- Irrational use of antibiotics.
- Overcrowding.
- Geographical variations.

Due to the geographical variations in antibiotic resistance and sensitivity that have been reported by many studies, this study was undertaken with the following objectives in a tertiary care teaching hospital in Vijayawada:
1) To identify the group of organisms isolated.
2) To know resistance and sensitivity patterns to various antibiotics.
3) To assess the possible factors that can favor the development of antimicrobial resistance.

**Methodology:**
This is a retrospective observational study conducted at the Dept of Pharmacology SMC Vijayawada. Approval from the Institutional Ethics and Research committee was obtained before the commencement of the study. Data regarding culture and sensitivity of the organisms isolated from different samples such as urine, blood, pus, and body fluids were collected from June 2019 to May 2020 from culture and sensitivity records of dept of Microbiology of SMC, Vijayawada. The obtained data were subjected to descriptive statistics.

**Results:**
Data were collected from June 2019 to May 2020. Total samples collected 2905. Among 2905 samples, 1347 samples are Pus and Body fluids, 632 Samples are blood, 926 samples are urine. Among these only 746 (25.67%) samples showed significant growth and the remaining samples didn’t show growth (Table 1).

| Type of samples      | sterile | Growth seen | Total  |
|----------------------|---------|-------------|--------|
| Pus and Body fluids  | 917     | 430         | 1347   |
| Blood                | 532     | 100         | 632    |
| Urine                | 710     | 216         | 926    |
| Total                | 2159    | 746         | 2905   |

**Isolated organisms**

**Pus and Body Fluids:**
Among 1347 samples of Pus and Body fluids only 31.9% (n=430) samples showed significant growth, remaining 68.07% (n=917) samples were sterile. Most common isolated organisms were Staphylococcus aureus 31.16% (n=134), Klebsiella 23.02% (n=99), Pseudomonas 14.65% (n=63), Escherichia coli 8.83% (n=38), Proteus spp 5.8% (n=24), *Methicillin Resistant Staphylococcus Aureus* (MRSA) 4.65% (n=20), *Coagulase Negative Staphylococcus* (CONS) 4.65% (n=20), *Methicillin Sensitive Staphylococcus aureus* (MSSA) 3.95% (n=17), Acinetobacter spp. 2.09% (n=9), Streptococcus spp. 0.93% (n=4), Enterococcus spp. 0.46% (n=2) respectively (Figure 1).
Blood:
Among 632 samples of blood, only 15.82%(n=100) samples showed significant growth, the remaining 84.17% (n=532) samples didn’t show any growth. Most common isolated organisms are Staphylococcus aureus 44%(n=44), Klebsiella 32%(n=32), Pseudomonas 8%(n=08), followed by MRSA (Methicillin-Resistant Staphylococcus Aureus) 5%(n=05), CNSA (Coagulase Negative Staphylococcus Aureus) 3%(n=03) MSSA (Methicillin Sensitive Staphylococcus Aureus) 3%(n=03), Acinetobacter 2%(n=02), E. coli 2%(n=02), Salmonella 1% (n=01) respectively (Figure 1).

Urine:
Among 926 urine samples only 23.32%(n=216) samples showed significant growth remaining 76.67%(n=710) samples were culture sterile. Most common isolated organisms were Escherichia coli 27.31%(n=259), Staphylococcus aureus 16.66%(n=136), Klebsiella spp. 16.66%(n=136), Pseudomonas spp. 10.18%(n=22), followed by Methicillin Resistant Staphylococcus Aureus (MRSA) 9.25%(n=20), Coagulase Negative Staphylococcus (CNSA) 9.25%(n=20), Methicillin Sensitive Staphylococcus aureus (MSSA) 2.31%(n=05), Acinetobacter spp. 1.85%(n=04), Citrobacter spp. 1.85%(n=04), Proteus spp. 1.38%(n=03). (Figure 1)

Resistance and Sensitivity Patterns
Pus and Body Fluids:
In this study, bacteria isolated from pus and body fluid samples showed resistance and sensitivity pattern as Amoxicillin + Clavulanic acid 58.60% & 41.39%(n=252 & 178), Co-trimoxazole 53.02% & 46.97%(n=228 & 202), Ciprofloxacin 51.16% & 48.85%(n=220 & 210), Ceftriaxone 48.85% & 51.16%(n=210 & 220), Cefotaxime 43.72% & 56.27%(n=188 & 212), Cefepime 42.79% & 57.20%(n=184 & 226) followed by Ceftazidime 31.16% & 68.85%(n=134 & 296), Piperacillin + Tazobactam 31.16% & 68.85%(n=134 & 296), Cefoperazone 16.74% & 83.25%(n=72 & 358), Amikacin 15.34% & 86.65%(n=66 & 364), Cefixime 12.55% & 87.44%(n=54 & 376), Levofloxacin 12.55% & 87.44%(n=54 & 376), Gentamicin 5.81% & 88.37%(n=27 & 26), Ceftazidime + Sulbactam 8.83% & 91.16%(n=54 & 376), Imipenem 5.11% & 94.88%(n=22 & 408), Vancomycin 2.79% & 97.20%(n=12 & 418) Linezolid 32.32% & 97.67%(n=10 & 420) respectively. No resistance seen with Ceftazidime + Clavulanic acid and sensitivity is 100%. (Figure 2)
Blood:
In this study bacteria isolated in blood samples showed resistance and sensitivity to Amoxicillin + Clavulanic acid: 60% & 40% (n=60 & 40), Cefoperazone: 54% & 46% (n=54 & 46), Cefepime: 52% & 48% (n=52 & 48), Cefotaxime: 40% & 60% (n=40 & 60), Ceftazidime: 32% & 68% (n=32 & 68), Ceftriaxone: 28% & 72% (n=28 & 72), Ciprofloxacin: 22% & 78% (n=22 & 78), Cotrimoxazole: 20% & 80% (n=20 & 80), Gentamicin: 20% & 80% (n=20 & 80), Piperacillin + Tazobactam: 18% & 82% (n=18 & 82), Amikacin: 16% & 84% (n=16 & 84), Levofoxacin: 16% & 84% (n=16 & 84), Azithromycin: 14% & 86% (n=14 & 86), followed by Cefixime: 12% & 82% (n=12 & 82), Vancomycin: 8% & 96% (N=08 & 96), Linezolid: 3% & 97% (N=3 & 97), Cefoperazone + Sulbactam: 2% & 98% (n=02 & 98), Imipenem: 1% & 99% (n=1 & 99) respectively and Ceftazidime + Clavulanic acid didn’t show any resistance. (Figure-3).
In this study, bacteria isolated from urine samples showed resistance & sensitivity to Nalidixic acid 82.87% & 17.21% (n=179 & 37), Norfloxacin 69.44% & 30.55% (n=150 & 66), Ceftriaxone 66.66% & 32.87% (n=145 & 71), Cefotaxime 61.11% & 38.87% (n=13 & 84), Amoxicillin+ Clavulanic acid 59.72% & 40.27% (n=129 & 87), Ceftazidime 53.24% & 46.75% (n=115 & 101), Nitrofurantoin 51.85% & 48.14% (n=112 & 48.14%), Cefixime 51.85% & 48.14% (n=112 & 104), Cefoperazone 49.50% & 50.46% (n=107 & 109), Co-trimoxazole 46.29% & 53.70% (n=100 & 106), Levofloxacin 46.29% & 53.70% (n=100 & 106), Ciprofloxacin 44.09% & 55.09% (n=97 & 119), Cefepime 27.77% & 72.22% (n=60 & 156), Amikacin 21.29% & 77.70% (n=48 & 168), Vancomycin 1.85% & 98.14% (n=4 & 212), Linezolid 1.38% & 98.61% (n=3 & 213), Ceftazidime + Clavulanic acid 0.92% & 99.07% (n=2 & 214), Imipenem 0.46% & 99.53% (n=1 & 21), No resistance is observed for Cefoperazone + Sulbactam (Figure 4).

Discussion:
Antibiotic resistance is one of the most common problems in the health care sector which is a challenging issue for healthcare professionals to combat infectious diseases and complications. This study is a retrospective observational study, collected data from microbiology department records from June 2019 to May 2020. The total number of samples collected was 2905. Tested samples were from Pus & Body fluids, Blood, and urine. Out of 2905 samples, only 25.67% (N=746) samples showed culture positivity which corresponds with studies conducted by Vijayalaxmi V. Mogasale et al. (19%), Revathy Saravanan et al. (12.5%).

Among 1347 Pus and Body fluids samples, only 31.9% (n=430) of culture positivity, remaining 68.07% (n=917) samples were culture negative. A study conducted by S. Ambwani et al. in pus samples showed 46.75% culture positivity. Another study conducted by Haritha Madigubba in sterile body fluids showed 29.9% culture positivity. The most common isolated organisms were Staphylococcus aureus 31.16% (n=134/430) which correlates with the study conducted by Perween N et al. Next most isolated organism is Klebsiella 23.02% (n=99), Pseudomonas 14.65% (n=63). Bacteria isolated from pus and body fluid samples were highly resistant to Amoxicillin + Clavulanic acid 58.60% and showed high sensitivity to Ceftazidime + Clavulanic acid (100%), Linezolid 97.67% (n=420), Vancomycin 97.20% (n=418). Imipenem 94.88% (n=408).

Among 632 blood samples, blood only 15.82% (n=100) samples showed significant growth, remaining 84.17% (n=532) samples didn’t show any growth. Most frequently, isolated bacteria were Staphylococcus aureus which is a Gram-positive bacteria. Among Gram-negative bacteria, the most frequent isolate was Klebsiella SPs, and Pseudomonas SPs. A Study conducted in Vijayawada, Andhra Pradesh by Dr. Tharangini Karicheti et al. and another study conducted in Ethiopia showed the same results. Isolated bacteria showed high resistance to Amoxicillin + Clavulanic acid.
Clavulanic acid 60% (n=60) and showed high sensitivity Ceftazidime + Clavulanic acid (100%), Imipenem 99% (n=99) Cefoperazone + Sulbactam 98% (n=98) Linezolid 97% (N=97). Bacteria isolated from blood, pus, and body fluid showed high Amoxicillin + Clavulanic acid resistance. A study conducted by K. V. Ramanath et al showed the same results.

Among 926 urine samples, only 23.32% (n=216) samples had shown significant growth remaining 76.67% (n=710) samples were culture negative. The most common isolated organisms were Escherichia coli 27.31% (n=59) which corresponds with a study conducted in Bangladesh by F. Tarannum Haque et al and in South India by Saligrama Chikkannasetty Somashekara et al. Next most commonly isolated organisms are Staphylococcus aureus 16.66% (n=36), Klebsiella spp. 16.66% (n=36). Bacteria isolated from urine samples showed high resistance to Nalidixic acid 82.87% (n=179), which is not used much in clinical practice.

Among frequently using antibiotics, uropathogens showed high resistance to Norfloxacin 69.44% (n=150) a study conducted in South India by Saligrama Chikkannasetty Somashekara et al. showed the same results. There is increased resistance to Fluoroquinolones and similar observations were reported from the studies from other parts of India. This may be due to the widespread use of fluoroquinolones as first-line empirical therapy for UTIs. Bacteria isolated from urine samples sensitive to Cefoperazone + Sulbactam (100%), Imipenem 99.53% (n=21) Ceftazidime + Clavulanic acid 99.07% (n=214), Linezolid 98.61% (n=213), Vancomycin 198.14% (n=212).

In this study after amoxicillin+ clavulanic acid, for 3rd generation, Cefalosporins bacteria showed a considerable amount of resistance. Considerable sensitivity is still retained to amikacin due to less use of these injectable antibiotics. Imipenem, Linezolid, Vancomycin-resistant bacteria and Ceftazidime+Clavulanic acid, Cefoperazone+Clavulanic acid-resistant bacteria also isolated, but very less number. This resistant pattern may be due to the inadvertent prescription of antibacterial drugs. But sensitivity to these drugs is very high.

Conclusion:-
In this retrospective observational study, among 2905 samples, only 746 (25.67%) samples showed significant growth. The most commonly isolated organisms were Staphylococcus aureus, Klebsiella, Pseudomonas from pus and body fluids and blood samples, Escherichia coli, Staphylococcus aureus, Klebsiella were the most common isolated organisms from Urine samples.

In this study, bacteria isolated from blood, pus, and body fluid samples showed more resistance to Amoxicillin + Clavulanic acid. Among bacteria isolated from urine samples showed more resistance to Fluoroquinolones like Norfloxacin and 3rd generation Cephalosporines like Ceftaxone, Cefotaxime. Parenterally used drugs like aminoglycosides (e.g. gentamicin and amikacin) and vancomycin have retained their sensitivity but bacteria also showed resistance to Imipenem, Vancomycin, new combinations like Cefoperazone + Sulbactam. From this study understood that organisms also developed resistance to even reserve group antibiotics (4th generation Cephalosporines, Linezolid).

Currently, we are in an antibiotic discovery void state, since 2007 there has been no new antibiotic intervention. So, it is essential to use antibiotics conservatively to prevent antibiotic resistance by following 4Ds (Right Drug, Right Dose, De-escalation to pathogen directed therapy, right Duration of therapy) and following antibiotic stewardship policies and culture sensitivity tests before prescribing. Every hospital should have an antibiotic policy. Regular antibiotic audits are needed. By following the above policies can prevent antimicrobial overuse, misuse, and abuse which helps to minimize the development of resistance at the hospital and community level. Not only do physicians, veterinary, and agricultural personnel also need to participate in preventing misuse of antibiotics also need to be controlled.

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There are no conflicts of interest.

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