ORIGINAL ARTICLE

Drug Utilization Pattern of Different Antibiotic and Evaluating the Cost of the Therapy in Patients With Enteric Fever admitted to KIMS Hospital and Research Center, Bangalore, India

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ABSTRACT

Aim: To study drug utilization pattern of various antibiotic and assessing the expense of the therapy in patients with enteric fever admitted to department of general medicine KIMS hospital and research center.

Methodology: A cross-sectional investigation was done in department of general medicine KIMS hospital and research center. between Aug-September 2018. Appropriateness in this examination was reviewed using Medication Appropriateness Index (MAI) criteria which incorporate sign, effectiveness, dose, right bearings, practical directions, drug-drug interactions, drug-disease collaborations, duplication, duration and cost

Result: Mean use of antibiotics in KIMS (2.18±0.87) was not basically one of a kind (P = 0.015). The Cephalosporin gathering of antibiotics was used by and large to treat enteric fever in medical clinics. By and large0.93 Cephalosporin per patient in KIMS was used. Overall, we found that 31.7% in of patient's medicines with antibiotics were inappropriate. Other normal sorts of inappropriateness are costly medications, duplication of antibiotics, prescribing higher generation antibiotics and useful bearing.

Conclusion: Conclusively, in excess of 30% of patients in KIMS hospitals treated for enteric fever got inappropriate antibiotics. Subsequently we prescribe future training or administrative intercession to improve appropriateness. Ceftriaxone emerged as the most commonly used antibiotic in years. Fever was seen in practically every one of the cases. Number of cases with widal tested as positive were 33. Number of cases impervious to cephalosporin were nil in years. Cephalosporin keep on being utilized normally. Use of ciprofloxacin has declined. Widal test keeps on being done ordinarily however it is of minimal practical value and effectively misinterpreted. Re-rise of chloramphenicol is an appreciated

Key words: Antibiotic Use, Enteric Fever, drug utilization, widal test

INTRODUCTION

Drug utilization has been characterized as the showcasing, circulation, prescription and usage of drugs in a general public with uncommon accentuation on the subsequent restorative and social results[5]. Drug usage is significant for each medication however particularly for antibiotics as they are generally utilized medications in health care and their excessive and inappropriate use in hospitals, health care facilities and network adds to the advancement of bacterial resistance[1]. The prevalence of antibiotic use is so high in India and extents from 24 to 67%[3]. Being the nation with most elevated weight of infectious disease India has most elevated rate of antibiotic prescribing prompting their irrational and indiscriminate use which has brought about in rapid increase in rate of antibiotic resistance[5]. Economically, antibiotics contribute fundamentally to the medication cost and are guaranteed worldwide to represent for 15 to 30 percent of the total health budget. Developing nations have constrained subsidizes accessible for health care and drugs and it becomes very important to prescribe drugs rationally so that the accessible assets can be used ideally[4]. Drug usage examine is a segment of medical audit that does observing and assessment of the medication prescribing patterns and recommends fundamental adjustments in prescribing practices to accomplish rational therapeutic practice as well as cost effective health care[2].

In the creating countries, the expense of medications is a major worry to therapeutic medicinal services experts and patients. It has been seen that antibiotic expenditures

uses utilizes speak to about half of an emergency clinic's complete medication budget[6]. Extensive abuse of antimicrobial medications has been accounted in the previous couple years, and almost 50% of all antibiotic drug prescriptions have been observed to be inadequately chosen. This is particularly valid for the general wards in tertiary medical centers (TMC) where errors in prescription, organization, and conveyance are normal. In such situations, the likelihood of drug interactions and adverse drug reactions are high, as huge quantities of medications are recommended. Furthermore, inappropriate and outlandish usage of antimicrobials can make microbial resistance to the normally endorsed antimicrobials[7].

Investigation of medication prescription practices is of uncommon enthusiasm as for expanding expenses of health service. The prescribing pattern can be surveyed in a knowing the past path through analysis of clinical records in a medical care focus[8]. The investigation of prescription pattern commonly a piece of a medical audit that searches for examination, and, whenever required, adjustment, in prescription pattern, to get rational and cost-effective medical care[9].

As indicated by WHO; Typhoid fever is a crucial disease achieved by Salmonella Typhi customarily through ingestion of polluted sustenance or water. The intense sickness is portrayed by delayed fever, cerebral pain, queasiness, loss of appetite, and obstruction or at times looseness of the bowels. Manifestations are often non-specific and clinically non- recognizable from other febrile sicknesses. Be that as it may, clinical severity changes and

extreme cases may prompt genuine complexities or even death. It happens overwhelmingly in relationship with poor sanitation and absence of clean drinking water. As per the latest evaluations, somewhere in the range of 11 and 21 million cases and 128 000 to 161 000 typhoid-related deaths happen every year around the world. A similar but often less severe disease, paratyphoid fever, is brought about by Salmonella Paratyphi A and B (or uncommonly Paratyphi C). WHO prescribes immunization to control endemic typhoid fever and for flare-up control. Among the accessible typhoid vaccines, TCV is favoured at all ages in perspective on its improved immunological properties, appropriateness for use in younger children and expected longer duration of security. WHO prescribes that all typhoid fever vaccination projects ought to be executed with regards to various endeavours to control the ailment, including health instruction, water quality and sanitation redesigns, and planning of health professionals in determination and treatment[10].

Enteric fever, for the most part known as typhoid fever, is an extreme fundamental diseases described by sustained fever and stomach side effects. Universally, enteric fever makes illnesses 21.6 million and passing to 216500 people reliably[11]. Typhoid rate differs considerably in Asia. High typhoid fever occurrence has been found in India and Pakistan. In comparison, typhoid fever recurrence was moderate in Vietnam and China and intermediate in Indonesia. Around the world, the rise of multidrug resistant S. Typhi and S. Paratyphi A strains has been appeared to be geographically heterogeneous, underscoring the significance of proceeding microbiological observation for Salmonella isolates by checking their antimicrobial obstruction profile at the nation level[12,13].

MATERIALS AND METHODS

It is an imminent, observational investigation directed on patients admitted to the Department of Medicine, KIMS Hospital and Research Center., who are diagnosed with enteric fever with positive Widal test. Data will be reviewed and collected on daily basis. The case reports of patients aged greater than 18 years who had been admitted will be enrolled in the study. Data will be collected from medication chart of the patients from the day of admission till the date of discharge of the patient from the hospital.

In this examination, we utilized the MAI (Medication Appropriateness Index) criteria to overview the appropriateness of antibiotics treatment. MAI is an endorsed and reliability quality tried instrument and was used in a couple of examinations surveying appropriateness. It has10 spaces which consolidate sign, adequacy, dosage, duration, direction, drug-drug interactions, drug-disease interactions, common sense, price and duplication of treatment. Each space has its own specific definition. In this examination, we have used balanced MAI basis which was detailed for evaluating antibiotic recommending in inpatients by Tayler et al. [14] Each paradigm was characterized regarding Enteric Fever utilizing WHO rule for Enteric Fever. [10] Appropriate, peripheral and inappropriate rating was given to every model for every patient.

Despite the fact that, the pervasiveness of enteric fever is higher in Asian nations, it lies between 0.3-1%1-4. example measure was then determined from equation n = Z2α/2 P (1-P) / M2Where, M = margin of error, P = Prevalence of the characteristic. Thus, the sample estimate (n) at 95% certainty interim and 5% margin of error will be n = 1.962 x 0.01 x 0.99 / (0.05)2 = 15.21 ~ 16 which is less. Consequently, we expanded the required sample size up to 100 in every emergency clinic with the goal that we can apply unmistakable measurements. Along these lines, all patients with enteric Fever treated with antibiotics agents amid the examination time frame were incorporated. Statistics: Descriptive measurements were utilized to examine the information utilizing Statistical Package for the Social Sciences (SPSS) for Windows Version 18.0 (SPSS Inc.; Chicago, IL, USA).

RESULT AND DISCUSION

demography of Patients experiencing Enteric Fever: The mean age of the patients was 22.81 ± 20.52 in KIMS (Table 1). We found enteric fever was increasingly pervasive in guys (54% in KIMS) in information from medical clinics, which is like investigation led by Malla et al [17].

The duration of the given treatment fluctuated from individual to individual, and was depended on the sort of antibiotic therapy. In our present investigation, the mean duration of clinic stay was 3.74 ±1.58 in KIMS. Be that as it may, in an examination directed by Walia et al [18]. in India found the remain in the emergency clinic to be around8.2-12.1 with various treatment regimens and another examination led by Farmakiotis D et al.[19]

Table 1: Demography of patients experiencing enteric fever

Demography	Parameter	KIMS hospital
Age	Mean	22.81 ± 20.52
Gender	Female	45
	Male	55
Duration of stay	Mean	3.74±1.58
Departments	Medicine	63

Altogether, 565 medications were utilized for the treatment of100 patients from KIMS. Mean number of prescriptions utilized in the medicines of KIMS (5.80±2.37). Anatomical therapeutic classification (ATC) of recommended prescription proposes antimicrobial class of medications were very endorsed for KIMS clinics.

Antibiotics agents remain the backbone of treatment of enteric fever. Different drugs are just symptomatic treatment. In our examination, other simultaneous medications utilized were drugs utilized in GIT, drugs utilized in skeleton-muscular system, drug used on nervous system etc. Although we did not find a similar study on concurrent prescription in enteric fever, an investigation led by Sharma et al.

A total of 218 antibiotics were endorsed in KIMS for the treatment clinic. Mean utilization of antibiotics in KIMS (2.18±.87. Further, consider found that over 20% of case was treated with3 antibiotics in the hospitals. This examination demonstrated that the Cephalosporin gathering of antibiotic was utilized broadly to treat enteric fever in KIMS emergency clinics. All things considered 1.12 Cephalosporin in KIMS.

Table 2 Category of antibiotics utilized per treatment

Group of Antibiotics	KIMS hospital	P-value
Aminoglycoside	0.33±.47	0.018
Cephalosporin	0.93±.38	0.052
Chloramphenicol	0.02±.14	-
Co-amoxiclav	0.02±.14	-
Macrolide	0.54±.50	0
Penicillin	0.05±.22	0.497
Fluoroquinolone	0.07±.26	0
Tetracycline	0.01±.10	0
Miscellaneous	0.21±.41	0.418

Among the drugs used for the treatment ceftriaxone emerged as the most commonly used in hospital, the incidence being 48%. The percent recovery is maximum for cephalosporin (100%) considering the number of patients treated with them and least for ciprofloxacin indicating the high rate of resistance against S. typhii. Percent recovery is 100% for cotrimoxazole and chloramphenicol also but the number of patients treated is very few. Oflaxacin has also shown a good 92% recovery rate. The criteria for recovery is clinical and it is a 48 hr. fever free interval after the culmination of a course of antibiotics. Table 3

Table 3 Utilization in Individual Drug Group

Drug Name	No. of patients treated	Percent recovery
Ceftriaxone	46	46 (100%)
Cefixime	14	14 (100%)
Ciprofloxacin	9	03 (33%)
Oflaxacin	14	13 (92%)
Sparfloxacin	2	01 (50%)
Amoxicillin	3	01 (33%)
Cotrimoxazole	2	02 (100%)
Gentamicin	6	04 (66%)
Chloramphenicol	0	0

Widal test was found to be positive only in 33 cases. Even blood culture which is a reliable test is positive only in 11 cases. In KIMS not a single case was found to be resistant to cephalosporin. As per the literature blood culture is positive in 90% in the first week of fever and in 75% in the second week. But to our surprise only 11.45% in 2002 was positive by culture. It could be possible that patients have taken some antibiotics prescribed by local doctors before coming to the hospital which has resulted in poor response to blood culture. Widal antigen test continues to be carried out commonly even though the fact is that it is of little practical value and easily misinterpreted [20]. The popularity of widal test in the determination of enteric fever is undeserved, thinking about its false notions and weaknesses [21]. The incidence of ultrasound abdomen is only 25%. But it has been demonstrated that ultrasound can be a non-invasive, efficient and a sensibly sensitive tool for diagnosing typhoid when serology is equivocal and societies are negative [22]. Hence ultrasound can be considered more often compared to widal test. Table 4
The use of ciprofloxacin has reduced considerably reassuring the fact that ciprofloxacin resistance is widespread. The widespread use of cephalosporin is not a good sign and re-emergence of chloramphenicol is a welcome sign. Response to oflaxacin seems to be good and hence can be prescribed more often.

Table 4 Microbiological discoveries

Microbiological	
Widal test +ve	34.37% (33)
Blood culture +ve	11.45% (11)
Sensitivity to all antibiotics	4.16% (4)
Resistance to cephalosporins	Nil

The mean expense of drug in enteric fever treatment in KIMS was not fundamentally extraordinary. Additionally, the mean expenses of antibiotics in enteric fever treatment in the emergency clinics was not measurably huge. The detail of expense is given in Table 5.

Table expense of per treatment of enteric fever in KIMS hospitals

Parameter	WRH	P-value
Mean cost of prescribed Medication	370.98±250.35	0.029
Mean cost of Antibiotics	350.49±200.28	0.422
Percentage of Antibiotic Cost	86	-

The drug-drug interactions among the endorsed drug were assessed utilizing Micromedex. There were drug-drug interactions in around 11% of patients endorsed drug. Some normal drug-drug interactions are given in Table 6.

The appropriateness examination of the treatment of enteric fever patients was finished utilizing Medication Appropriateness Index(MAI) 10 pointer (Table 7) and every marker was assessed by scientist utilizing WHO rules as showed in strategy. While surveying we found that larger part of signs was inappropriate based on WHO rules.

Therapy: Appropriate utilization of antibiotics is the key component in the treatment every single bacterial disease. We suitability the appropriateness of antibiotic therapy utilizing MAI criteria. By and large, 31.7% in KIMS of patients with recommended antibiotics were inappropriate which is nearly lesser than found in an investigation led by Tobia et al[15] in the US, where around two-thirds of patients got at any rate one inappropriate antibiotic and Tobgay et al[16].

The lesser frequency of inappropriateness in our investigation might be because our examination was led on in-patients though these two investigations were directed on the out-patients with respiratory tract infection in Tobia et al. and in overall out-patients in Tobgay et al. study. In our investigation we found that basic type of inappropriateness incorporates the duplication of antibiotics, cost, recommending high generation antibiotics, and commonsense bearings. There were comparative discoveries as far as cost from Tobia et al[15].
In this investigation, mean number of antibiotics for the treatment of enteric fever was 2.13±1.11 in KIMS which was not fundamentally extraordinary (P = 0.015). These recommend the abuse of antibiotics in the treatment of enteric fever in the medical clinics. WHO rules for the treatment of enteric fever advocates the utilization of fluoroquinolone as first line treatment even in serious enteric fever. Interestingly, greater part of patients from either medical clinic got Ceftriaxone as first line treatment in the present investigation showing aimless utilization of more current generation antibiotics.

Table 6 Common drug-drug interactions

Drug	Drug	Interaction	Severity	Documentation	KIMS
Amikacin	Furosemide	Concurrent use may result in increased amikacin plasma & tissue concentrations & additive ototoxicity and/or nephrotoxicity	Major	Fair	√
Ketorolac	Norfloxacin	Concurrent use may result in an increased risk of seizures	Moderate	Fair	√
Ampicillin	Pantoprazole	Concurrent use may result in loss of ampicillin efficacy	Moderate	Fair	√
Antacid	Ciprofloxacin	Concurrent use may result in decreased ciprofloxacin effectiveness	Moderate	Good	-
Ciprofloxacin	Diclofenac	Concurrent use may result in increasedciprofloxacin plasma concentrations	Moderate	Excellent	-
Doxycycline	Ferrous sulphate	Concurrent use may result in decreased tetracycline and iron effectiveness.	Moderate	Good	-

Table 7 Appropriateness examination for Enteric Fever Treatment (n=100/medical clinic)

Criterion	Appropriate of KIMS	Marginally appropriate of KIMS	Inappropriate of KIMS
Indication	12	8	80
Effectiveness	12	44	44
Correct dosage	95	1	4
Correct direction	95	2	3
Drug-drug interactions	89	0	11
Drug-disease interaction	100	0	0
Practical directions	65	18	17
Least expensive alternative	7	3	90
Duplication with other drug	46	1	53
Duration of therapy	75	10	15
Average Score	59.6	8.7	31.7

CONCLUSION

Our establishing proposes that in excess of 30% of patients in KIMS emergency clinics treated for enteric fever got inappropriate antibiotics. Cost, recommending higher generation antibiotics and duplication with antibiotics were normal sorts of inappropriateness. It is verifiable truth that inappropriate utilization of antibiotic leads to antibiotic resistance, so such practice should be debilitated. Consequently, we trust that this examination will help in arranging and deciding kinds of intervention and we prescribe future instructive and administrative mediations to improve appropriateness.

Ceftriaxone emerged as the most commonly used antibiotic in years. Fever was seen in almost all the cases. Number of cases with widal tested as positive were 33. Number of cases impervious to cephalosporin were nil in years. Cephalosporin keep on being utilized ordinarily. Utilization of ciprofloxacin has declined. Widal test keeps on being completed usually however it is of minimal practical value and effectively misinterpreted. Re-development of chloramphenicol is an appreciated sign.

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