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# ASSESSMENT OF SENSITIVITY PATTERN OF ANTIMICROBIALS PRESCRIBED IN ONCOLOGY DEPARTMENT OF A TERTIARY CARE HOSPITAL

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## ABSTRACT

**Background:** Antimicrobials are prescribed empirically and prophylactically without performing culture sensitivity tests. However, inappropriate prescribing pattern of antibiotics directs to increase in mortality, medical expenses and drug-resistant strains of bacteria. Antibiotic therapy on the initial use in febrile neutropenia episodes should be based on local bacterial susceptibility and sensitivity pattern to prevent failure of treatment with increased morbidity and mortality. This prospective study describes the antimicrobial sensitivity pattern of common organisms in isolates of clinical samples of oncology patients. **Objectives:** • To assess the antimicrobial sensitivity pattern of common organisms in clinical samples of neutropenic and non-neutropenic patients admitted in oncology department. **Method:** The proposed prospective study was conducted over 145 patients of Oncology department in Aster CMI hospital, Bangalore for duration of 6 months. **Result:** A total of 145 patients were included in the study. Out of 145, 82 patients were male and female consisted of 63 sample. 76.6% of the population was found to be non-neutropenic and 23.4% was neutropenic. Gram negative bacteria showed high resistance to ciprofloxacin and cefuroxime. Aminoglycosides like gentamycin exhibit resistance to gram positive bacteria. **Conclusion:** The data was collected to identify the resistance pattern of antimicrobials. Antibiotic therapy on the initial

use in febrile neutropenia episodes should be based on local bacterial susceptibility and sensitivity pattern to prevent failure of treatment with increased morbidity and mortality.

**KEYWORDS:** Neutropenia, non-neutropenia, cancer.

## INTRODUCTION

Cancer increases a patient's threat of having serious infection. In spite of many advances made in most cancer treatments, infections continue to be a main reason of morbidity and mortality in oncology patients.[1] The risk factors for getting infections include catheterization [long term], stem cell transplantation and neutropenia.[2]

Neutropenia is expounded as the value of ANC less than 500 cells/mm3. Mild neutropenia is decided as ANC of much less than 1500 cells/mm3. A value less than 1,000 cells/mm3 is considered as average. ANC below 500 cells/mm3 is considered as severe neutropenia.[3]

Antimicrobials are prescribed empirically and prophylactically without performing culture sensitivity tests in most of the cases. Resistance towards most of the antimicrobials is one amongst the rising problems especially among the ICU patients, CCU patients etc. Both Gram negative and Gram-positive microbes have obtained resistance to many of the antibiotics and is a one of the major causes of HAI (hospital acquired infections). ICU commonly faces antimicrobial resistant bacteria due to overuse of broad-spectrum antibiotics, paucity of supporting staff and increased crowding of patient in a small region of hospital, prolonged hospitalization and economic pressure.[4] Bacterial infection is a type of customary complication noticed in patients diagnosed with haematological malignancy, mainly neutropenic patients. 5% to 11% increase in mortality rate is seen in patients with neutropenia. Timely administration of suitable antimicrobial therapy is crucial for easy management of bacterial infections in neutropenic patients. However, unnecessary prescribing pattern of antibiotics directs to increase in mortality, medical expenses and strain that yields resistance to bacteria.[5]

Hospitalisation with febrile or non-febrile neutropenia conduct to major economic and social burden for the patient as well as hospitals. Various international organisation such as Infectious Disease Society of America and European Conference on Infection in leukaemia has established algorithmic approaches for neutropenic and fever and infection prophylaxis.

Antibiotic sensitivity pattern governs the 1st line antibiotics prescribed among these ill patients, even if these guidelines provide empirical choices.[6]

**CAUSES OF ANTIMICROBIAL RESISTANCE:**

- Inappropriate prescribing

Erroneously prescribed antibiotics leads to increase in bacterial resistance. Studies have revealed that choice of antimicrobial and antibiotic therapy duration is inappropriate in about thirty to sixty reports.[7] In reckoning, 30% to 75% of the antibiotics prescribed in ICUs have been based to be, inappropriate and suboptimal.[8] Alterations to first line empirical therapy given to patients who are at a greater risk of acquiring antibiotic resistant organisms, especially if the patient feels instability and the patient which gives positive culture results in blood. These consist of Gram-negative bacteria, and carbapenems -producing organisms.[7]

- Overuse of antibiotics

The antibiotic overuse can lead to the era of resistance. Researches have claimed a strong relationship between antibiotic consumption and the emergence and spreading of organisms. The horizontal gene transfer (HGT) can reinforce antibiotic resistance to pass on against rare species of bacteria. Antibiotics dispose drug-sensitive participants, leaving behind resistant bacteria to reproduce. Despite of warnings regarding overuse, antibiotics are still over-prescribed throughout the world.

Empiric antibiotic therapy must be carried out immediately in all febrile neutropenic patients. Cefepime, Meropenem, Imipenem and Piperacillin-tazobactam have been validated to be optimistic as mono therapy. Non β-lactam alternatives.

- Clindamycin + ciprofloxacin
- vancomycin + aztreonam

Addition of an aminoglycoside like gentamicin or vancomycin is better, if the patient shows hemodynamic instability.[9]

- Lack of new antibiotic being developed

There is a lack of antibiotic development, as people no longer consider it as an economically sensible funding for the pharmaceutical industry. Antibiotics, to a extent are mostly given for less duration and are often curable. Prophylaxis to cowl the duration of neutropenia may also be regarded as the first cycle of treatment in patients who are diagnosed with solid tumours or lymphoma who regularly receives regimens that purpose extreme neutropenia.[7] Excessive

confined levels of resistance to Fluoroquinolones caused by Clostridium difficile and related to fluoroquinolones have a instantaneous reconsideration of this policy. Lack of economic appeal of low cost of antibiotics is another component that causes antibiotic development. The availability, ease of use, and typically low price of antibiotics has additionally triggered to understand about low fee amongst payers and the citizens.[10]

WAYS TO SLOW DOWN ANTIBIOTIC RESISTANCE.

- INDIVIDUAL

Antibiotics should only be prescribed by a licensed medical professional.[10] If you have started antibiotic therapy, you should complete the course duration even if you start getting healthier, due to the fact "stopping remedy early promotes the increase of drug-resistant bacteria" [11]

- HEALTHCARE PROFFESSIONALS

Unnecessary prescribing and dispensing of antibiotics unless you have made all efforts to check which antimicrobial the patient needs to have. It is assumed that in half of antimicrobials prescribed are for infection caused by viruses. More ways to reduce or stop infections is by monitoring your hands, instruments are clean, and using vaccines were used appropriately.[11]

- Improve global surveillance of drug resistance and microbial consumption

Improve international observation for drug resistance and microbial usage for researchers and doctors to eliminate the mechanisms of obtaining resistance, display and assessing the instances that exists and to expect future complications. For these surveillance 3 areas require better information.

1. resistance rates for the available drugs.
2. antibiotic consumption in the population
3. research information on the molecular structure of Anti-microbial resistance [13]

- PREVENTION OF INFECTION

Hand hygiene is the main preventative measure. Hematopoietic HSCT patients should be in HEPA filtered rooms, and should evade contact to phytogeography.[14]

Nosocomial infections amongst the most common type infections acquired by patients which are life threatening.[15] The optimal selection, dose of antibiotics duration, and would help in

slowing down the emergence of resistance within organism during antimicrobial stewardship. Driven factor of concern is the antimicrobial usage in developing resistance.[15] Proper monitoring and implementation of antimicrobial use and sensitivity pattern examines in having a control on resistance. Inborn contributing factors like amplification of genes point mutation, and superficial factors like horizontal transfer of resistant genes within and Integrins and across species by transposons in bacteria etc, led to concerns for the resistance development.[17] According to WHO irrational and inappropriate use of antibiotics in humans and animals for non-therapeutic and therapeutic purposes have also posed a cause of antibiotic resistance in community and hospital acquired conditions.[16]

Gram-negative bacteria as in, A. baumannii, E. coli, Pseudomonas Aeruginosa and K. pneumoniae were main microorganisms seen in neutropenic patients A large percentage of ESBL-generating Enterobacteriaceae, P. aeruginosa, and Acinetobacter baumannii from neutropenic patients were segregated. Hence, empirical antibiotic therapy for neutropenic patients should address as early from these Gram-negative pathogens.

Among non-neutropenic patients, GPB (Enterococcus faecalis, Staphylococcus aureus) were the most often isolated organisms. Prevention of the development and spreading of resistant microorganisms will lessen the unfavourable events. [5] To bring down AM resistance, usage regulation is vital. Continuous checking of AMs and evaluating the sensitivity patterns are obligatory.[18]

## METHODOLOGY

### Study Site

The proposed study was conducted in Department of Oncology at Aster CMI hospital, Hebbal, Bangalore, Karnataka.

### Study design

Retrospective cohort study.

### Study duration

6 months.

### Sample size

As per the department of Oncology, Aster CMI Hospital Hebbal, Bengaluru, sample size is 145 patients.

**Study criteria**

**Inclusion criteria**

• Neutropenic or non-neutropenic patients admitted in Oncology department were included in our study.

**Exclusion criteria**

• Outpatients.

• Day care patients

• Covid patients

• Pregnant women

**Study procedure/ methodology**

The study was approved by the institutional human ethics committee KLE COP, Bengaluru. Patients which satisfied the inclusion requirements were enrolled in the study. The information such as demographic, medication, clinical data and antibiotic culture and sensitivity reports are obtained and documented in specially created patient data collection form. The sensitivity pattern and drug resistance of antibiotics prescribed will be analysed. Prescription pattern of antimicrobials is analysed and compared with the local guidelines of Aster CMI hospital. These guidelines are extracted from the NHS guidelines.

**RESULTS**

To assess sensitivity pattern of antimicrobials prescribed in the oncology department, our study was carried out for span of five to six months in a tertiary care hospital. In total 145 patients data was collected and analyzed and observations are as follows:

**Table 1: Gender Distribution.**

| S. No | GENDER | FREQUENCY (N = 145) n (%) |
|---|---|---|
| 1 | MALE | 82 (58) |
| 2 | FEMALE | 63(42) |

**AGE DISTRIBUTION**

In this study, 145 patients' record was obtained and analyzed. Out of 145 patients, 20 were <40 years of age and 125 were above 40 years of age.

**TABLE 2: Age group distribution among males and females.**

| *AGE GROUP IN YEARS* | *MALE* | *FEMALE* | *TOTAL* |
|---|---|---|---|
| ***11-20*** | 2 | 1 | **3** |
| ***21-30*** | 5 | 5 | **10** |
| ***31-40*** | 4 | 3 | **7** |
| ***41-50*** | 9 | 14 | **23** |
| ***51-60*** | 22 | 14 | **36** |
| ***61-70*** | 23 | 19 | **42** |
| ***71-80*** | 14 | 6 | **20** |
| ***81-90*** | 3 | 1 | **4** |
| ***TOTAL*** | | | **145** |

**NEUTROPENIC STATUS**

Out of the total study population, 76.6% was found to be non-neutropenic and 23.4% was neutropenic.

**Table 3: Neutropenic status.**

| Neutropenic status | N | % |
|---|---|---|
| **Neutropenic** | 34 | 23 |
| **Non-neutropenic** | 111 | 77 |

**Figure 3: Neutropenic status.**

**COMMONLY PRESCRIBED DRUG CLASS**

**TABLE 4: Commonly Prescribed Drug Class.**

| DRUG CLASS | NO OF DRUGS |
|---|---|
| **PENICILLINS** | 9(36%) |
| **CEPHALOSPORINS** | 8(32%) |
| **CARBAPENEM** | 4(16%) |
| **FLUOROQUINOLONES** | 2(8%) |
| **ECHINOCANDINS** | 2(8%) |

Pencillin(9) and cephalosporins(8) are the commonly prescribed drug class.

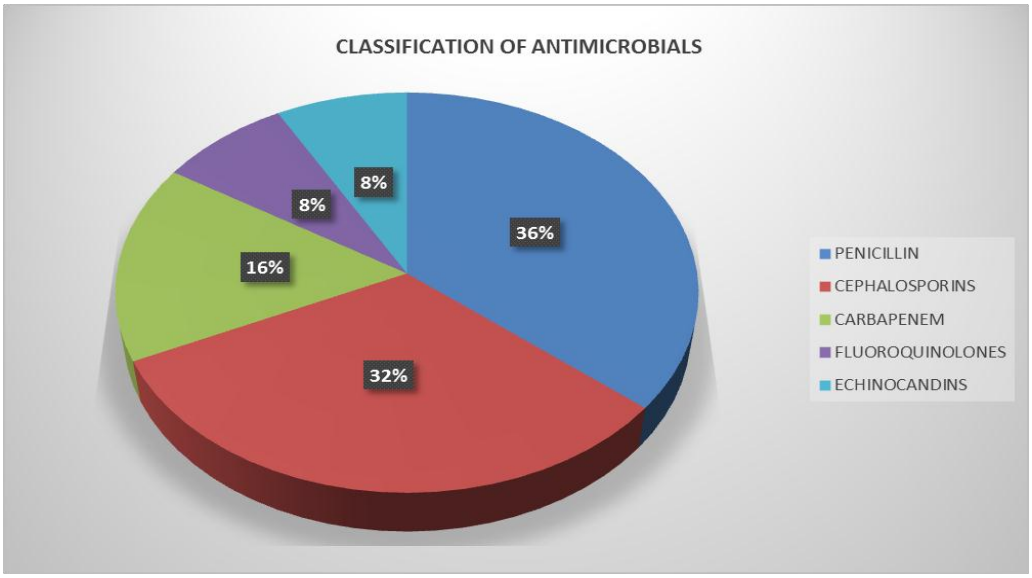


**FIGURE 4: Classification of antimicrobials.**

## ANTIMICROBIAL RESISTANCE PATTERN

High resistance was observed among total gram-negative bacteria, to ciprofloxacin (42) and Cefuroxime (39). Similarly high resistance rates to gentamycin were observed among gram positive organisms.

**Table 5: Antimicrobial resistance pattern of GNB.**

| ANTIMICROBIAL | E. aerogenes (n=31) | ECL (n=6) | E. coli (n=115) | K. pneumoniae (n=2) | K. pneumonia ssp (n=39) | P. mirabilis (n=3) | Proteus spp (n=-3) | P. aeruginosa (n=6) | Salmonella spp (n=2) | TOTAL |
|---|---|---|---|---|---|---|---|---|---|---|
| **CIPROFLOXACIN** | 5(11.9) | | 28(66.6) | | 5(11.9) | 1(2.3) | 1(2.3) | 2(2.3) | | 42 |
| **GENTAMYCIN** | 2(11.1) | | 7(38.8) | | 5(27.7) | 1(5.5) | | 2(11.1) | 1(5.5) | 18 |
| **TRIMETHOPRIM/ SULFAMETHOXAZOLE** | 4 (15.3) | | 16(61.5) | | 5(19.2) | 1(3.8) | | | | 26 |
| **PIPERACILLIN** | 3(30) | 1(10) | 3(30) | | 3(30) | | | | | 10 |
| **AMIKACIN** | | | 3(50) | | 3(50) | | | | | 6 |
| **CEFTRIAXONE** | 3(9.6) | 1(3.2) | 21(67.7) | 1(3.2) | 5(16.1) | | | | | 31 |
| **CEFUROXIME** | 5 (12.8) | 2(5.1) | 21(53.8) | 1(2.5) | 6(15.3) | | 1(2.5) | 2(5.1) | 1(2.5) | 39 |
| **AMOXICILLIN/CLAVULANIC ACID** | 5 (25) | 2(10) | 9(45) | | 3(15) | | 1(5) | | | 20 |
| **MEROPENEM** | 2(22.2) | | 4(44.4) | | 3(33.3) | | | | | 9 |
| **CEFOPERAZONE** | 2 (25) | | 3(37.5) | | 3(37.5) | | | | | 8 |

**TABLE 6: Antimicrobial resistance pattern of GPB.**

| ANTIMICROBIAL | S. aureus (n=8 | E. faecalis (n=1) | TOTAL |
|---|---|---|---|
| CIPROFLOXACIN | 3(75) | 1(25) | 4 |
| GENTAMYCIN | 3(100) | | 3 |
| AMOXICILLIN/CLAVULANIC ACID | 2(100) | | 2 |

**PROPORTION OF BACTERIAL GROWTH**

**TABLE 7: Bacterial isolates obtained from different culture samples.**

| Sample | n(51) | % |
|---|---|---|
| Blood | 21 | 47 |
| Pus | 5 | 14 |
| Urine | 14 | 24 |
| Body fluids | 4 | 8 |
| Bronchio alveolar lavage | 2 | 4 |
| Foley's tip | 1 | 2 |
| Peri anal abscess | 1 | 2 |

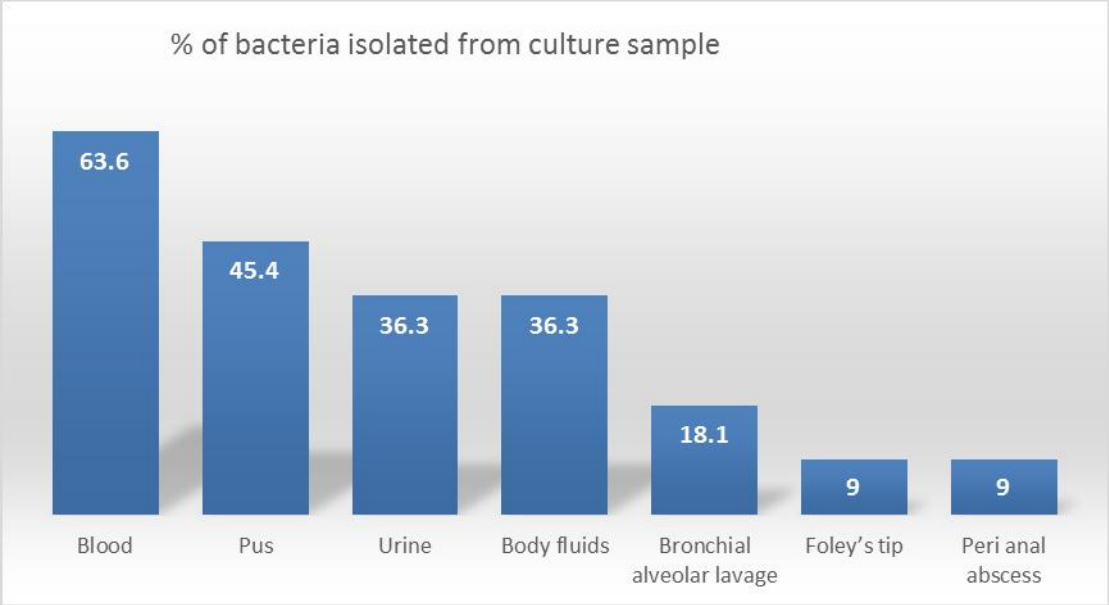


**FIGURE 5: bacterial isolates from different culture samples.**

**PRESCRIBED FORM OF DRUG**

The number of antimicrobial agents prescribed in generic name (13.6%) were comparatively less than brand name (86.4%).

**Table 8: Prescribed Form of Drug.**

| PRESCRIBED FORM OF DRUG | FREQUENCY (n=37) | PERCENTAGE |
|---|---|---|
| Brand Name | 32 | 86.4% |
| Generic Name | 5 | 13.6% |

**FIGURE 6: PRESCRIBED FORM OF DRUG**

**MDR**

We found out that the prevalence of MDR was 21, while 12 bacterial isolates were resistant to quinolones, aminoglycosides, di amino pyrimidines, beta lactams.

**Table 9: Multiple drug resistance pattern.**

| | A0 | A1 | A2 | A3 | A4 | MDR |
|---|---|---|---|---|---|---|
| **E. aerogenes** | 0 | | | | 4(33.33) | 4(19.04) |
| **ECL** | 3(18.75) | 1(33.33) | | | | 0 |
| **E. coli** | 0 | | | | 4(33.33) | 4(19.04) |
| **K. pneumoniae** | 3(18.75) | 1(33.33) | | | | 0 |
| **K. pneumonia ssp** | 0 | | | | 4(33.33) | 4(19.04) |
| **P. mirabilis** | 1(6.25) | | | 3(33.33) | | 3(14.28) |
| **Proteus spp** | 2(12.5) | | 2(50) | | | 0 |
| **P. aeruginosa** | 1(6.25) | | | 3(33.33) | | 3(14.28) |
| **S. aureus** | 1(6.25) | | | 3(33.33) | | 3(14.28) |
| **E. faecalis** | 3(18.75) | 1(33.33) | | | | 0 |
| **Salmonella spp** | 2(12.5) | | 2(50) | | | 0 |
| **Total** | 16 | 3 | 4 | 9 | 12 | 21(47.7) |

**Note: A0: Sensitive to every class of antibiotics; A1: Resistant to I class of antibiotic;A2: Resistant to II classes of antibiotic;A3: Resistant to III classes of antibiotic;A4: Resistant to IV classes of antibiotic.**

**DISCUSSION**

The sensitivity pattern of antimicrobials prescribed in the oncology department was assessed in the study period. A total of 145 patients culture sensitivity report and the drug chart was analysed.

Among 145 patients 58% were males and 42% were females. Out of the total study population of 145 patients, 34 (23.4%) of the patients were neutropenic and 111(76.6%) were non-neutropenic.

Out of the 145 patients selected for the study, 48 (33.1%) of the bacterial culture was positive. Our calculation was similar to a prospective study conducted in iran. This finding was low when compared with studies conducted. The alteration was due to the differences in geographical locations. Sensitive blood culture system use can increase culture positivity rate.[18] Out of 48 culture positive cases 21 (43.7%), 14(29.1%), 5(10.4%) bacteria were isolated from blood, urine and pus respectively. Other culture includes body fluid-4 (8.6%),

bronchoalveolar lavage- 2(4.16%), foley tip-1(2.08%) and stool-1 (2.08). Our study was comparable to the retrospective study carried out by Mahendrakumar B J which shows that majority of the patients had growth in blood culture.[19] Blood stream infection was higher which is probably due to higher patients had absolute neutrophil count (ANC) <100. Among all the isolates the predominant isolates in our study were Escherichia coli 20(41.6%) followed by Klebsiella pneumonia ssp pneumoniae 6 (12.5%). Infection risk associated with Multi drug resistant bacteria has been related to a plethora of factors including antimicrobial therapy, cross transmission and length of stay in hospital, conducted by Cornejo. P. et.al.

In our study GNB was found dominant to GPB. Gram-negative organism attributed to 62.5% of total organism and the remaining organism were gram positive (25%) and fungal pathogen (12.5%). Our finding was in line with the studies conducted by Africa, which stated that GNB was the most predominant isolates from cancer patients and current values alerts the re occurrence of GNB cancer patients along with neutropenia.[18] Amongst the gram-negative organisms, E. coli has been consistently the most commonly isolated organism, followed by Klebsiella pneumonia ssp pneumoniae. Similarly in the gram-positive bacteraemia group, Enterobacter aerogenes continue to represent the majority of isolates. On the other hand, there were two episodes of fungal pathogen were also identified.

The number of antimicrobial agents prescribed in generic name (13.6) was less than brand name (86.4) The rate of gram-negative bacteria in febrile neutropenic patients was 75%. Generally, the result obtained from this study is similar to recent reports that demonstrated the re-emergence of gram- negative bacteria as the main cause of infection. However, in contrast with our data Nejad et.al reported that majority (66%) of isolated bacteria was gram positive.[18] Determination of AM susceptibility profile of bacterial isolates in neutropenia can be beneficial in selecting the proper antimicrobial agents.[20] In the current study, species of Staphylococcus aureus and Staphylococcus epidermidis were isolated from blood culture with a frequency of 2.08 and 4.16 respectively. Echerichia coli was the main isolated organism from both the non-neutropenic and neutropenic patients.

Although the increase in number of MDR is a common phenomenon, a high increase in number of immunocompromised conditions like cancer, increases multi resistance to drugs. The overall count of multi drug resistance was 21 (47.7%) which was comparatevely lower than a study conducted by safdar et.al.[19] Among the bacteria which was isolated, escherichia coli and enterobacter aerugens were the principal MDR strains found.

Second generation cephalosporins, third generation cephalosporins and fluoroquinolones are characterized by high resistance to gram negative organisms, whereas fluroquinolones have shown high resistance to gram positive organisms. Adverse effects in febrile neutropenia are a serios complication in chemotherapy in cancer patients. Antibiotic therapy on the initial use in febrile neutropenia episodes should be based on local bacterial susceptibility and sensitivity pattern to prevent failure of treatment with increased morbidity and mortality.

## CONCLUSION

In the current clinical setting, DAPT is most preferred in ACS patients who underwent PTCA with lesser incidence of complications in comparison with monotherapy and triple therapy. In DAPT, occurrence of MI, CHF and unstable angina were comparatively less in Aspirin-Ticagrelor combination with reduced dyspnea and bleeding events. The study concluded that Aspirin-Ticagrelor combination is the safest and better therapeutic option with minimum cardiovascular events.

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