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Original Research Article

Rapid Cycle Analysis and Daily-Defined Dose as Tools to Audit Antibiotic Policy on the Usage of Restricted Antibiotics: Suggesting Corrective Changes

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ABSTRACT

Antibiotics are medicines, which are used under restricted conditions. Sometimes it has become essential for controlling serious infections. Administration of Antibiotics is governed by certain policies of the hospital. Further these policies usually undergo a periodic review at the regular interval. Antibiotics have both positive and negative impact, it depends how best it is used for the right purposes. Basically it contributes significantly to decrease morbidity and mortality by the way of minimizing the risk of health-associated infections. On the other hand, unregulated use of antibiotics could lead to serious problems to the patients. Hence, appropriate guidelines, policies and protocol is essential to ensure right use of antibiotics. The study focuses on the factors that contribute to make better policies, which will have greater impact on the use of antibiotics. To achieve an effective result of antibiotic policy audit, approach was adopted to study "restricted antibiotics", which are the newer antibiotics scheduled under schedule H1 which will be accessible only in tertiary care hospitals. A retrospective study was done with samples collection, which was guided by ICD codes. A total of 120 samples were assessed which was 20% of total data of 699 cases with probability of using restricted antibiotic. A three way approach adoption was suggested with Rapid cycle analysis of clinical case data from Medical Records Department, DDD (daily defined dose) utilization data from pharmacy department, and third, which was not implemented due to permission issues, sending out Google forms to clinical staff to get understanding of clarity of policy to staff. Analysis was done by excel and SPSS. The results show that there has been some gap between the policies and practice. It is important to match that the best practices to be adopted in the policies document at the regular interval and similarly the approved policies to be implement strictly by the professionals.

Keywords: Antibiotic policy, Rapid cycle analysis, DDD (daily defined dose), Antibiotic policy audit, restricted antibiotics

INTRODUCTION

The antibiotic policy has been implemented in the particular tertiary care hospital as per rules and requirements, which have been continued without changes in years 2013 & 2014. There were some review and changes implemented in 2015 &2016. The audit would be to check compliance on the restricted drugs prescription on clinical case data entry with antibiotic policy and to comparatively study utilization of these drugs by daily-defined dose indicator.

The basic purpose of antibiotic policy is to provide guidelines on usage of antibiotic. In order to have separate regulation to check unauthorized usage of ``restricted antibiotic'', a separate schedule

as Schedule H1 of third generation antibiotics and all newer molecules like Carbapenems (Ertapenem, Imipenem, Meropenem), Tigecycline, Daptomycin may be put in place restricting their access to only tertiary hospitals as per the Drugs and Cosmetics Rules. [1] Antibiotic formulary restrictions are to reduce the cost and resistant microorganisms in hospitals. [2] The antibiotic policy drafting should include microbiologist, pharmacist, pathologists, Doctors, Nursing staff, and infection committee members from administration. [3] Currently used methods for antibiotic policy are not very clear and only a few studies are done to understand system of auditing [4] but the possible auditing methods may include the resistance and antibiotic policy may be recorded by predictor variable. [5] (DDD) daily defined dose OR Average local daily administration (DDD) PER 100 Patient days may be monitored, [6,7] Segmented regression analysis of pharmacy stock data and Design of the Alert Antibiotic Intervention to monitor the changing professional behavior in the EPOC (Effective Practice and Organization of Care) [8] or Use standards, Generate reliable numerator, Express resistance as incidence rate as per SEARO guidelines. In *India*, according to Ministry of health and family welfare specific intervention measures such as rational use of antibiotics and antibiotic policies in hospitals may be implemented as early as possible, by Formulation of antibiotic policy, Education and Training of all prescribers, Implementation of infection Control guidelines. [9,10] Also in cases like urinary tract infection direct usage of third generation cephalosporin was reported as 1st line drugs showing need to improve adherence to antibiotic policies [11] *Internationally*-In modern medical practice serious medical conditions are supplemented by antibiotics, but non responsiveness to these antibiotics are reported commonly. [12] In studies conducted in Dutch association of chest observed and promoted empirical treatment which was supported by antibiotic policy. [13] In Europe there have been studies done to audit antibiotic usage by European Surveillance of Antimicrobial Consumption (ESAC-tool). [14] The effort was to assess policy by peers who are not the members of the policy development group should review policy. Antimicrobial stewardship which refers to the multifaceted approach (including policies, guidelines, surveillance, prevalence reports, education and audit of practice) that healthcare organizations have adopted to optimize prescribing. [15]

Objectives

- To explore factors that determine requirement of antibiotic policy and regulation.
- To assess the compliance of the restricted drugs usage with the existing antibiotic policy
- To understand and establish corrective changes those are required in the policy.

METHODOLOGY

The Methodology was based on the literature review mentioned in the references. The audit was performed on perceived GAPS found, by a multi approach of Rapid cycle analysis, [16] Utilization DDD Indicator. The key informants were from Clinical departments, Infection control committee, Pathology department, Pharmacy department, Manager operations and quality management department. The infection control officer gave guidelines and other data available on dispatch of restricted medicines. Selection of sample was on grounds of ICD 10 coding data of infectious diseases, which had probability of restricted antibiotics usage, [17] from the Medical records department. Data collection- the purposive random sampling was conducted, as per ICD 10. A total of 699 cases were found from data of eight months with the relevant ICD10 codes. [18] Every 5th sample was collected. 120 Samples were assessed (20% of total sample size attained from ICD CODE samples collected.ICD-10 A00-A09, A10-A49, I-33, J09-J18, K58-59, N39, R19, R50, T 85, 86 based on infectious diseases

requiring antibiotic were found in data entry. Analysis of compliance was done with antibiotic policy draft compared with case data detailed, drugs prescribed and its empirical relation. DDD indicator was also calculated and compared. [19] Analysis was done using EXCEL (/Applications/Microsoft Office 2011) and SPSS 23.0.0.0

A gap analysis was mainly done at the beginning. Initial assessments suggested perceived gaps were in 1.Patient disease profile requirements and resistances guidelines effectiveness to be assessed from Daily Drug Dosage and antimicrobial stewardship 2 No Gap in wrong service quality standards as benchmark practices e.g. NABH followed.3.The service performance gap and policy not matching actual delivery to be checked by rapid cycle analysis 4. The difference between Policy requirements perception, expectation and knowledge of antibiotic policy which may be assessed byA Target - self assessment tool [20] Google sheet may be mailed to receive response which were a suggestion made but were not utilized due to permission constraints.

Table 1.The Rapid cycle analysisformat was edited as per need of study

SR. NO	ADMISSION NO CODED	SEX	AGE	DATE OF ADMISSION	DISCHARGE DATE	SPECIALTY	REASON FORADM	ICD CODE	ICD GROUP	ICDDESCRIPTION	CLINICALDATA	TREATMENT GIVEN	TREATMENT ADVISED	CONSULTATIONOPDTYPE	COMPLIANCE Y/N	COMPLIANCE WITH	RECOMENDATION

RESULT

Factors that determine requirement of antibiotic policy and regulation

There are certain common factors that indicate a constant monitoring of antibiotic policies, which include social, political, economical, cultural and ecological factors (SPECE).

Social Aspects: There has been increase in antibiotic resistance observed, with which interests has turned to whether antibiotic policies can reduce the spread of resistance and even reverse current high levels. Early studies indicated towards feasibility. [21]

Political Aspects: The guidelines draw a pathway to government policies and how to tackle population at large. Improve awareness and understanding through effective communication, education and training. Reduce the incidence of infection through effective infection prevention and control. Optimize the use of antimicrobial agents in healthcare. Promote investments for Antimicrobial resistance (AMR) activities, research and innovations. [22]

Economical Aspects-various control measures have been shown to be useful in reducing costs of therapy and total amounts of prescribing, while maintaining quality of care. Impact of policy and cost-benefit analysis and Resource mobilization plan documented is an essential to assess the economic effects of policy [23]

Cultural Aspects-Specific cultural communities have shown patterns of specific antibiotic resistance. E.g. quoted from research papers .In the community, outbreaks of resistant group have been controlled by major reductions in prescribing of erythromycin and penicillin, respectively; firstly in Japan [24] and Hungary [25] and, more recently, in Finland [26] and Iceland. [27]

Ecological Aspects -

Where resistance previously was not present, Acquisition of resistance by a few previously susceptible strains through genetic mutation or through transfer of genetic material, inducible resistance that is already present in a few strains in the bacterial population or of a small resistant subpopulation of organisms, usually from direct selection by antibiotic prescribing or due to poor infection control procedures. With monitoring and forming efficient antibiotic policies these unwanted issues might be surpassed [28] also studies on worldwide population was done to

understand the effect antibiotic resistance. The combination therapy was concluded to be more effective [29]

Compliance of the restricted drugs usage with the existing antibiotic policy

A 68.3% of positive compliance was observed (Frequency 82), whereas 31. 7% (Frequency 38.) Of samples showed non-compliance out of total 120 samples. Department wise compliance was studied and the maximum compliance was found to be from departments of Nephrology (100%-9 Compliances, 0 Non compliances) Critical care (94%-16 Compliances, 1 Non compliances), Cardiology (91%-10 Compliances, 1 Non compliances), Chest Medicine (88%, 16Compliances, 2 Non compliances), Cardiology (91%-10 Compliances, 1 Non compliances), Physical and internal medicine (68%-13 Compliances, 6 Non compliances), Non - compliance was highest from Pediatrics department (Pediatric Surgery& Pediatric Hemato-Oncology-100%, Pediatrics, 93.75%, (Total-1 Compliances,20 Non compliances) followed by Physical and internal medicine(31%-13 Compliances,6 Non compliances), Gastroenterology (42%-, 4 Compliances,3 Non compliances) Gynecology (33%-2Compliances, 1Non compliances), Clinical Hematology(50% -2 Compliances, 2 Non compliances), the reason for non-compliance is mentioned below.

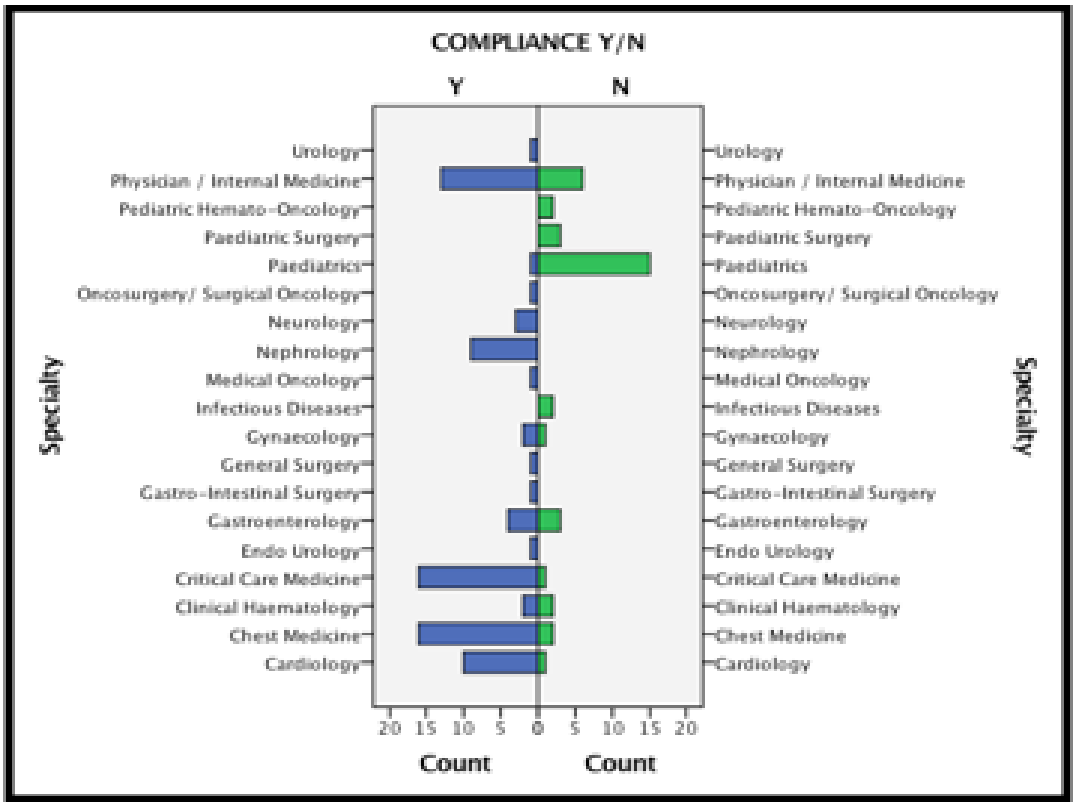

Figure 1 Showing department wise compliance and non-compliance

OBSERVATIONSFOR COMPLIANCE AND NON-COMPLIANCE

There has been a good compliance in general. Viral Pneumonia guidelines will improve compliance but as such pneumonia guidelines were well in place.

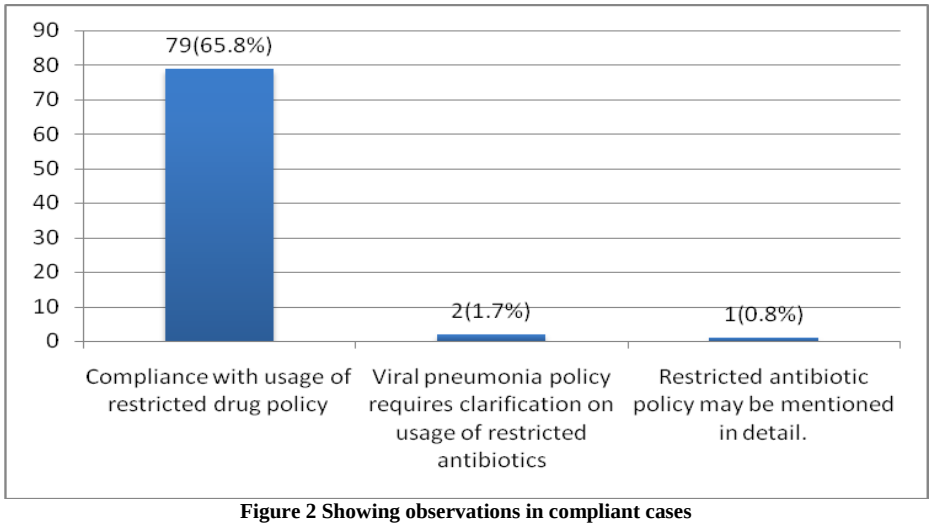

Figure 2 Showing observations in compliant cases

The non-compliances findings are enumerated below in presentation

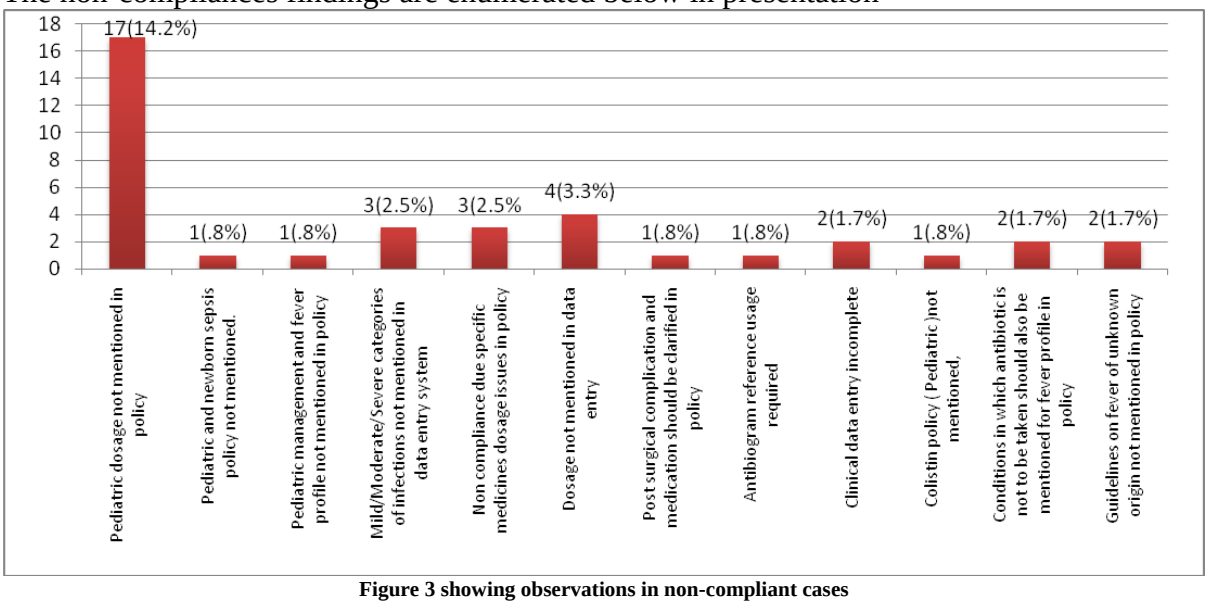

Figure 3 showing observations in non-compliant cases

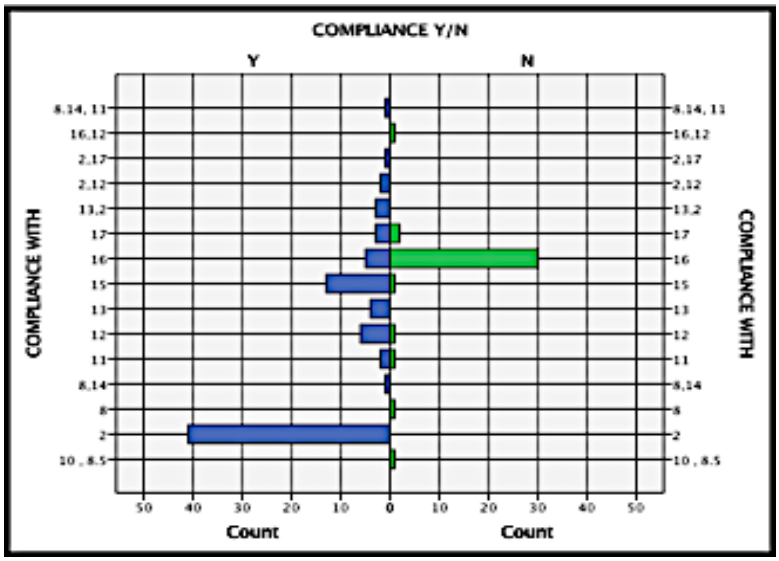

Figure 4 – High compliance was with section 2 and 15 showing 34.1% and 10% positive responses respectively with highest non-compliance with section 16 showing 25% negative responses

COMPLIANCE WITH THE SECTIONS OF ANTIBIOTIC POLICY-

The policy has Sections, which indicated guidelines of antibiotic policy. The section 2, which is suggestive of compliance due to appropriate usage of antibiotic policy. The non - compliance was majorly in section 16 due to the drug dosage not mentioned for restricted drugs, with missing guidelines on Pediatrics, fever profiles, where no antibiotic prescriptions might be required but only palliative treatment might help.

THE FREQUENCY OF PRESCRIBING THE RESTRICTED ANTIBIOTICS-

The restricted antibiotics are administered to IPD patients in injection form. The data was assessed for June and July for the No. Of ampules utilized (Table 2). There are specific trade names of drugs, which showed higher usage. But the content of the ampule have to be converted on the similar scale for better accuracy. For this the DDD (daily defined dose) was calculated. All the brands available for use in IPD of hospital were studied by calculating dosage in grams and the multiplying by units used (Figure 5). For antibiotic Colistin (MIU) the comparison was done separately due to unit MIU (Figure 6)

Table 2 - Restricted antibiotic usage Generic details and Trade Names with maximum usage.In Prescription of Meropenem was highest with Inj. Meronem 1gm and Inj. Penmer 500mg

Name of Antibiotic	No. of ampule June	No. of ampule July	Trade names which were found to have had higher usage
Imipenem	9	37	No special finding
Meropenem	1720	1872	Inj. Penmer 1gm, Inj. Meronem 1gm Inj. Penmer 500mg
Cefepime	75	18	No special finding
Cefpirome	242	289	No special finding
Amikacin	383	630	Inj. Alfakim 500mgInj. Lupamik 250mg
Vancomycin	270	148	No special finding
Teicoplanin	448	419	Inj. Targocid 400mg
Linezolid	29	9	No special finding
Aztreonam	216	114	Inj. Azom 1gm
Tigecycline	274	213	Inj. Tygacil 50mg
Colistin	426	703	Inj. Coly-Monas 2 miu,Inj. Coly-Monas 4.5 miu
Piperacillin Tazobacatam	1568	1756	Inj. Biopiper TZ 4.5MG ,Inj. Zosyn 4.5mg

The DDD Indicator

The DDD Data gives an idea about the average utilization for a drug. A comparative review may be observed from the table and graphs.

UTILISATION IN DDD=NUMBER OF PACKAGESUSED (provided by Pharmacy) *** NUMBER OF DDD PACKAGES (**dosage mentioned)

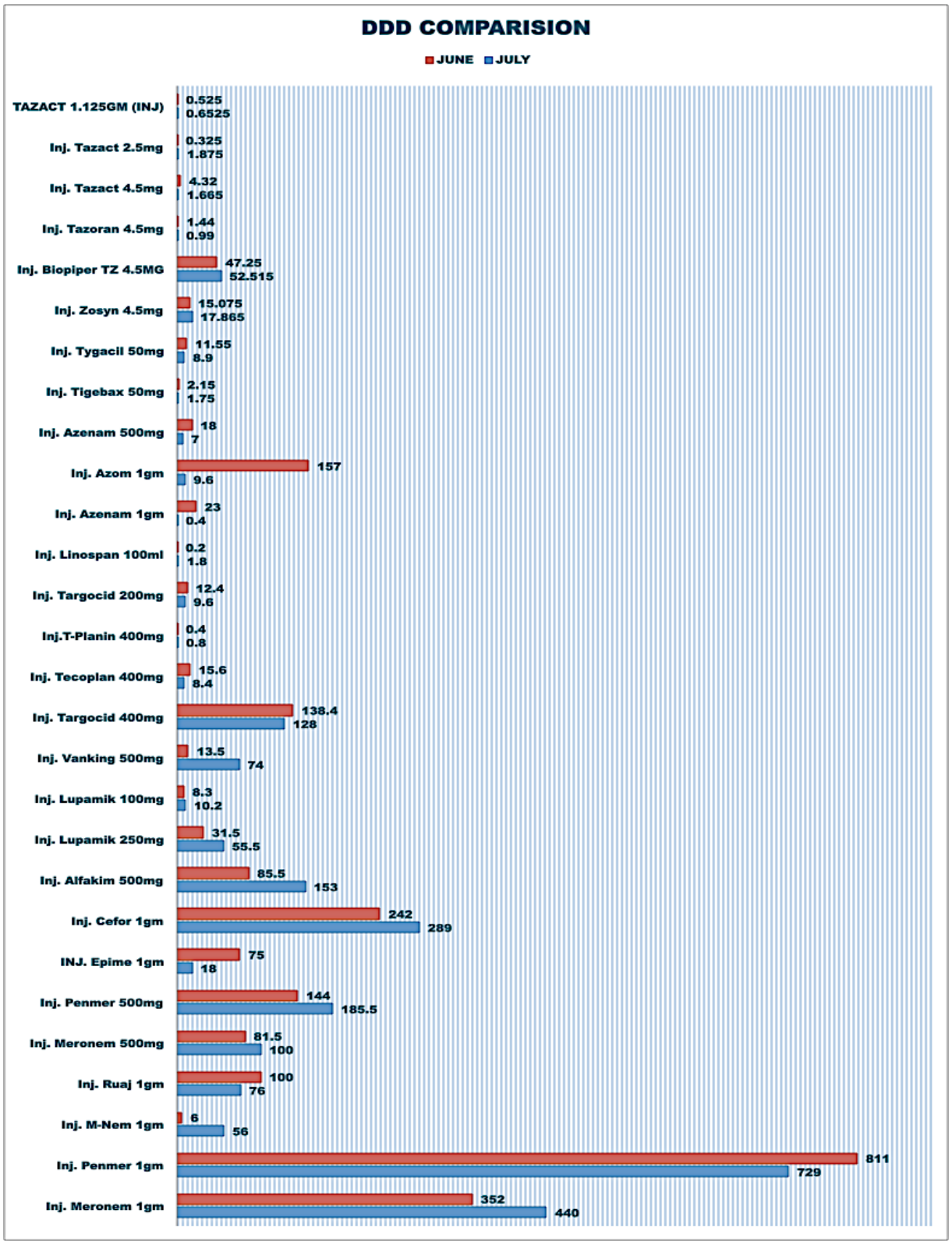

Figure 5: Shows Comparative Defined Daily Dose for Restricted antibiotics (Grams) **DDD Calculations and comparative study of restricted drugs.All drugs compared were converted in Grams.**

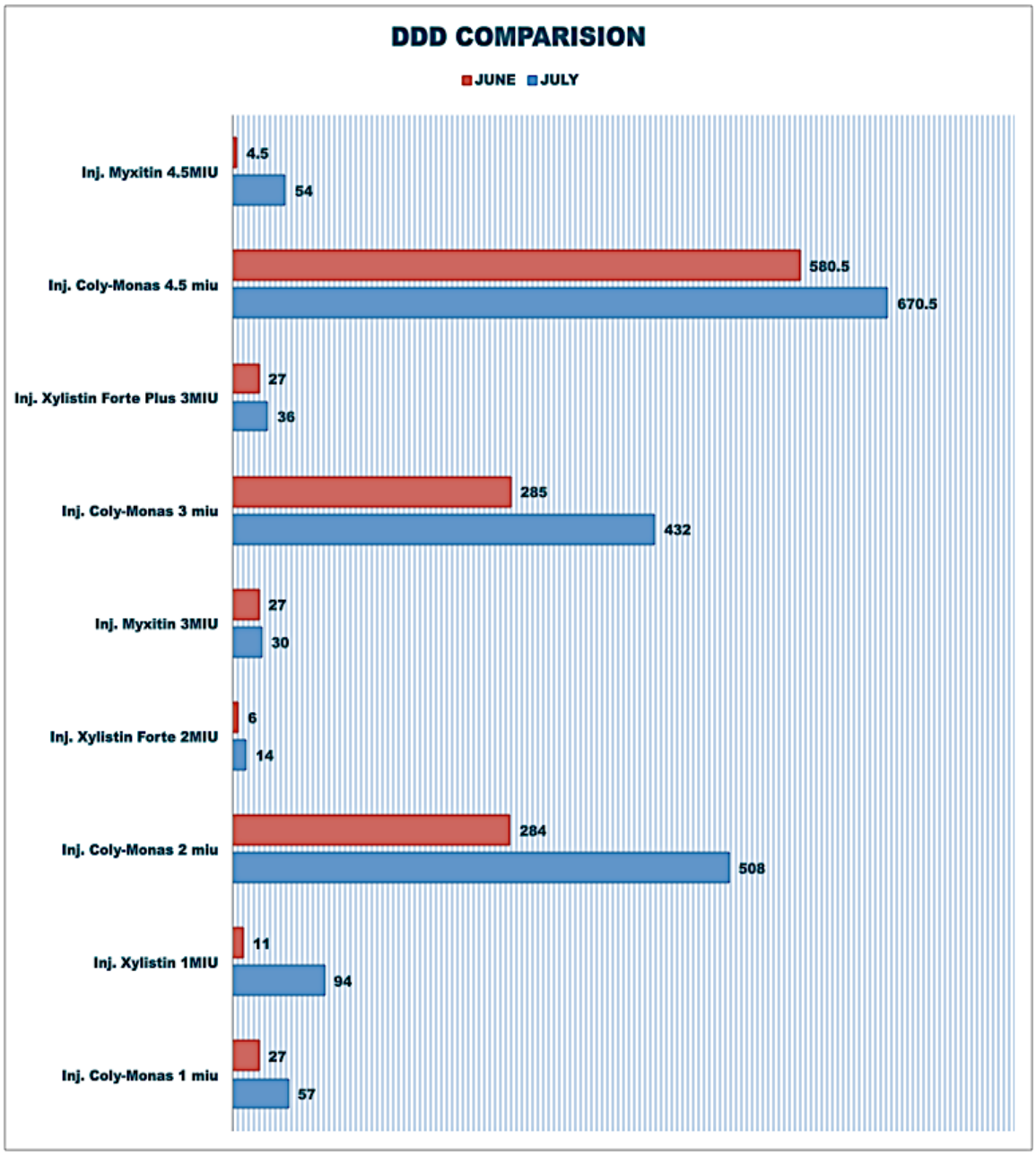

Figure 6 Comparative Defined Daily Dose for Restricted antibiotic Colistin (MIU)

DISCUSSION

There may be more detailing done in context of corrective and preventive actions suggested as given below

Corrective actions suggested-

Total of 68.3% compliance was observed but scope of improvement may be with permission to be granted by nodal officer in the restricted drug entry system with drop down menu including Infectious disease specialist's name too. In 1.7% compliant cases requirement of clarification on viral pneumonia antibiotic prescription policy is suggested as many cases of pneumonia are received by hospital.

A total of 31.7% non compliant cases were observed

Table 3- Shows observations with recommendations of non-compliant cases

1	In 14.2% cases the pediatric dosage was not mentioned in the policy for which a separate section on pediatrics patients should be made. Dosage formulas (young's rule and Clark's rule) should be mentioned.
2	Pediatric and newborn sepsis policy, or pre post surgical guidelines showed 0.8% of non-compliant cases, a high no. Of sepsis cases are received hence guidelines should also be framed on sepsis policy and pediatric sepsis.
3	Pediatric fever profile management and usage on restricted antibiotics elaboration would increase the utility of policy by 0.8%. Pediatric policy needs to be framed with guidance from pediatric staff.
4	The Mild/Moderate/Severe categories and dosage were not mentioned in the data entry system .To assess compliance of prescription is tough through clinical data in retrospective audits. The electronic data entry portal may be added up with options of Mild / Moderate / Severe Infection for increasing compliance by 2.5%. This would make data entered similar to categories mentioned in policies.
5	2.5% non-compliance was mentioned in condition when compliance was there with correct usage of antibiotic policy but dosage not mentioned in data entry. So data entry is in treatment given should be made a mandatory entry to understand compliance. In case of medicine prescribed not guided. (As in case with Amikamycin). The usage may be discussed with clinical staff and may be included in policy
6	3.3% Non-compliance was also found due to dosage not mentioned in data entry, which should be made mandatory for good assessment.
7	Post surgical complication and medication found for 0.8% cases may be clarified further .The references for pre and post surgical cases may be detailed more with reference from a senior consultant in every department to.
8	For better understanding of the dosages Antibiogram reference may be used to understand resistance, to improve compliance by 0.8%
9	In 1.7% cases the Clinical data entry was found incomplete which is requirement .The clinical data acts as a justification to medication prescribed and should be mentioned in detail
10	In 0.8% cases non compliance was due to Colistin prescription was not mentioned in policy, unlike many other essential medicine, detailing is recommended for same
11	Conditions in which antibiotic is not to be taken should also be mentioned for fever profile. This would be corrective to 1.7% non compliance observed due to fever Profile cases requiring no antibiotic but only palliative treatment,
12	1.7% cases non-compliance resulted from guidelines on fever of unknown origin. Details should be mentioned as many patients are prescribed restricted medicines in fever of unknown origin but no guidelines are present to understand them.

Preventive actions-

1.A Target form should be designed which may be circulated by mails / through Google form to analyze GAP found in the difference between Policy requirements perception, expectation and knowledge of antibiotic policy.

2.Following the steps may make the Annual review on antibiotic policy below-

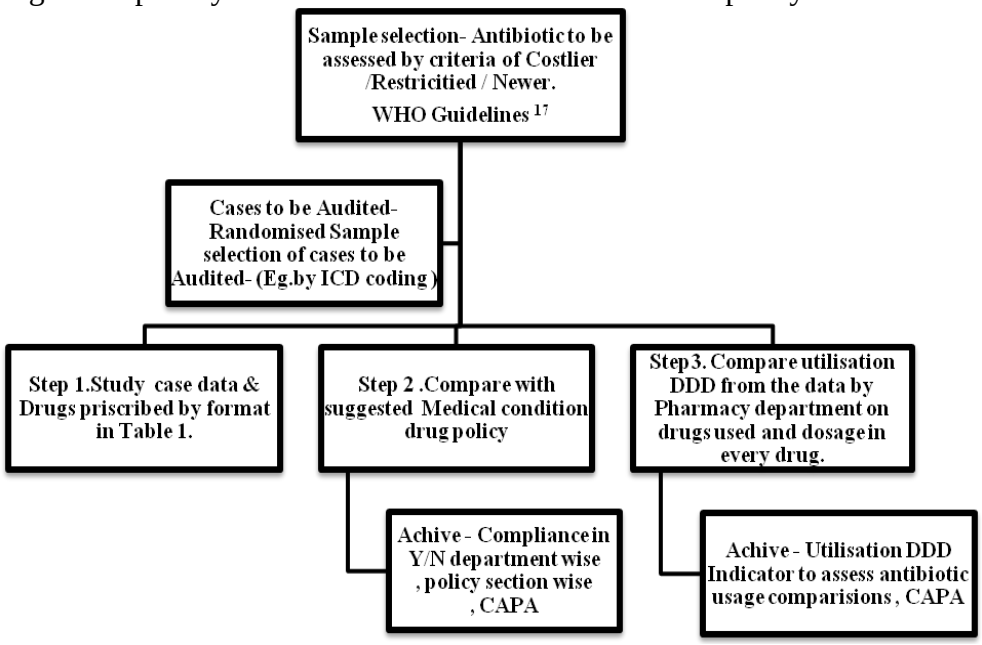

Figure 7. Suggested steps for annual review of antibiotic policy

CONCLUSION

The Doctors were found to be following guidelines of antibiotic policies majorly which was shown in 68.3% compliance but the reason of 31.7 % of non-compliance was found due to the guidelines not mentioned in the policy. The suggested corrective actions and preventive actions on Pediatric, Fever profiles and corresponding usage of drugs, conditions where no drugs are not to be used, are required. I.T. system entries as – MILD/ MODERATE/ SEVERE

cases and DDD would increase compliance. The steps mentioned in figure 7 including the DDD formula with rapid cycle analysis wound lead to elaborate and enriching results on corrections and preventive actions required. In brief of study more than the clinical compliance the issue was found in the detailing of the policy has been suggested by the finding.

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REFERENCES

1. Ministry of Health & Family Welfare, Government of India. National Policy for containment of Antimicrobial Resistance. Directorate General of Health Services, Delhi. October 2018. Available from: https://mohfw.gov.in/sites/default/files/3203490350abpolicy%20%281%29.pdf
2. Vlahovic-Palcevski V, Morovic M, Palcevski G. Antibiotic utilization at the university hospital after introducing an antibiotic policy. European journal of clinical pharmacology. 2000 Apr 1; 56(1): 97-101.
3. Dancer SJ, Kirkpatrick P, Corcoran DS, Christison F, Farmer D, Robertson C. Approaching zero: temporal effects of a restrictive antibiotic policy on hospital-acquired Clostridium difficile, extended-spectrum β-lactamase-producing coliforms and meticillin-resistant Staphylococcus aureus. International journal of antimicrobial agents. 2013 Feb 1; 41(2): 137-42.
4. Löffler C, Böhmer F. The effect of interventions aiming to optimise the prescription of antibiotics in dental care - a systematic review. PloS one. 2017 Nov 14;12(11):e0188061.
5. Struelens MJ, Byl B, Vincent JL. Antibiotic policy: a tool for controlling resistance of hospital pathogens. Clinical microbiology and infection. 1999 Mar; 5:S19-24.
6. Morris AM. Antimicrobial stewardship programs: appropriate measures and metrics to study their impact. Current treatment options in infectious diseases. 2014 Jun 1;6(2):101-12.
7. MacDougall C, Polk RE. Antimicrobial stewardship programs in health care systems. Clinical microbiology reviews. 2005 Oct 1;18(4):638-56.
8. Ansari F, Gray K, Nathwani D, Phillips G, Ogston S, Ramsay C, Davey P. Outcomes of an intervention to improve hospital antibiotic prescribing: interrupted time series with segmented regression analysis. Journal of Antimicrobial Chemotherapy. 2003 Nov 1;52(5):842-8.
9. Global Antibiotic Resistance Partnership (GARP)-India Working Group. Rationalizing antibiotic use to limit antibiotic resistance in India+. The Indian journal of medical research. 2011 Sep;134 (3):281.
10. Deshmukh AC, Ghadlinge MS, Tamboli SB, Deshmukh JB, Chhabra RR. Study of rationality and utilization pattern of antimicrobials in ear, nose, throat outpatient department of Tertiary Care Hospital, Nanded. International Journal of Basic & Clinical Pharmacology. 2017 Jan 19;4(4):734-8.
11. Sundaran, S., Reghu, A., Janardhanan, A., Das, C. M., Raju, T., & Hassan, U. A. (2018). study on antibiotic utilization pattern for urinary tract infection at a tertiary care hospital in calicut. World journal of pharmacy and pharmaceutical sciencesVolume 7, Issue 4, 1147-1154
12. Laxminarayan R, Malani A. Extending the cure: policy responses to the growing threat of antibiotic resistance. Earthscan; 2007.
13. Wiersinga WJ, Bonten MJ, Boersma WG, Jonkers RE, Aleva RM, Kullberg BJ, Schouten JA, Degener JE, Janknegt R, Verheij TJ, Sachs AP. SWAB/NVALT (Dutch Working Party on Antibiotic Policy and Dutch Association of Chest Physicians) guidelines on the management of community-acquired pneumonia in adults. Neth J Med. 2012 Mar; 70(2): 90-101.
14. Aldeyab MA, Kearney MP, McElnay JC, Magee FA, Conlon G, Gill D, Davey P, Muller A, Goossens H, Scott MG, ESAC Hospital Care Subproject Group. A point

prevalence survey of antibiotic prescriptions: benchmarking and patterns of use. British journal of clinical pharmacology. 2011 Feb; 71(2): 293-6.
15. Charani E, Cooke J, Holmes A. Antibiotic stewardship programmes-what's missing?. Journal of antimicrobial chemotherapy. 2010 Sep 16; 65(11):2275-7.
16. Antimicrobial Stewardship (AMS) Policy for Your Practice - HSE.updated on November 2012. Available from: https://www.hse.ie/eng/services/list/2/gp/antibiotic-prescribing/antibicrobial-stewardship-audit-tools/ Sep 16, 2018
17. Adopted from World Health Organisation. (2011). Step-by-step approach for development and implementation of hospital and antibiotic policy and standard treatment guidelines. Available from: http://apps.searo.who.int/PDS_DOCS/B4691.pdf?ua=1
18. ICD10Data.2018.Available from: https://www.icd10data.com/ICD10CM/Codes
19. WHO (2018). Essential medicines and health products.(Internet) DDD Indicators.p2. Updated 2018. Available from: http://www.who.int/medicines/regulation/medicines-safety/toolkit_indicators/en/index1.html#.W9bfx4uCz1I.gmail
20. Owens R, Jones LF, Moore M, Pilat D, McNulty C. Self-Assessment of Antimicrobial Stewardship in Primary Care: Self-Reported Practice Using the TARGET Primary Care Self-Assessment Tool. Antibiotics. 2017 Aug 16;6(3):16.
21. Gould IM. A review of the role of antibiotic policies in the control of antibiotic resistance. Journal of Antimicrobial Chemotherapy. 1999 Apr 1;43(4):459-65.
22. Government of India (2017). National Action Plan on Antimicrobial Resistance (NAP-AMR) 2017–2021 The Ministry of Health & Family Welfare (MoHFW),WHO.India.p4.Availablefrom:http://www.searo.who.int/india/topics/antimicrobial_resistance/nap_amr.pdf
23. Wyatt TD, Passmore CM, Morrow NC, Reilly PM. Antibiotic prescribing: the need for a policy in general practice. Bmj. 1990 Feb 17;300(6722):441-4.
24. Fujita K, Murono K, Yoshikawa M, Murai T. Decline of erythromycin resistance of group A streptococci in Japan. The Pediatric infectious disease journal. 1994 Dec;13(12):1075-8.
25. Nowak R, Rachel, Hungary sees an improvement in penicillin resistance. (Science (New York, NY), 1994 Apr 15 ;264(5157):364
26. Seppala H, Klaukka T, Vuopio-varkila J, Muotiala A, Helenius H, Lager K, Huovinen P. The effect of changes in the consumption of macrolide antibiotics on erythromycin resistance in group A streptococci in Finland. The New England journal of medicine. 1997 Aug 14;337(7):441-6.
27. Arason VA, Kristinsson KG, Sigurdsson JA, Stefansdottir G, Molstad S, Gudmundsson S. Do antimicrobials increase the carriage rate of penicillin resistant pneumococci in children? Cross sectional prevalence study. Bmj. 1996 Aug 17;313(7054):387-91.
28. McElnay JC, Scott MG, Sidara JY, Kearney P. Audit of antibiotic usage in a medium-sized general hospital over an 11-year period. Pharmacy World and Science. 1995 Nov 1; 17(6): 207-13
29. Bonhoeffer S, Lipsitch M, Levin BR. Evaluating treatment protocols to prevent antibiotic resistance. Proceedings of the National Academy of Sciences. 1997 Oct 28; 94(22): 12106-11.

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