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A Study on Prescribing Pattern of Antimicrobial Agents Used in Treating Sepsis

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ABSTRACT

Sepsis is defined as life threatening systemic or local infection due to dysregulated host response, which can lead to organ or tissue damage or death. Hence it is necessary to monitor the disease. Due to lack of data on prescription patterns, it is essential to conduct such studies. To analyze prescribing patterns of Antimicrobial agents used in treating sepsis.: It was a Prospective and Observational study which was conducted for a period of 6 months in all the departments of Apollo multi-specialty hospital. All the patients admitted with sepsis during the study period were screened for the use of any Antimicrobials. Those who met the inclusion and exclusion criteria, were enrolled for the study. Therapeutic data such as name of drugs, doses, route of administration, duration & other laboratory data was collected and documented in a suitably designed data collection form. The Data was evaluated by using suitable statistical tools. Out of 146 patients, 95 patients (28.28%) were prescribed with Carbapenem. In this study, blood was majorly used as specimen. The commonly found causative organism was E.coli in 50 patients (32.17%) which largely effected females than males. Meropenem was found to be the major drug sensitive to E.coli. Septic shock and death were the major complications found. Health care professionals must understand the usage of antimicrobial agents for specific conditions in sepsis patients so as to minimize adverse drug reactions, complications, antimicrobial agent resistance and improve patient quality of life. The number of antimicrobial drugs prescribed to this group of patients must be minimized so as to reduce toxic effects, burden of resistance, to ensure effective treatment and improve patient safety.

Keywords: Sepsis; Prescription pattern; Antimicrobial agents.

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INTRODUCTION

Sepsis is defined as life threatening organ dysfunction due to dysregulated host response to infection that can lead to tissue damage, organ failure and death. Sepsis is derived from the ancient Greek term "*make rotten".* It is the host response to microbial pathogens resulting in significant morbidity and mortality[1]. Sepsis occurs when chemicals are released into the blood stream to fight the infection, triggers the inflammatory responses throughout the body[1].Infection triggers both pro-inflammatory and anti-inflammatory process and ultimately contribute to the clearance of infection and the tissue damage that lead to organ failure[2]. In general, the pro-inflammatory process are triggered by the infection agents and are focused on the elimination of the pathogen, whereas the anti-inflammatory processes are triggered by the host response to promote tissue repair and healing[3]. An imbalance of these mechanism may lead to either excess tissue damage (pro-inflammatory) or immunosuppression and increased susceptibility to secondary infection (anti-inflammatory)[4]. The individual patient response is dependent on characteristic of both the host (comorbidities and immunosuppression) and the pathogen (organism load and virulence)[5]. Furthermore coagulation abnormalities such as intravascular coagulation and fibrinolysis result in endothelial dysfunction, microvascular thrombi, and impaired tissue oxygenation[6]. The impairment combined with the systemic vasodilation and hypotension cause tissue hypoperfusion and decreased tissue oxygenation[7]. Further complicated by mitochondrial oxygen utilization secondary to oxidative stress. These mechanism results in further tissue damage and ultimately contribute to multi organ failure[8]. It is a common and lethal condition that carries a substantial financial burden and is a primary cause of death in intensive care units[9].Sepsis remains in the top 10 leading causes of death despite plentiful investigative attention toward new therapies and adjuncts to mitigate poor outcome[9].

The source of infection can be lung, genitourinary tract, gastrointestinal tract, skin or soft tissue, and so on. Pathogenesis of bacteria due to the structural components of the Gram negative and Gram positive bacteria is responsible for initiating sepsis[10]. Diagnosis of infection in septic patients is critical. Early treatment of patients has been early shown to improve prognosis. Therefore, early diagnosis of infections and control of primary infection site are fundamental to improving patients prognosis[11]. Procalcitonin (PCT) is currently an FDA approved test to aid in the diagnosis of sepsis but with questionable efficacy. Blood culture remains one of the most important investigations in the management of sepsis. Clinical correlation of positive (as well as negative) blood culture is an important aspect of investigation where a clinical microbiologist can significantly on the management of sepsis[12]. The latest guidelines for the management of severe sepsis and septic shock

provided by the surviving sepsis campaign consortium recommend to timely commence appropriate IV broad spectrum antibiotics after performing a probable diagnosis and obtaining culture tests (1B/1C grated recommended to administer antibiotics within 1hour after diagnosis of either sepsis or septic shock. In general, "appropriate" treatment is defined as treatment matching the in vitro susceptibility of the pathogen[13]. Antimicrobial agents are any substance that kill (or) slow the growth of microbes. These substances can be derived from naturally occurring substance (or) can be synthetic. The aim of Prescription Pattern Monitoring Studies (PPMS) is to facilitate the rational use of drugs in a population[14].

There is no specific treatment for patients with sepsis, the management therefore relies on infection control with source removal and effective antibiotics- and organ function support. There is good evidence that early treatment is associated with improved outcomes in these patients, and the ability to recognize the condition as soon as possible is therefore important, so that treatment can be started early in the course of disease to prevent deterioration. However, the early diagnosis of patients with sepsis remains a challenge for clinicians at the beside[15]. Optimization of antimicrobial therapy in severe sepsis and septic shocks crucial to reducing the microbial load in a prompt and effective manner. Early, appropriate empirical antimicrobial therapy employing aggressive dosing strategies to maximize pharmacokinetic and pharmacodynamics indices and therefore killing activity are vital to reducing mortality. Timely antimicrobial de-escalation based on microbiologic identification and susceptibility testing and clinical improvement are likewise essential strategies to conserve the effectiveness of existing antimicrobials and prevent the emergence of resistance[16]. There is a lack of data on prescription pattern studies and it is essential to define prescribing. This study is designed to assess the usage of antimicrobials in sepsis treatment which includes analysis of prescribing pattern of antimicrobial agents in sepsis according to the standard guidelines followed by the hospital assessing and evaluating culture sensitivity test and to analyze complication of sepsis[17].

METHOD

This was a Prospective and Observational study performed on 146 patients over a period of six months starting from October 2018 to March 2019 to assess the prescribing pattern of antimicrobial agents used in treating sepsis. A total of 146 patients from all department of Apollo Multi Specialty Hospital & Imperial Research Center. Ethical committee clearance was obtained by the Institutional Ethical Committee of Apollo Multi Specialty Hospital &Imperial Research Center. Patient demographics, clinical findings and therapeutic data were collected from inpatients and the main sources for the collection of data were Patient's case note, Treatment chart, Lab data reports

(especially WBC & CULTURE SENSITIVITY test), Patient discharge cards. Inclusion criteria were Patients with sepsis along with comorbidities and being prescribed with antimicrobial agents. Exclusion criteria were Pregnant and lactating woman, Outpatient department and Patient who stay less than 24 hours in hospital.

Method of data collection

All patients with sepsis who met with the inclusion and exclusion criteria, who were admitted to all departments of the Apollo multi-specialty hospital & Imperial Research Centre in Bengaluru, during this study period were included in the study. Follow ups were carried out from the day of admission to the day of discharge for the enrolled patients. After the diagnosis were confirmed by the physician, the relevant & necessary baseline information (socio-demographic details of the patient & details of visit for the treatment) was obtained from patient's case notes (patient's age, date of admission, date of discharge, CBC reports, culture sensitivity tests) are collected. Therapeutic data (name of drugs, doses, and route of administration, duration & other laboratory data) were collected in a suitably designed data collection form.

Determination of prescribing patterns:

The treatment chart of the patient was checked on a daily basis. Patients laboratory values, vital signs, general examination and progress chart were recorded before and after the treatment with antimicrobial drugs. If indicating biomarkers such as decrease in WBC count and decrease in platelet count and other parameters were also recorded. The different antimicrobial agents used as treatment ware assessed. Statistical evaluation was done based on the data collected.

Statistical Methods:

Descriptive statistical analysis has been carried out in the present study. Chi-Square test has been used to find the significance of study parameters on categorical findings among different groups.

P value or significant considerations: Actual range ($0.05<p<0.5$). Strongly Significant if P value is = 0.01, Significant if P value is </= 0.05, Moderately Significant if P value is >0.05 and <0.1, Not Significant if P value is >/=0.1. The statistical software called SPSS (IBM) 25th version was used for the analysis. Microsoft Word and Excel were used to generate tables and graphs respectively.

RESULTS AND DISCUSSION

Demographics

As shown in Table 1 in the current study, Out of 146 patients, males were 81 and females were 65 patients with 67.5% and 32.5% respectively. Similar findings were found in a study conducted by Scott T. Micek on "Empiric combination therapy associated with improved outcome against sepsis". The number of male and female patients was almost same however, there were slightly more males

(52.5%) than female (47.5%) patients. This shows that, gender influences the prevalence of sepsis and males are highly prone to develop systemic infections when compared to females. in the current study the involvement of patients was of various age groups and it was found that maximum participants were seen in the age group of ≥60years having 87 patients with 59.58% compared to other age group which are ≤29years having 04 patients with 2.73%, 30-49yrs having 22 patients with 15.06%, 50-59yrs having 33 patients by giving 22.60%. Thus the lowest number of participants was seen in the age group ≤29 years. Similar findings were found in a study conducted by Scott T. Weiss on "Sepsis Prevalence, Outcome, and Therapies Study".

Table 1: Age and gender wise distribution of patient's data.

Age	Male	Female	Total	Percentage
</= 29	3	1	04	2.73
30-39	5	4	9	6.16
40-49	8	5	13	8.90
50-59	20	19	39	26.71
>/= 60	45	36	81	55.47
Total	**81**	**65**	**146**	**100**

Micro-organism Present:

As shown in table 2, out of 146 patients evaluated for causative organism, it was found that the percentage and order of various micro-organism isolated as; E.coli was found in 50 patients with 32.67%, out of which 19 were male and 31 were females (females were largely effected than males) >Klebsiella pneumonia was found in 33 patients with 21.56%, out of which 25 were males and 8 were females (males were largely effected than females) >Staphylolococcus aureus was found in 14 patient with 9.15%, out of which 10 were males and 4 were females (males were largely effected than females) >Enterococcus cloacae was found in 12 patients with a7.84%, out of which 8 were male and 4 were female (males were more effected than females) >Pseudomonas aeuroginosa was found in 11 patients with 7.18%, out of which 5 were males and 6 were females (females were more effected than males) >E.coli ESBL producing was found in 9 patients with 5.88%, out of which 5 were males and 4 were females (males were more effected than females) >Citrobacter was found in 8 patients with 5.22%, out of which 5 were males and 3 were females (males were more effected than females) > Candida tropical is was found in 7 patients with 4.57%, out of which 5 were males and 2 were females (males were more effected than females) > Clostridium difficile was found in 3 patients with 1.96%, out of which 2 were male and 1 is female >Acinobacterboumanii was found in 2 patients i.e. 01 male and 01 female with 1.30% > Enterococcus faecalis, Strreptococcusanginosus,

Serratiamarcecens are found in 01 male patient each with 0.65% >Acinobacterboumanii was found in 01 female patient with 0.65%.

Similar findings were found in a study conducted by Subhash KR on "Prescription of antibiotics utilization at a tertiary care hospital" was studied. There were 61% Gram Negative organisms which includes E.coli, Klebsiella pneumonia, Enterobacter and Pseudomonas. The rest 39% were Gram Positive organisms which includes staphylococcus aureus, staphylococcus epidermidis.

Table 2: Distribution of Micro-organism Present:

Microorganism	Male	Female	Total	Percentage
E.Coli	19	31	50	32.67
E.Coli ESBL producing	5	4	9	5.88
Klebsiella Pneumomiae	25	8	33	21.56
Psedomonas aeroginosa	5	6	11	7.18
Acinobacter boumanii	1	1	2	1.30
Acinobacter iwoffi	0	1	1	0.65
Candida tropicalis	5	2	7	4.57
Enterococcus faecalis	1	0	1	0.65
Citrobacter	5	3	8	5.22
Streptococcus anginosus	1	0	1	0.65
Enterococcus cloacae	8	4	12	7.84
Clostridium difficile	2	1	3	1.96
Serratia marcecens	1	0	1	0.65
Staphyllococcus aureus	10	4	14	9.15
Total	**88**	**65**	**153**	**100**

P=0.875, Non-significant, Chi-Square test

Prescribed Antimicrobial agents:

According to table 03, out of 146 patients, the antimicrobial drug distribution shows the order of prescribing patterns of various class of agents like, carbapenem in 95 patients (28.18%)>Penicillins and Cephalosporinsin 42 patients (12.46%), > Macrolides in 23 patients (6.82%) >poplypeptidein 21 patients (6.23%) >Glycopeptidein 19 patient (5.63%) >oxazoladinonein 17 patients (5.04%) >Lincomycinin 16 patients (4.74%) >Rifamycine derivatives and Azoles in 11 patients (3.26%) > Antivirals and Nitroimidazole in 09 patients (2.67%)>Echinocandin07 patient (2.07%)> Tetracycline in 03 patients (1.48%) >Glycylcycline andphosphonic acid derivatives in 03 patients (0.89%)> Sulfonamides in 02 patients (0.59%) >Flouroquinolon and Nitrofuran derivatives in 01 patient (0.29%). Similar findings are found in a study conducted by Ana Diaz-Martin on "Antibiotic prescription pattern in the empiric therapy of severe sepsis: combination of antimicrobials with different mechanism of action reduces mortality". This shows that carbapenem (25.1%) was most frequently prescribed antibiotics in empiric therapy in patients with severe sepsis and septic shock.

Table 3: Distribution of prescribed Antimicrobial agents:

Class of the Drug	Antimicrobial drugs	No. Of subjects/ Drug	No. Of drugs prescribed per class	Total No. Of subjects	Percentage
Carbepenems	Meropenem	85	03	95	28.18
	Ertapenem	07			
	Imepenem	03			
Penicillins	Amoxicillin	02	3	42	12.46
	Flucoxacillin	02			
	Piperacillin + Tazobactam	38			
Cephalosporins	Cefipime	03	6	42	12.46
	Cefipime + Tazobactam	01			
	Cefotaxim	01			
	Cefaperazone	10			
	Cefaperazone + Sulbactam	05			
	Ceftriaxone	22			
Macrolide	Azithromycine	16	02	23	6.82
	Clarithromycine	07			
Polypeptide	Polymyxin B	06	02	21	6.23
	Colistin	15			
Glycopeptide	Teicoplanin	16	02	19	5.63
	Vancomycine	03			
Oxazolidinone	Linezolid	17	01	17	5.04
Lincomycine	Clindamycine	16	01	16	4.74
Rifamycine Derivatives	Rifamycine	02	02	11	3.26
	Rifamixine	09			
Azoles	Fluconazole	09	02	11	3.26
	Voriconazole	02			
Antivirals	Oseltamivir	08	02	09	2.67
	Acyclovir	01			
Nitromidazole	Metronidazole	09	01	09	2.67
Echinocandin	Anidulafungin	07	01	07	2.07
Tetracyclines	Doxycycline	05	01	05	1.48
Glycylcyclines	Tigecycline	03	01	03	0.89
Phosphonic acid derivative	Fosfomycine	03	01	03	0.89
Sulfonamides	Cotrimoxazole	02	01	02	0.59
Flouroquinolones	Levofloxacin	01	01	01	0.29
Nitrofyran derivatives	Nitrofurantoin	01	01	01	0.29
TOTAL				337	100

Complications

As shown in figure 1, out of 146 patients evaluated for complications from septicemia, the various complications found were, Septic Shock (17.53%) in 37 patients (30 males and 07 females) >Death (13.74%) in 29 patients (16 males and 13 females) > Acute Kidney Injury (12.32%) in 26 patients (17 males and 09 females) and Respiratory Distress (12.32%) in 26 patients (19 males and 07 females) and MODS (12.32%) in 26 patients (21 males and 05)> Thrombocytopenia (10.90%) in 23 patients (19 males and 04 females) > Cardiogenic shock (5.68%) in 12 patients (08 males and 04 females) > Chronic Kidney Disease (5.21%) in 11 patient (09 males and 02 females) > Encephalopathy (3.79%) in 08 patients (03 males and 05 female) > Cardiac Myopathy (3.31%) in 07 patients (05 male and 02 females) > Metabolic Acidosis (2.84%) in 06 patients (04 males and 02 females).Out of 146 patients, 36 patients (14.57%) were not found with any complications. Similar findings were found in a study conducted by Khalilullah Hayatzaki on "Prophylactic antibiotics reduces sepsis after biopsy of the prostrate" in which severe infectious complications seems to be correlated with bacteria resistant to antibiotics.

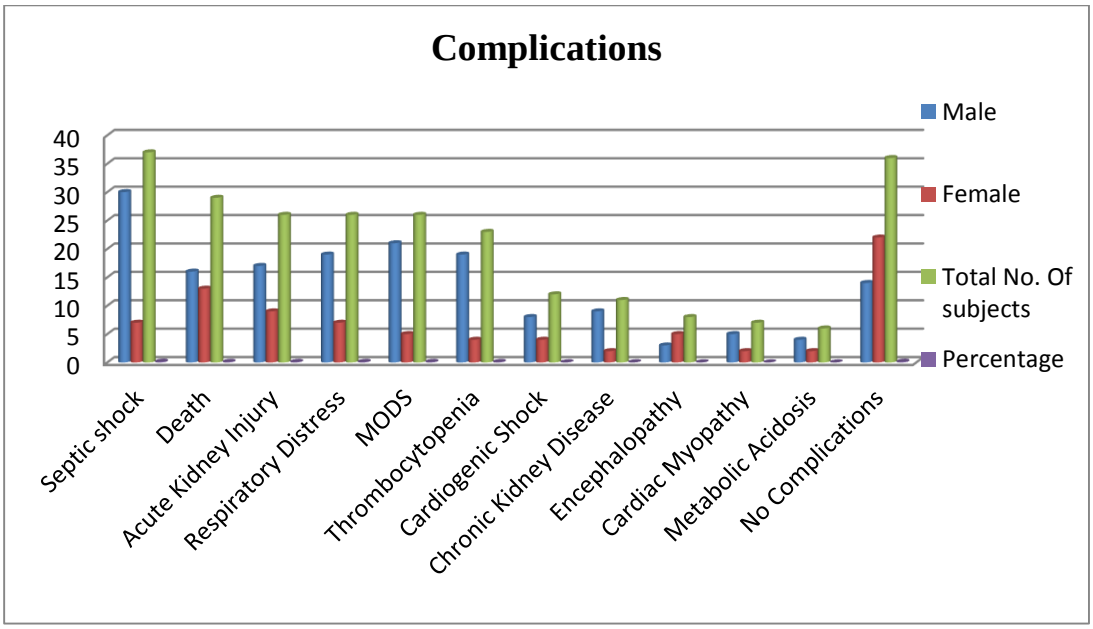

Figure 1: Distribution of complication:

CONCLUSION

Culture and sensitivity test was done which shows micro-organism found with maximum distribution of organisms were E.coli which is sensitive to Meropenem. The most frequently prescribed antimicrobial agents were carbapenem. Various complications were found, among which septic shock were majorly effected. Health care professionals must understand the usage of Antimicrobial agents for specific conditions in Sepsis patients so as to minimize adverse drug reactions, complications and improve patient quality of life. The number of antimicrobial drugs

prescribed to this group of patients must be minimized so as to reduce toxic effects involve in excessive use of antimicrobial agents.

REFERNCES

1. Roger G, Gordon R. "Introduction of sepsis. National institute of General Medical Science", ISF. 2014 Nov;(2).
2. H. Bryant N, Emanuel P R. "Severe sepsis and septic shock: Review of the literature and emergency department management guidelines", AEM. 2006 Jul;1(48).
3. Neeru P, Chetan P, "Profile of fungal septicemia in new born at tertiary care hospital in North India", IJCP. 2017 March;4(2).
4. Meghan R F, Joanne T, "Antiviral prevention of sepsis induced cytomegalovirus reactivation in immune competent mice, NIH Public Access", 2010 March;85(3).
5. LE. Lopez C, B. Almirante, "Empirical targeted therapy of candidemia with fluconazole versus echinocandins", CMI.2016.
6. K Ashwin R, S Uday K, "Bacteriological profile and antibiotic sensitivity patterns of blood cultures", IJCP.2016 Nov;3(4).
7. Dr. Narendra B, Dr. Jayanti P B, "Drug Utilization Pattern Of Antimicrobials In Neonatal Sepsis in Tertiary Care Teaching Hospital", IJNMR. 2017 Jul;5(3).
8. Subash KR, Shanmugapriyan S, "Study of Prescription of Antibiotics Utilization in Neonatal Intensive Care At a tertiary care", IJMRSH. 2015;4(2).
9. Sarah A S,W.Ryan M, "The impact of timing of antibiotics on outcomes in severe sepsis and septic shock:A systemic review and meta analysis. HHS public Access", CCM. 2015 Sept;43(9).
10. Anand J A,Prashant C.S, "Drug Utilization study of Antimicrobial agents in patients of neonatal sepsis in neonatal intensive care unit at a tertiary care hospital in western part of India", IJBCP, 2015 Sept-Oct;4(5).
11. Stephen Y L, Anand K, "Empiric Antimicrobial Therapy In Severe Sepsis and Septic Shock: Optimizing pathogens clearance. HHS Public Access", CIDR. 2015Jul;17(7)
12. Caroline MA VD B, Marlies EJL, "Development of quality indicator for antimicrobial treatment in adults with sepsis", BMC Infectious Disease. 2014.
13. Aline F, Julia B, "Reviewing the WHO guidelines for Antibiotic use for sepsis in neonates and children", PICH. 2018;(08).

14. Khalilullah H, Sveinar M, Karsten N, "Prophylactic antibiotics reduces sepsis after biopsy of the prostrate", DMJ. 2014;61(11).
15. Heena R H, Jayendra R. G, "Correlation of blood culture results with the sepsis score and sepsis screen in the diagnosis of early onset neonatal septicaemia", JCN. 2016 Aug;3(5).
16. Fatema A, Nicolette L T V, Emine A, Mehmet D, "Treatment of sepsis: what is the antibiotic choice in bacteremia due to carbpenem resistant enterobacteriaceae". 2017 Aug16;5(8).
17. Paula K.O.Y, Alexander R.M, "Impact of appropriate anti microbial therapy for patients with severe sepsis and septic shock- Quality improvement study". 2014 Nov;9(11).