CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.1117312

Available online at: http://www.iajps.com Research Article

A PROSPECTIVE OBSERVATIONAL STUDY ON EMPIRICAL ANTIMICROBIAL USE IN MEDICAL INTENSIVE CARE UNIT

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Abstract:
Empirical treatment is given without knowledge of the cause or nature of the disease and based on experience rather than logic. Bacterial resistance to antibiotics create a challenge for clinicians when treating a patient with infection and thereby empirical antimicrobial therapy is important as it decreases the emerging resistance and reduce the economic burden to society. This study was done among 75 patients for 2 months to analyse the empirical antimicrobials used in the medical intensive care unit. It was found from the study that lungs was the major site of infection and E.coli was the most grown microorganism in the culture. In the treatment with empirical antimicrobials, azithromycin was the most common antibiotic used among the patients and there was no change in the treatment pattern after obtaining the culture results.

Key words: *Empirical Antimicrobials, Medical Intensive Care Unit, Escalation, De-escalation, Culture*

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Please cite this article in press as Alwin Jose et al., ***A Prospective Observational Study on Empirical Antimicrobial Use in Medical Intensive Care Unit****, Indo Am. J. P. Sci, 2017; 4(12).*

INTRODUCTION:

The empirical antimicrobial therapy is intended to cover the multiple possible pathogens that are associated with the specific clinical syndrome [1]. The adequate initial therapy has a protective effect for critically ill patients which will significantly lower the mortality rate [2]. Optimal antibiotic use is crucial in the hospital settings as there is increased antibiotic resistance and lack of new antimicrobial development. Use of antibiotics in Medical Intensive Care Units (MICUs) settings are difficult for various reasons like severity of infections, withdrawing or postponing antibiotics, disease- long continuity and lack of expertise [3]. While selecting an empirical antimicrobial therapy, several factors must be considered such as site of infection and organism most likely to colonize that site, prior knowledge of bacteria and the local bacterial resistance that can occur. Empirical antibiotics are typically broad-spectrum, in that they treat both a multitude of either gram positive or gram-negative bacteria. When more information is known, treatment may be changed to a narrow spectrum antibiotic which more specifically targets the bacterium known to be causing disease [3].

In some cases, urgency dictates empirical treatment, when a dangerous infection by an unknown organism is treated with a broad-spectrum antibiotic while the bacterial culture and other tests are awaited [1]. The timing of initial therapy is based on the urgency of situation or condition of the patients. In some circumstances, for those with septic shock or febrile neutropenia with bacterial meningitis, empiric therapy should be initiated immediately, this premature initiation of antimicrobial therapy will supress the bacterial growth and it gives an opportunity to establish a microbiological diagnosis which is important in the management of such patients. Obtaining cultures before antibiotic use improves the chances of identifying the offending microorganism which improves patient care. Empiric therapy is most often used when antibiotics are given to a person before the specific bacterium causing an infection is known. Fighting an infection sooner rather than later is important to minimize morbidity, risk and complications. As soon as the microbiology results are arrived, the therapy should be changed to the specific antibiotic spectrum in order to reduce the cost, toxicity and emergence of resistance. The identification of organism plays a major role as it will influence diagnosis, therapy and prognosis. This will be benefited by providing appropriate and definitive treatment and also by controlling the emergence of antimicrobial resistance. [2] Prompt selection of empirical antimicrobial therapy for positive blood culture is a complex and difficult decision. Appropriate evaluation and correct treatment regimen are of paramount importance as there is high morbidity and mortality rate associated with bacteraemia. Once an organism has been fully identified, the antimicrobial selection can be modified [4]. In this study, the empirical antimicrobial use in MICU and their escalation and de-escalation pattern were analysed. The types of antimicrobials used, empirical treatment given and its appropriateness were also evaluated.

METHODOLOGY:

A prospective observational study was done on the empirical use of antimicrobials in a medical intensive care unit of a tertiary care hospital. This study was done among 75 patients for 2 months. Patients who were directly admitted in medical ICU receiving antimicrobials for 3 or more than 3 days were included. Patients who came from wards to MICU, those have undergone total knee or hip replacement surgeries and those who were admitted for less than 3 days were not considered in this study.

RESULTS AND DISCUSSION:

During this study period, a total of 75 patients were admitted in Medical ICU. In these 48 patients were males and 27 were females. Taking appropriate cultures before starting antimicrobial therapy plays an important role in patient care. This will provide more appropriate and definitive treatment, and also helps to control the raising of antibiotic resistance by reducing the use of broad-spectrum antimicrobials. It will also improve the chances of identifying the causative microorganism. If the cultures are obtained after starting the antimicrobial therapy, it may give unconvincing reports as the organisms may not grow after exposure to the antimicrobials. In this study, 87% of cases had their culture sent before starting antimicrobials and only 13% of them did not have sent it. This compliance is due to the restrictive antimicrobial policy of the hospital and tracking the patients and auditing for the same on daily basis by the clinical pharmacist who play a major role in identifying appropriate antimicrobial for a particular patient and reason to start or stop the same respectively [5]. In some cases like chemo patients, dialysis patients clinical diagnosis is enough to start antimicrobial therapy and the culture will not be sent before starting antibiotics. Identifying the site of infection plays a major role in empirical antimicrobial therapy. It also highlights which antimicrobials should be used for a specific infection site. [1] The subjects were classified according to the site of infection. Here, out of 75 patients, 44 patients (47%) have the lung related infections, 21 patients (23 %) came with genitourinary infections followed by 9 % of subjects (n=8) had intra-abdominal infections. The infections on other sites were comparatively less. Remaining 8 % (n=7) of infections were related to kidney, 4% (n=4) infections were related to surgical sites, 2% (n=2) infections occurred in CNS, Pleural, skin, and blood stream.

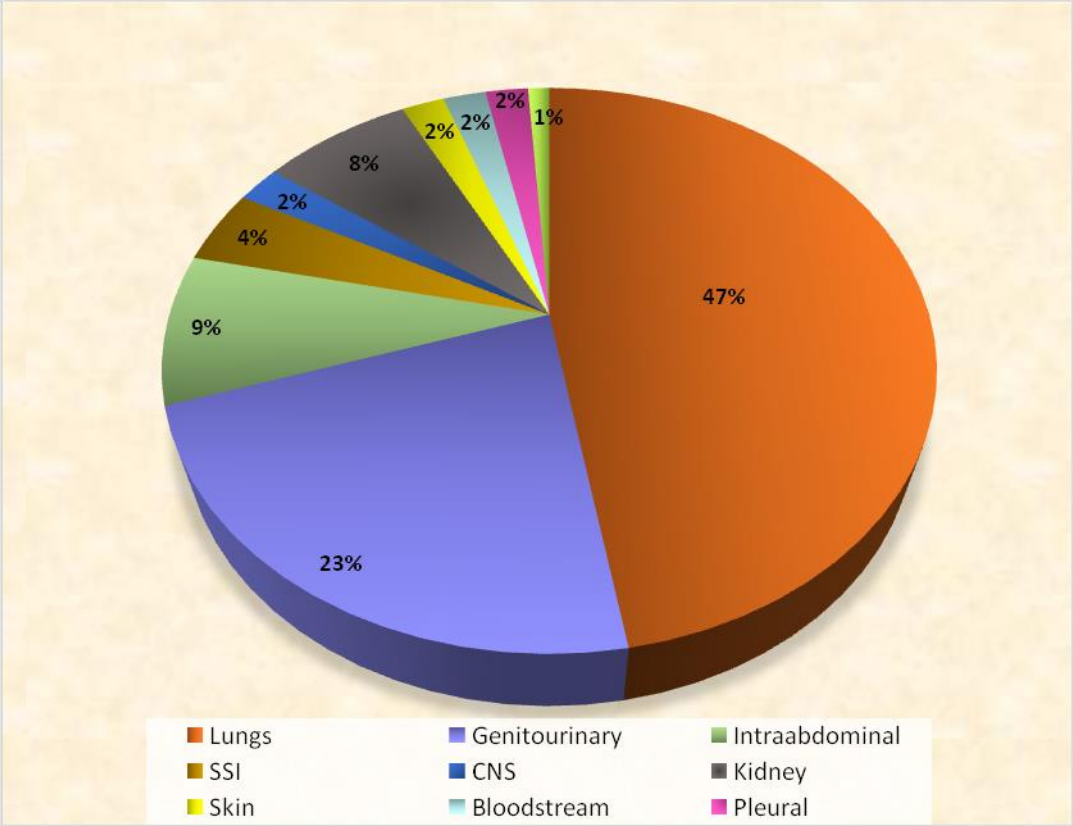

Fig No.1: DISTRIBUTION OF PATIENTS BASED ON THE SITE OF INFECTION

The most commonly used antibiotics for empirical antimicrobial therapy were Azithromycin (n=38) which is a macrolide antibiotic and an extended spectrum antibiotic, Piperacillin/ Tazobactum (n=33). Meropenem (n=26) which is a carbapenem is the next highly used antimicrobial agent in Medical ICU. Ceftriaxone (n=12) which is a cephalosporin antibiotic and Metronidazole which is an nitroimidazole antimicrobial agent were used less when compared to the above antibiotics. All other antimicrobials were used in lesser amount in Medical ICU. Starting of Azithromycin at the earliest signs of a respiratory tract infection was effective in reducing the risk of experiencing progression to severe respiratory tract infections. [6] Piperacillin/Tazobactum was usually started as empirical treatment because of its broader coverage on both gram positive and gram-negative organisms. As the infection, clinical symptoms or infected site doesn't give a clear idea about possible type of organism infecting it, giving a broader spectrum can help reduce the severity of the same. [7] Piperacillin/Tazobactum and Meropenem, exhibit similar action but, chances of resistance to beta-lactamase is more and hence escalation to Meropenem becomes a necessity. Patients with persisting infection, worsening clinical symptoms and long stay in ICU were escalated to or given with Meropenem in view of a Multi Drug Resistant infection (MDR). This was tracked based on laboratory parameters, clinical prognosis and no improvement with the current treatment given. Meropenem being a higher end antibiotic, gives a better coverage for severe and life-threatening infections and also for MDR infections and patients having history of the same. Use of Meropenem is high in ICU like areas because of the critical conditions, where patients are chronically ill or are severely infected. [8],[9]

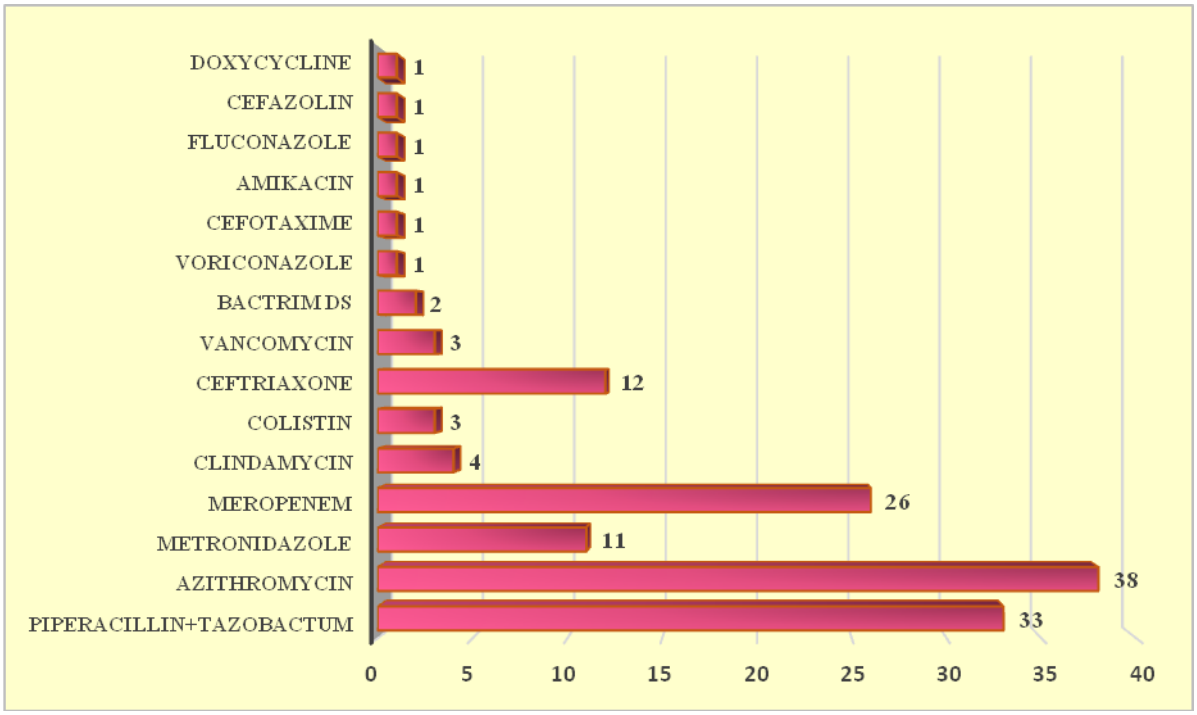

Fig No. 2: DISTRIBUTION OF PATIENTS BASED ON THE TYPE OF DRUGS

The below graph shows the escalation and de-escalation done after receiving the culture reports. Out of 75 subjects, 53 do not have any change in their treatment. In 14 patients, the treatment got escalated to a higher antimicrobial and in 8 cases, the antimicrobial got de-escalated. Escalation to a higher antibiotic depends on the type of culture being isolated and severity of infection. Main reason for escalation after culture reports was multi drug infections in which the usual treatment is not effective and patient shows a resistance to the treatment. Patients who got better and showed a progress in their clinical prognosis and culture reports negative were de-escalated from higher antibiotics. Within the sample size, most of the patients did not undergo any change in their treatment because they were showing improvement with the given treatment.

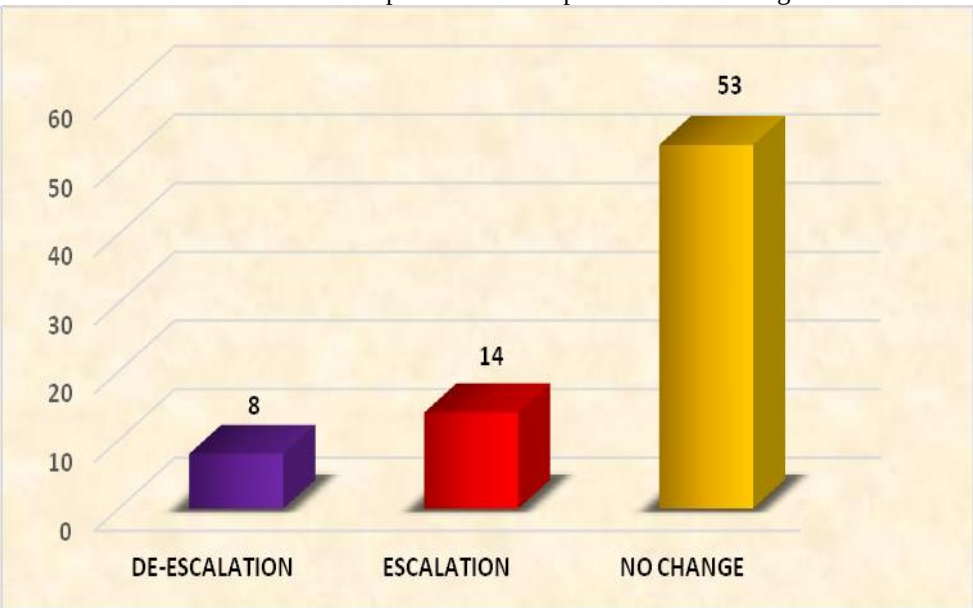

Fig No.3: DISTRIBUTION OF PATIENTS BASED ON ESCALATIONS AND DE-ESCALATIONS

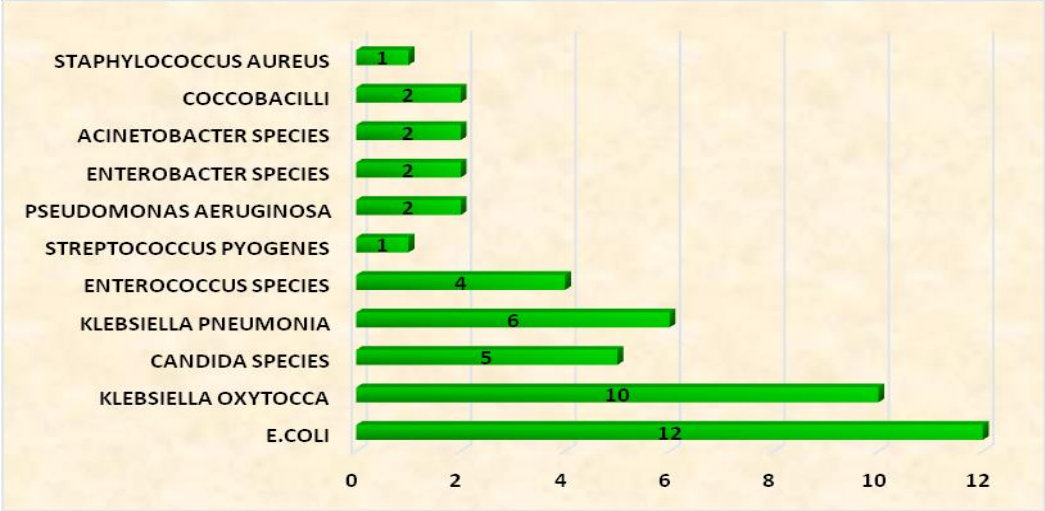

Fig No.4: DISTRIBUTION BASED ON ORGANISM PRESENT IN CULTURE

Identifying the causative organism helps us to choose the appropriate antimicrobial therapy for the patient. It switches the antimicrobials from broad-spectrum to a narrow spectrum and reduces the chance of developing the antimicrobial resistance. From the graph we can understand that Escherichia coli (n=12) was the most grown microorganism in cultures followed by Klebsiella oxytoca (n=10), both are gram negative microorganisms. Compared to other microorganisms, Klebsiella pneumoniae (n=6) and Candida species (n=5) showed significant growth.

The graph shows the distribution of patients based on the type of the patients admitted in hospital. From the graph, it is clear that 47% (n=35) patients were of Type 3 and 42% (n=32) patients were Type 2. Comparing to Type 3 and Type 2, Type 1 (3%, n=2) and Type 4 (8%, n=6) patients were very less.

Type 1 patients - Those who have no contact with health care system for the past 90 days, no prior antibiotic treatment during last 90 days, Patient young with no or few co-morbid conditions.

Type 2 patients - This type of patients have contact with health care system (e.g. Recent hospital admission, nursing home, dialysis) without invasive procedure, Recent antibiotic therapy in last 3 months, Patients old (> 65 years) with few co-morbidities.

Type 3 patients - Patients hospitalized for more than 5-7 days and infection following major invasive procedures, Recent antibiotic therapies, Patient old (> 65 years) + multiple co-morbidities (e.g. structural lung disease, immunodeficiency).

Type 4 patients – Type 3 patients with fever despite antibiotic therapy more than 5 days with no obvious source/ after appropriate source control, Patients with severe sepsis/ septic shock, One of the following (but not limited to) risk factors for invasive fungal infections: TPN, Haemodialysis, Immunodeficiency of variable origin, Major abdominal surgery, Multi-focal candida colonization, Diabetes.

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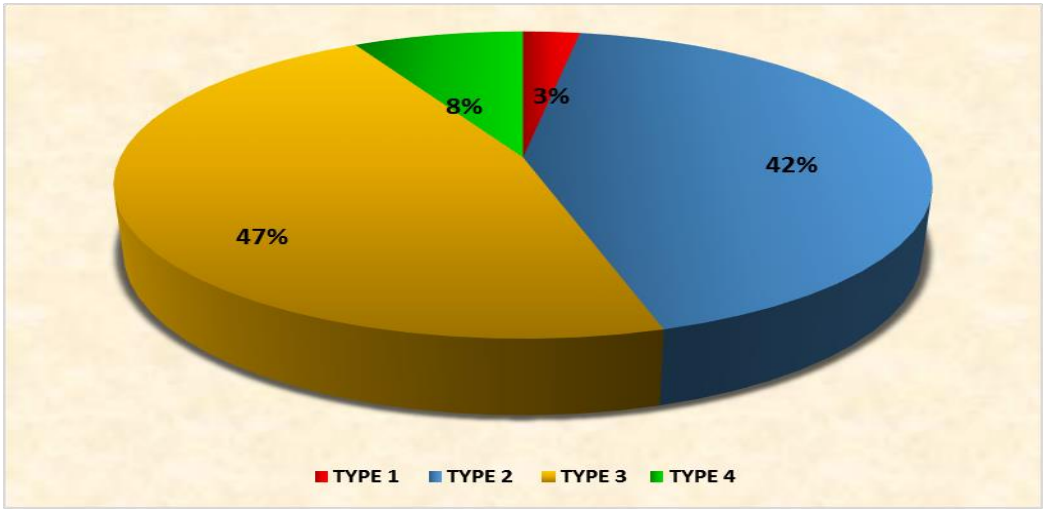

Fig No.5: DISTRIBUTION BASED ON TYPE OF PATIENTS

CONCLUSION:

Prescribing an empirical treatment in any suspected infection plays an important role in the pharmacotherapy. In severe infections without knowing the cause and the causative organism, empirical management often helps in reducing the worsening of patient condition. In present study, it was seen that, in the Medical ICU, the major site of infection were lungs and genitourinary and E.coli was the common microorganism present in the culture. Based on the site of infection, Azithromycin was maximally used for the patients. Piperacillin/ Tazobactum and Meropenem were observed to be given as broad spectrum antibiotics in patients with worsening infections and MDR infections as they have similar spectrum of activity. Escalations from Piperacillin/ Tazobactum to Meropenem were carried out after the culture reports and specific sensitivity tests. A better compliance was seen in obtaining cultures before starting a definitive antimicrobial treatment.

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