Antimicrobial Stewardship Program Implementation in a Medical Intensive Care Unit at a Tertiary Care Hospital in Saudi Arabia

مستشفى الملك فيصل التخصصي ومركز الأبحاث
King Faisal Specialist Hospital & Research Centre
Gen. Org. مؤسسة عامة

eahp european association of hospital pharmacists

Marwa Amer, Post Graduate Year 1 (PGY1) Resident, Nada Al Qadheeb Pharm.D., BCPS, FCCP, Wafeeq A. Mahmood, MD, FRCPC, Abdulrazaq S. Al-Jazairi, Pharm.D, FCCP, BCPS {AQ Cardiology}, Nathem S. Akhras, PharmD, BCPS {AQ Cardiology}

BACKGROUND

◆The inappropriate antimicrobials use, that is currently observed in intensive care units (ICUs) results in increased selection of resistant pathogens, health care cost, as well as significant impact on patients' mortality [1].

◆ Published data from Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) has shown antimicrobial stewardship program (ASP) implementation to minimize emergence of antimicrobial resistance associated with inappropriate antimicrobial use [2-5].

◆ King Faisal Specialist Hospital & Research Center (KFSHRC), ICUs in particular, presents one setting where such a program is essential to promote antimicrobials standard of practice, and improve patients' clinical outcomes [1-5, 6,7].

OBJECTIVE

Primary Objective: Compare the appropriateness rate of empirical antibiotics therapy (initial and final) before and after implementation of "proactive" antimicrobial stewardship program. Initial appropriateness was defined as the first intervention initiated by physicians while final appropriateness was assessed following ASP team interventions.

Secondary Objectives: The rate of clostridium difficile-associated diarrhea (CDAD), frequency of multi-drug resistant organisms (MDR) including methicillin-resistant staphylococcus aureus (MRSA), extended spectrum beta-lactamases producing strains (ESBL), and physicians' acceptance rate for the ASP recommendations.

METHODS

Study Design: This is a comparative, non-randomized, historical-controlled study. Adult medical ICU patients were enrolled, in a prospective fashion, under active ASP arm and compared with historical patients who were admitted to the same unit before the ASP implementation (Figure 1)

Setting: KFSHRC-Riyadh is an 894-bed multi-facility, multi-entity tertiary care hospital with 20 adult male and female beds at medical intensive care unit (MICU). Adult critically ill patients (> 14 years old) were defined as those requiring mechanical ventilation (invasive or noninvasive); and/or those with a fraction of inspired oxygen (FiO2) concentration ≥ 0.6; and/or those requiring intravenous infusion of inotropic or vasopressor medications.

Patients' Selection: " Please refer to figure 2,3 and table 1 "

Inclusion criteria:

◆Patients on five targeted antibiotics piperacillin/tazobactam, imipenem/ cilastatin, meropenem, vancomycin, and tigecycline.

◆No official Infectious disease (ID) service consultation.

Exclusion Criteria:

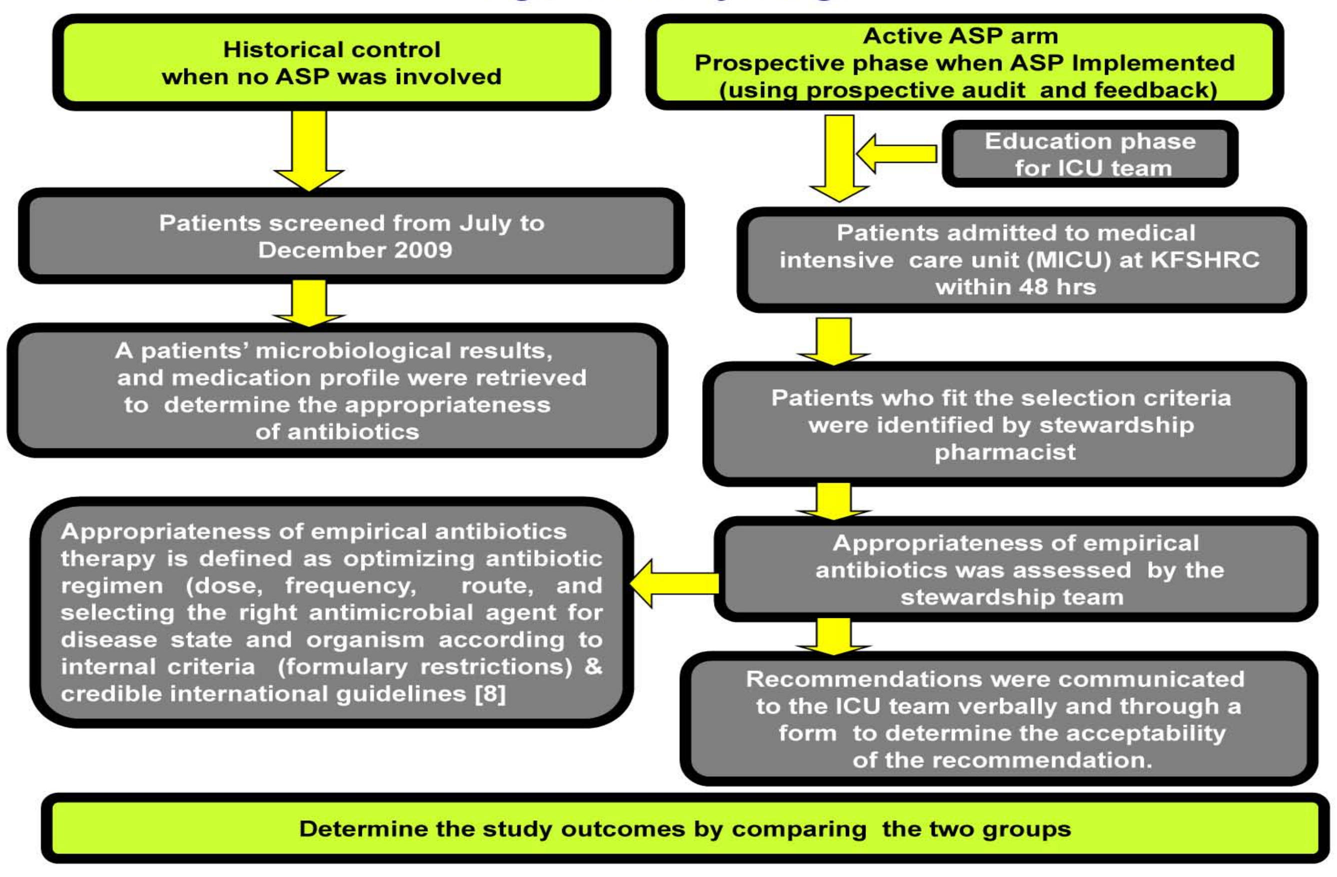
◆Patients were excluded if they didn't fit the previously mentioned inclusion criteria

Statistical analysis:

◆ A sample size of 73 participants (49 in historical control arm and 24 in active ASP arm) based on alpha of 0.05 would yield 90 % power to detect a difference of 20 % between groups for the primary outcome.

◆Descriptive data were analyzed by using chi-square test for categorical data and student t-test for continuous data. The commercial software SPSS system (version 19) was used for statistical analyzes.

Figure 1 : study design



RESULTS

Figure 2 : study population

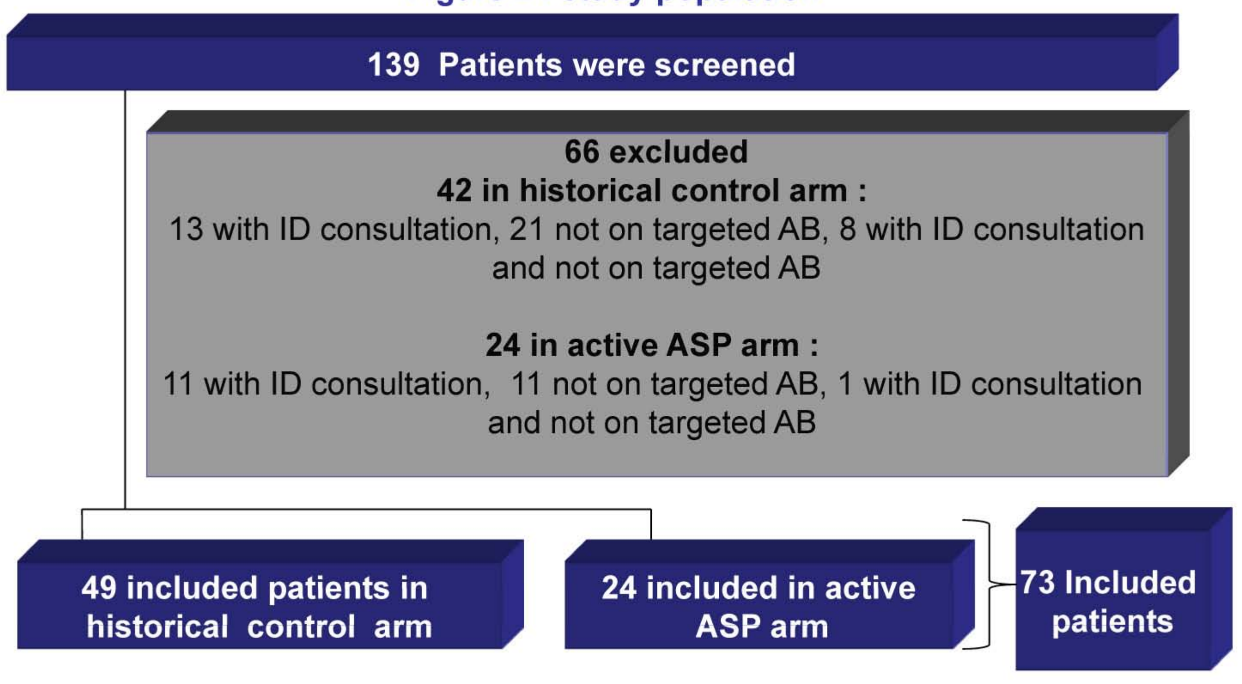
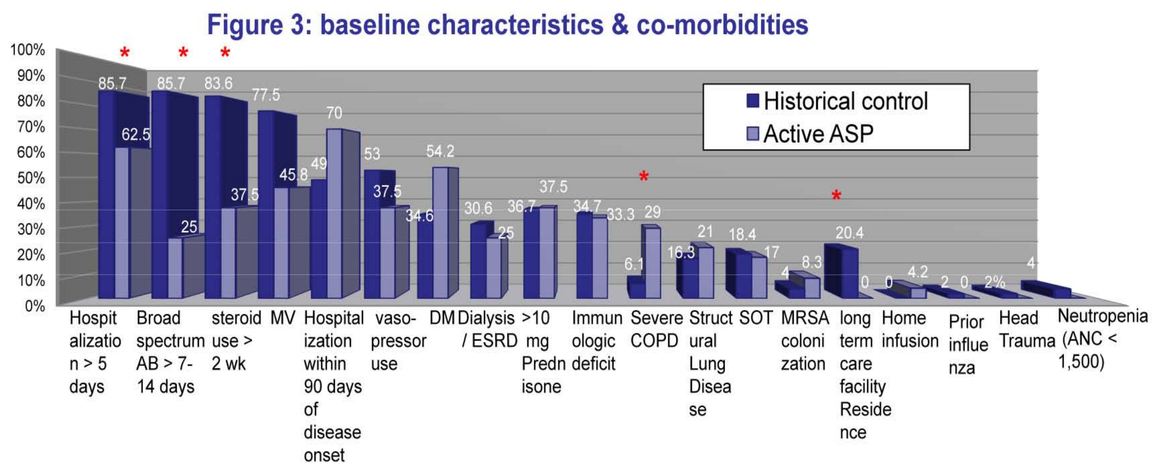


Table 1: baseline characteristics & demographics

Arm	Control N= 49	Active ASP N=24	P value
Gender Male, no. (%) Female, no. (%)	31 (63 %) 18 (37 %)	15 (63%) 9 (38%)	0.949
Age (mean years) (interquartile range)	52.37 30	59.75 24	0.087
APACHE II score* (mean)	10.51	19.38	<0.0001

*APACHE II score was calculated within 24 hours of ICU admission

Figure 3: baseline characteristics & co-morbidities



- No significant differences between historical control and active ASP arm except for the factors presented with red asterisks (P < 0.05)
- COPD: chronic obstructive pulmonary disease, DM: diabetes mellitus, ESRD: end stage renal disease, MV: mechanical ventilation, SOT: solid organ transplant

Table 2: primary and secondary outcomes

Arm	Control N= 49	Active ASP N=24	P value
Primary outcome (*empirical* antibiotics therapy appropriateness)			
Initial appropriateness *			
Appropriate, no. (%)	15 (30.6%)	5 (20.8%)	0.379
Inappropriate, no. (%)	34 (69.38%)	1 9 (79.1%)	
Final appropriateness *			
Appropriate, no. (%)	15 (30.6%)	24 (100%)	0.0001
Inappropriate, no. (%)	34 (69.38%)	0 (0 %)	
Secondary outcome			
Clostridium difficile-associated diarrhea (CDAD)	1 (2 %)	0 (0 %)	1
Microbiological outcome			
MDR, no. (%)	15 (30.6%)	2 (8.3%)	0.034
MRSA , no. (%)	2 (4.1 %)	0 (0 %)	1
ESBL, no. (%)	11 (22.4%)	3 (12.5%)	0.36
MRSA/MDR, no. (%)	1 (2%)	0 (0 %)	1
Physician acceptance rate for ASP recommendations	*Please refer to figure 4 "note section"*		
Patients' ICU course			
Deceased, no. (%)	16 (32.65%)	4 (16.7%)	0.150
Transferred to floor, no. (%)	29 (59.2%)	20 (83.3%)	0.091
Transfer to another hospital, no. (%)	1 (2%)	0 (0 %)	1
Still active at the MICU, no. (%)	3 (6.1 %)	0 (0 %)	0.55

* Initial antibiotics appropriateness was defined as the first intervention initiated by physicians "*please refer to table 3 for the reasons of initial antibiotics inappropriateness* " while final antibiotics appropriateness was assessed following ASP team I interventions "*please refer to figure 4 for interventions made in the active ASP arm to overcome inappropriateness*"

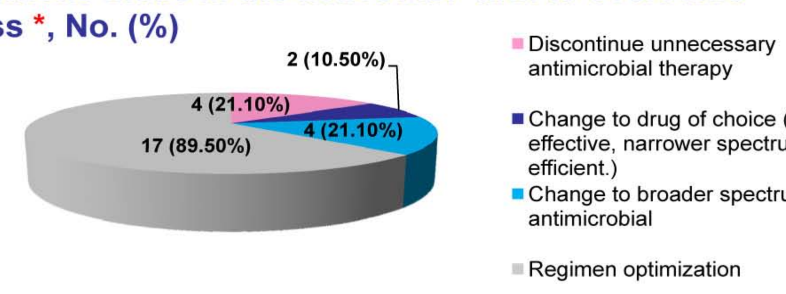
Table 3 : Reasons of initial antibiotics inappropriateness, no.

Arm	Control * N= 49	Active ASP ** N=24	P value
No current treatment for positive culture	9	0	0.02
No indication (e.g. colonization) for current treatment	5	0	0.15
Inadequate empiric coverage for indication	14	10	0.37
Excessive empiric coverage for indication	2	2	0.6
Resistant to current antibiotic	12	1	.02
Regimen excessive (failure to de-escalate)	8	0	.04
Regimen inadequate (wrong dose or frequency)	6	10	.006
Total	56	23	

* In the historical control arm: each patients with initial inappropriate AB(34 pts) had ≥ 1 reason for inappropriateness

** In the active ASP arm: each patients with initial inappropriate AB (19 pts) had ≥ 1 reason for inappropriateness

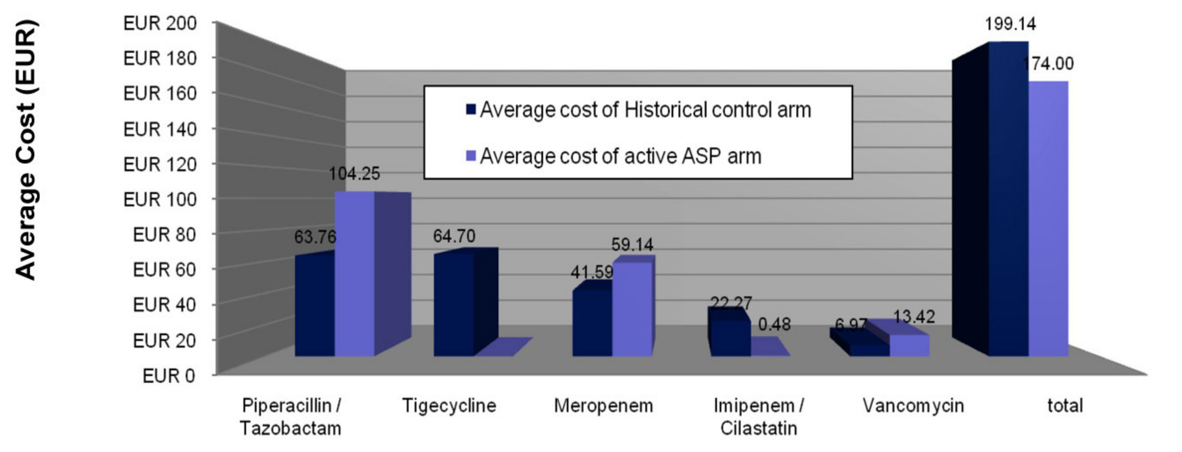
Figure 4: interventions made in the active ASP arm to overcome inappropriateness *, No. (%)



Note: A total of 27 interventions were made, with an acceptance rate of 26 (96.3 %) and 1 (3.7 %) accepted with minor modifications

* In the active ASP arm: each patient with inappropriate AB (19 pts) had ≥1 interventions

Figure 5: direct cost of antibiotics utilization per patient in both groups



DISCUSSION

◆ASP implementation in the MICU at tertiary care hospital resulted in optimal utilization of antibiotics. The significant appropriateness of antibiotics in the active arm is contributed by ASP and the proactive nature of its implementation.

◆A positive outcome was noted on emergence of multi-drug resistant organisms (MDR), however, the rate of clostridium difficile-associated diarrhea was comparable between the groups.

◆The results of our study are consistent with the Cochrane meta-analysis which showed a positive impact of interventions for optimization of antibiotics use and MDR emergence [9].

◆Limitations of our study included lack of randomization, single institution's population, and difficulty in controlling confounding variables.

CONCLUSION

Antimicrobial stewardship program is important in many healthcare settings; the ICU presents one setting where it is greatly needed. Therefore, utilizing such data can improve clinical outcomes and the cost-effectiveness of antimicrobial therapy by increasing the likelihood that the appropriate antibiotic treatment will be prescribed.

Acknowledgment:
Ted Morton, Pharm.D. BCPS (AQ-ID), King Saud University, Ali Al-Zahrani, Dep Exec Dir, Research center, Salah Al-Gain and Abdelmuniem Eldali, statistician and epidemiologist, , Research center, Mohammed Al sharhan, KFSH resident.

Disclosure:
Authors of this presentation have nothing to disclose concerning possible financial or personal relationship with the commercial entities that may have a direct or indirect interest in the subject matter of this presentation.

References availale upon request