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Impact of Rational Antibiotic Use on Antimicrobial Resistance Pattern in Pediatric ICU

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Abstract
Background and Objectives: *There is ever growing increase in antimicrobial resistance worldwide mostly due to injudicious and irrational use of antimicrobials in health care institutions and probably due to lack of knowledge among health care professionals about antimicrobial resistance to add to this there is a constant stagnation in development of newer antimicrobials.ICU's represent the heaviest antibiotic burden within hospital often described as 'factory creating and amplifying antibiotic resistance. We decided to conduct this before and after study to test the feasibility of a clinical ASP with respect to effect on resistance pattern in pediatric ICU in our hospital with the purpose of finding out the change in resistance pattern with implementation of antimicrobial stewardship programme .*
Methods: *This study was a prospective before and after study design which was divided into 3 phases over a span of 12 months. A pre- implementation audit (phase 1) was conducted for 1st 3 months studying various prescription practices that were being followed in ICU and general observation. Antimicrobial stewardship was implemented in phase 2 for a period of 6 months. After the implementation of ASP in PICU, a similar audit on antimicrobial prescription and usage was done in next three months (phase 3) and theresults compared with the audit of pre-implementation period.*
Results: *Our study was designed to note effect of antimicrobial stewardship on antimicrobial resistance pattern. Our findings revealed that there was a significant reduction in multidrug resistant (MDR) organisms after implementation of antimicrobial stewardship programme (ASP) (from 58% to 17 % between two phases).*
Keywords: *antimicrobial stewardship, antimicrobial resistance, multi drug resistant.*

Introduction

There is ever growing increase in antimicrobial resistance worldwide mostly due to injudicious and irrational use of antimicrobials in health care institutions and probably due to lack of knowledge among health care professionals about antimicrobial resistance to add to this there is a constant stagnation in development of newer

antimicrobials.[1] The main purpose of antimicrobial stewardship programme is to optimize antimicrobial use with maximum impact on subsequent development of antimicrobial resistance[2]

According to a WHO report, *Escherichia Coli* and *Klebsiella pneumoniae* in majority of world have over 50% resistance to 3rd generation cephalosporins and fluoroquinolones[3]. Antibiotic resistant organisms are not only becoming increasingly difficult to treat but also lead to increased treatment costs, longer duration of hospital stay and in some cases even death; over 30% of deaths have been attributed to antimicrobial resistance (AMR).The effectiveness of any drug is jeopardized by development of tolerance and resistance to that drug from the time it was first employed.

ICU's represent the heaviest antibiotic burden within hospital often described as 'factory creating and amplifying antibiotic resistance.(3) ICU's in emerging economies report notably higher prevalence of extended spectrum betà-lactamase (ESBL) producers and carbapenam resistant organisms.[4][5] The increasing AMR possess significant challenge to patient safety and management especially in intensive care units.[6] Therefore it is amply clear that judicious use of antibiotics is an important measure to limit AMR and its subsequent complications. This concept led to the development of antimicrobial stewardship programs (ASPs) to assist in optimal selection, dosage and duration of antibiotic treatment so as to improve patient safety and outcome and decrease resistance. Most of the studies on ASP are in adults and that too from developed countries. Emerging economies contribute significantly to the burden of AMR, mainly due to indiscriminate use, and poor prescribing guidelines. To add to this the higher sickness level of patients, and coexisting co- morbidities like malnutrition, pushes clinicians toward frequent empiric use of antibiotics. We therefore decided to conduct this before and after study to test the feasibility of a clinical ASP with respect to effect on resistance pattern in pediatratic ICU in our hospital.

Materials & Methods

This study was a prospective before and after study design which was divided into 3 phases over a span of 12 months. A pre- implementation audit was conducted for 1st 3 months studying various prescription practices that were being followed in ICU and general observation were made on prevailing antimicrobial resistance pattern, and methods being undertaken to prevent emergence of antimicrobial resistance. This audit was on a structured pre-designed proforma (appendix)

A stewardship programme 'ASP' was implemented in PICU over a period of 6 months following 1st phase .The residents were on the very 1st day of the PICU rotation about technique and need of hand washing, other hygienic measures during procedure and patient care, donning and doffing of universal precautions and various critical care bundles (including VAP, BSI, CLABSI etc.). The message was disseminated with help of posters, pamphlets, power point presentations, didactic lectures (in formal and informal settings), electronic communication to resident groups and mock codes. Updates on antibiotic prescribing, antibiotic resistance, and infectious disease management were provided and queries of resident were discussed and addressed. Similarly weekly classes for nursing staff were also taken on topics as described above. A checklist to follow in each patient was provided to both doctors and nurses Injudicious use of antimicrobials was strongly discouraged. Posters and written instructions pertaining to general hygiene and precaution before contacting patient in isolation rooms were pasted on doors. Nurses were also encouraged to take basic hygiene classes of parents and attendants. Common clinical infectious syndromes treated in PICU (e.g., pneumonia, diarrhea, CLABSI, VAP, UTI), specific/ pathogens, specific antimicrobial agents and clinical pathway were outlined and protocolized. Use of Vancomycin, Colistin, and

Amphotericin were restricted. It was ensured that before initiation of these drugs the indication was reviewed with a senior consultant either in person or over phone. Feedbacks as external reviews of antibiotic therapy by an expert in antibiotic use were also obtained. After the implementation of ASP in PICU, a similar audit on antimicrobial prescription and usage was done in next three months and the results compared with the audit of pre-implementation period (3 months),

Results

A total of 99 children admitted to PICU during phase I received empirical antibiotics for longer than 24 hours and were enrolled in this phase. The mean ± SD (range) and median (IQR) age of children enrolled in phase I was 3 ± 3.3 (1 month to 12 years) and 1 (3 months to 4 years) respectively. Out of the 99 children started on empirical antibiotics, 35(35.4%) required empirical upgradation for various reasons like clinical/radiological worsening, persistent fever etc. and in 28(28%), antibiotics were upgraded in response to specific culture reports. In remaining 36(36%) no change in antibiotic regimes were made. It was noted that 26(26%) patients grew organism in their cultures and of these 19(58%) were MDR and remaining 8(42.1%) were resistant to a single drug.

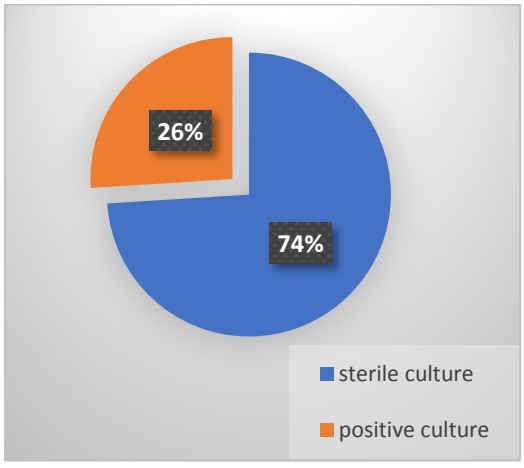

Fig. 1: No. of culture positive patients

During the post implementation phase A total of 89 children admitted to PICU during phase III received empirical antibiotics for longer than 24 hours and were enrolled in the phase. Out of the total of 89 patients evaluated 50(56.2%) were boys an 39(43.8%) were girls with boys:girls of 1.2. The mean ± SD (range) and median (IQR) age of children enrolled in phase III was 4 ± 3.3 (1 month to 12 years) and 3 (1.3 to 6.5) years respectively. It was noted that 23(26.2%) patient grew organism in their cultures and out of these 4(17%) were MDR and remaining 19(83%) were resistant to single drug The incidence of MDR organisms in Post ASP phase was significantly less than in pre-implementation phase (17% vs 58% ; p=0.010)

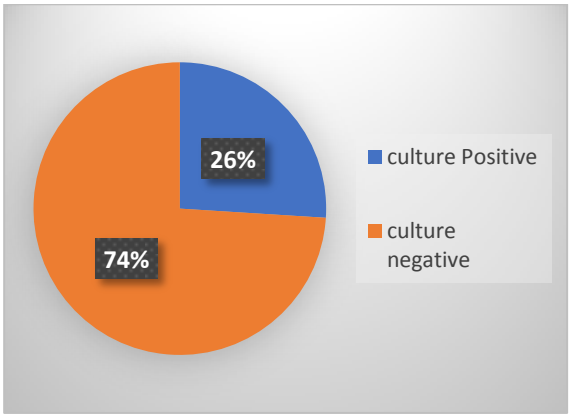

Fig.2: Number of culture positive patients

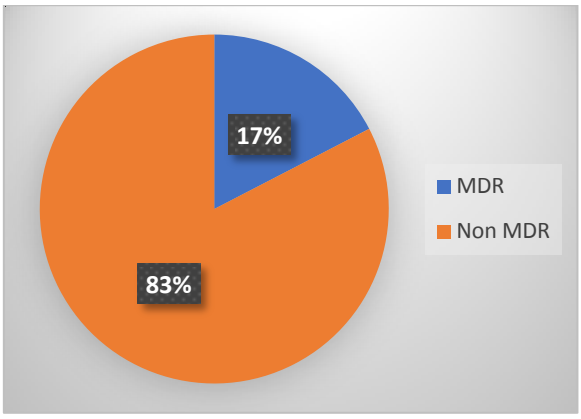

Fig.3: Resistance pattern among culture positive patients

Comparison between pre and post implementation phase

The incidence of MDR organisms in Post ASP phase was significantly less than in pre-implementation phase (17% vs 58%; p=0.010)

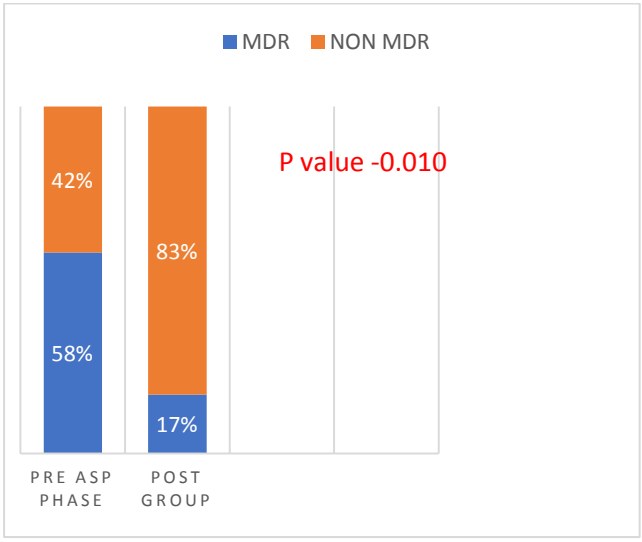

Fig.5. Comparison of incidence of MDR in pre and post ASP cohort

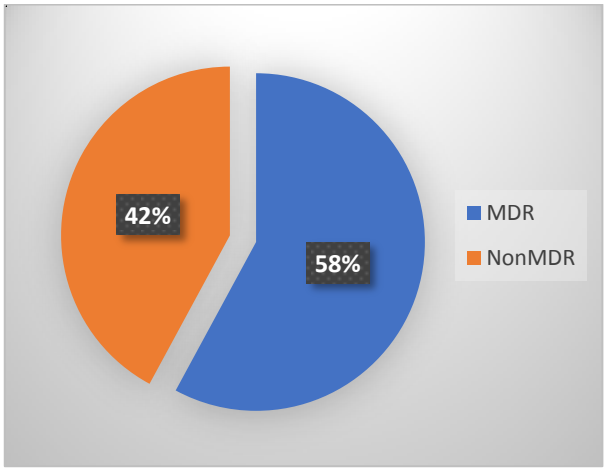

Fig. 6: Resistance pattern among culture positive patients

Discussion

Our study was designed to note effect of antimicrobial stewardship on various antimicrobial resistance pattern. Our findings revealed that there was a significant reduction in multidrug resistant (MDR) organisms after implementation of antimicrobial stewardship programme (ASP) (from 58% to 17 %between two phases). Our findings are in concordance with Ma et al. who showed similar decrease in MDR organisms from 48% to 29%(P=0.001) after implementation of antimicrobial stewardship.[7] Wu et al. in their study also showed a significant change in antimicrobial resistance pattern in gram positive (p=0.013) and gram negative bacteria (p=0.001) between pre and post ASP phases[8]. Similar findings of significantly reduced resistance pattern in gram positive and gram negative bacteria were reported by Raymond et al.[9] Allegranzi B et al. also described decrease in resistance of *Staph. Aureus* (93 % vs 73%) and *Pseudomonas* (67% vs 29%) after changing the ongoing antimicrobial practices (10). Hou D et al in their study demonstrated a 40 % decrease in antimicrobial resistance after implementation of antimicrobial stewardship program[11]. However some contradictory reports regarding resistance pattern has also been reported; Morrill HJ et al observed no change in resistance pattern after implementation of ASP[12]. Our findings along with observations of others reiterate the fact that AMR is linked to excessive antibiotic use and reduces with decrease in antibiotic use.

Conclusion

We found that there is a significant reduction in resistance pattern with significant decrease in number of MDR (multidrug resistant) cases following successful implementation of antimicrobial stewardship programme

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