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Role of Microbiological Culture Results in Optimizing Antimicrobial De-escalation: Evidence from *Escherichia coli* and MSSA Infections

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ABSTRACT

De-escalation of antibiotic therapy represents a fundamental pillar of antimicrobial stewardship efforts designed to limit the emergence and spread of drug resistance. The present research was carried out to determine how positive culture and sensitivity findings for *Escherichia coli* or Methicillin-sensitive Staphylococcus aureus (MSSA) influence the de-escalation of prescribed antibiotics. A total of 256 patients with confirmed infections were included in this prospective observational investigation. Clinical specimens were largely obtained from purulent material at infection sites for microbial identification and subsequent susceptibility profiling. Patient-level data were retrieved from medical charts and included demographic characteristics, specimen origin, the pathogen identified, and whether the antimicrobial regimen was initiated empirically or tailored definitively according to culture results. Data processing was performed with SPSS. Of the 256 recovered microorganisms, 138 (53.9%) were MSSA and 118 (46.1%) were *E. coli*. MSSA isolates displayed complete (100%) susceptibility to cefoxitin, oxacillin, vancomycin, fosfomycin, and colistin, and greater than 90% susceptibility to linezolid (95.3%), tigecycline (93.1%), chloramphenicol (92.2%), and amikacin (90.2%). *E. coli* strains were fully susceptible only to fosfomycin, with susceptibility levels exceeding 90% for colistin (96.7%), polymyxin-B (95.1%), and tigecycline (92.9%). Empiric therapy was characterized by frequent administration of cefoperazone+sulbactam (151), amikacin (149), ceftriaxone (33), metronidazole (30), and piperacillin+tazobactam (22). Once susceptibility data became available, the antibiotics most commonly selected for *E. coli* included intravenous meropenem (34), amikacin (34), ciprofloxacin (29), and cefoperazone+sulbactam (25). For MSSA infections, linezolid (48), clindamycin (30), intravenous cefoperazone+sulbactam (16), and amikacin (15) were frequently prescribed. Overall, antibiotic consumption fell by 23% among *E. coli* cases and by 43% in the MSSA group. Access to culture-sensitivity data enabled antimicrobial de-escalation, particularly reducing reliance on broad-spectrum agents. Hence, individual hospitals should formulate local guidance rooted in facility-specific antimicrobial susceptibility trends while curtailing unwarranted empiric use of broad-spectrum antibiotics.

Keywords: Antimicrobial resistance, Antimicrobial stewardship, Culture sensitivity reports, Definitive treatment, Empirical treatment, De-escalation

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Introduction

The 10th International Conference on Emerging Infectious Diseases (EID) estimated that emerging pathogens are implicated in roughly 15% of all human infections [1]. Drug-resistant organisms are frequently the culprits behind healthcare-associated infections, a problem that has intensified with the widespread overuse of broad-spectrum antibiotics [2-6]. This is particularly alarming given the slowdown in both novel antibiotic development and the

repurposing of older agents [3, 7]. Additionally, the Centers for Disease Control and Prevention (CDC) has determined that between 20% and 50% of all antibiotic prescriptions in US critical care settings are either superfluous or ill-chosen [8]. It is therefore imperative to optimize antimicrobial prescribing to tackle the mounting tide of nosocomial infections caused by resistant bacteria [9]. Susceptibility profiles and microbiological data should guide the selection of suitable antibiotics to refine prescribing practices within healthcare facilities [10, 11]. Likewise, any empirical administration of broad-spectrum agents must be based on local antibiogram findings and later modified in light of culture sensitivity results [12-14]. Among the strategies proposed to enhance antibiotic use are de-escalation and active monitoring of therapeutic effectiveness, both of which have the potential to reduce costs [15]. This type of oversight can support hospital stewardship teams in striking a balance between delivering effective treatment and limiting the emergence and spread of resistant organisms [8].

Antibiotic de-escalation is a crucial pillar of stewardship, encouraging rational prescribing by either limiting the spectrum of antimicrobial coverage or directing treatment to an identified pathogen, ultimately lowering the risk of antimicrobial resistance (AMR) [16-18]. This strategy is also associated with reductions in inappropriate prescribing, hospitalization costs, length of stay, and mortality [19]. De-escalation is considered both safe and effective in the management of numerous infectious diseases (IDs), including hospital-acquired and community-acquired pneumonia, bacteremia, urinary tract infections (UTIs), sepsis with concomitant bloodstream infection (BSI), severe sepsis among neutropenic patients, and pneumococcal bacteremia [20-25]. Nevertheless, a host of barriers contribute to inconsistent de-escalation practices across hospitals in different nations. These obstacles include a shortage of diagnostic resources, insufficient training, inadequate multidisciplinary coordination, and a reluctance to de-escalate in critically ill individuals who are already responding favorably to broad-spectrum treatment [26-28].

Methicillin-sensitive Staphylococcus aureus (MSSA) commonly exhibits high levels of resistance and is the most prevalent pathogen underlying various hospital-acquired infections, making such infections particularly difficult to treat [29]. Together, MSSA and *Escherichia coli* (*E. coli*) constitute the most frequently encountered organisms in orthopedic infections [30]. MSSA is also responsible for both nosocomial and community outbreak infections, with multidrug resistance further complicating clinical management [31, 32]. *E. coli*, likewise, ranks among the common pathogens in animals [33]. Distinct pathogenic strains of *E. coli* cause a range of infections, including UTIs, bloodstream infections, wounds, and other complications [30]. Moreover, *E. coli* contributes to the burden of hospital-acquired infections. For this reason, any de-escalation that follows empiric treatment, anchored in local antibiograms, must be implemented, where applicable, once culture results are available, to forestall complications associated with resistant MSSA and *E. coli* infections [34]. In Pakistani healthcare environments, however, there is currently an overreliance on broad-spectrum antibiotics as initial empiric therapy [35]. This trend is concerning, not least because, to our knowledge, no published information currently exists on antibiotic de-escalation practices within Pakistani hospitals. That said, efforts have been undertaken to strengthen antibiotic use through the implementation of antimicrobial stewardship programs (ASP) in Pakistan [36, 37]. With this context in mind, we set out to evaluate the effect of positive culture sensitivity reports for *E. coli* or MSSA on subsequent antibiotic prescribing behavior in a prominent teaching hospital in Pakistan. We believe that the findings will offer value not only to this institution but also to hospitals across Pakistan and beyond as they strive to curb AMR for these two leading nosocomial pathogens in alignment with the National Action Plan to mitigate AMR in Pakistan [38].

Materials and Methods

Study design and study setting

This prospective, observational investigation was conducted in the orthopedic ward of Ghurki Trust Teaching Hospital (GTTH) and aimed to assess the impact of positive culture reports for MSSA and *E. coli* on antimicrobial de-escalation from September 2020 through December 2020.

Ghurki Trust Teaching Hospital, a 600-bed teaching institution, is one of Pakistan's largest charitable hospitals, holds certification from the Pakistan Center of Philanthropy, and maintains a particular focus on orthopedic care. Accordingly, the successful introduction of stewardship initiatives within this facility to foster de-escalation could potentially serve as a model for the broader Pakistani healthcare landscape.

Ethical clearance was secured from the hospital administration and the Research Ethics Committee, Discipline of Pharmacy Practice, Faculty of Pharmacy, University of Lahore (REC/DPP/FOP/8-2020) before the study was initiated. Informed consent was obtained either from the patients themselves or, for those under 18 years, from

their parents or legal guardians before data collection. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Inclusion and exclusion criteria

Subjects whose clinical specimens returned positive culture results for *E. coli* or MSSA while admitted to the orthopedic unit were eligible for enrollment. Every participant had already been initiated on empirical antibiotics, and treatment was subsequently tailored when culture and sensitivity data were available. Individuals were not considered for participation if their medical documentation was incomplete, if death occurred before culture results became available, if hospital discharge occurred before data capture, if cultures yielded microorganisms other than *E. coli* or MSSA, if culture results were negative, or if the collected samples were judged to be contaminated. Patients managed in wards outside of orthopedics were also excluded from the study.

Sample for culture sensitivity

Specimens destined for pathogen identification and antimicrobial susceptibility assays were collected directly from the infected sites of study participants. The obtained material was then placed into dedicated transport containers and delivered promptly to the microbiology laboratory at room temperature. Each patient with a confirmed positive culture was systematically followed to document the evolution of their antibiotic regimen, the overall duration of their inpatient stay, and the drug sensitivities of the drugs administered. It is noteworthy that each patient provided a single culture report rather than multiple samples.

Data collection

A standardized, preformatted data collection sheet was used to collect information from patients in the orthopedic ward. The tool recorded demographic details, history of prior surgical interventions, clinical diagnosis, microbiological profiles, and the antimicrobials prescribed both empirically and as definitive therapy after susceptibility results were returned. Data collection was performed by institutional staff following patient consent. The structure of the data collection instrument was informed by published literature and the substantial experience of the co-investigators working within this domain.

Antibiotic de-escalation was defined as the act of narrowing therapy—moving from a broad-spectrum empiric antimicrobial regimen to a more targeted, narrow-spectrum alternative—guided by a reassessment of the patient's clinical trajectory, microbiological findings, and inflammatory marker trends [39].

Statistical analysis

Data were processed using the Statistical Package for Social Sciences (SPSS), version 21.0. Study outcomes were summarized as frequencies and percentages, and results were presented in both graphical and tabular formats.

Results and Discussion

Demographic characteristics of patients

The baseline demographic attributes of the enrolled population are outlined in **Table 1.** This study encompassed 256 patients, of whom a substantial majority were male (n = 159, 62.1%), with an average age of 65 years. Surgical site infections were the dominant clinical presentation (59.4%), and the most frequently observed comorbid illness was diabetes mellitus (n = 57, 22%). Clinical specimens were obtained from various infected sites, with pus as the predominant sample type (n = 171, 66.8%). Of the 256 microbiological isolates recovered, 118 were classified as *E. coli* (46.1%) and 138 as MSSA (53.9%).

Table 1. Demographic characteristics of selected patients.

Characteristics	Percentage (%)	Frequency (N)
Gender		
Male	62.1	159
Female	37.9	97
Age group		
Less than 18 years	11.0	28

19–40 years	12.7	32
41–60 years	15.4	39
61–85 years	63.1	161
Sample		
Pus	66.8	171
Urine	21.1	54
Tissue	6.6	17
Dead Bone	2.3	6
Blood	1.6	4
Tracheal secretion	1.2	3
CSF	0.4	1
Isolated microbes		
MSSA	53.9	138
E. coli	46.1	118
Past surgical history		
Yes	59.4	152
No	40.6	104
Ward		
Orthopedic	100	256
CRP		
No	84.4	216
Yes	15.7	40
ESR		
Yes	15.2	39
No	84.8	217
Other complications		
Diabetes	22.2	57
Hepatitis C	13.6	35
Hypertension	11.7	30
TB	3.1	8
IHD	2.3	6
Hepatitis B	1.5	4

Abbreviations: CSF = Cerebrospinal Fluid; MSSA = Methicillin-sensitive *Staphylococcus aureus*; *E. coli*, *Escherichia coli*; NICU = Neonatal Intensive Care Units; CRP = C-reactive protein; ESR = Erythrocyte Sedimentation rate; TB = tuberculosis; IHD = Ischemic Heart Disease.

Sensitivity pattern of antibiotics

The antibiotic susceptibility data are displayed in **Table 2.** Against *E. coli*, fosfomycin demonstrated the highest activity (100%), followed by colistin (96.7%), polymyxin-B (95.1%), tigecycline (92.9%), and chloramphenicol (80.5%). For MSSA, complete susceptibility (100%) was recorded for cefoxitin, oxacillin, fosfomycin, vancomycin, and colistin. The identification of linezolid-resistant variants within the MSSA collection is a worrisome finding.

Table 2. Antibiotic sensitivity pattern of *E. coli* and MSSA isolates.

Antibiotics	***MSSA***	***E. coli***
	Sensitivity n (%)	**Sensitivity n (%)**
Cephalosporin		
Cefoxitin	130/130 (100)	NT
Cefazolin	(85.7)	NT
Cefuroxime	30/47 (63.8)	5/88 (5.7)

Cefoperazone + Sulbactam	NT	18/30 (60)
Ceftriaxone	26/45 (57.8)	8/100 (8)
Ceftazidime	6/16 (37.5)	9/29 (31)
Cefipime	5/16 (31.3)	11/52 (21.2)
Cefixime	5/17 (29.4)	2/58 (3.5)
Cefoperazone	NT	1/23 (4.4)
Quinolones		
Levofloxacin	32/45 (71.1)	28/82 (34.2)
Ciprofloxacin	49/92 (53.3)	17/74 (23)
Norfloxacin	26/55 (47.3)	10/44 (22.7)
Ofloxacin	6/11 (54.5)	6/29 (20.7)
Nalidixic	NT	7/40 (17.5)
Penicillin		
Oxacillin	8/8 (100)	NT
Piperacillin + tazobactam	10/17 (58.8)	71/111 (71)
Co-Amoxiclav	13/25 (52)	12/86 (14)
Penicillin	30/104 (28.9)	NT
Ampicillin	12/46 (26.1)	7/104 (6.7)
Carbapenems		
Imipenem	12/17 (70.6)	81/101 (80.2)
Ertapenem	NT	49/69 (71)
Meropenem	18/24 (75)	81/108 (75)
Macrolide		
Clarithromycin	16/19 (84.2)	NT
Erythromycin	89/133 (66.9)	NT
Aminoglycoside		
Amikacin	101/112 (90.2)	87/103 (84.5)
Gentamicin	85/108 (78.7)	51/96 (53.1)
Tobramycin	39/59 (66.1)	30/59 (50.9)
Oxalidone		
Linezolid	121/127 (95.3)	NT
Glycopeptide		
Vancomycin	122/122 (100)	NT
Teicoplanin	46/66 (69.7)	NT
Lincomycin		
Clindamycin	96/125 (76.8)	NT
Phosphonic acid Antibiotics		
Fosfomycin	3/3 (100)	48/48 (100)
Polymyxin		
Colistin	11/11 (100)	58/60 (96.7)
Polymyxin B	11/12 (91.7)	58/61 (95.1)
Antimycobacterials		
Rifampicin	51/58 (87.9)	NT
Tetracycline		
Tigecycline	54/58 (93.1)	52/56 (92.9)
Minocycline	33/38 (86.8)	20/44 (45.5)
Tetracycline	43/80 (53.7)	17/80 (21.3)
Sulfonamide		
Nitrofurantoin	NT	13/14 (76.5)
Co-Trimoxazole	21/83 (25.3)	12/81 (14.8)
Others		
Chloramphenicol	71/77 (92.2)	33/41 (80.5)

Abbreviation: NT = Not Tested.

Antibiotic prescribing trend

With respect to empiric prescribing for both *E. coli* and MSSA infections, heavy reliance was placed on cefoperazone+sulbactam (151), amikacin (149), ceftriaxone (33), metronidazole (30), and piperacillin+tazobactam (22). After susceptibility results were available, the therapeutic agents most frequently selected for *E. coli* included intravenous meropenem (34), amikacin (34), ciprofloxacin (29), and cefoperazone+sulbactam (25). For MSSA infections, the antibiotics predominantly prescribed following sensitivity testing were linezolid (48), clindamycin (30), intravenous cefoperazone+sulbactam (16), and amikacin (15). When both groups were combined, antibiotic consumption fell by 23% in the *E. coli* cohort and by 43% in the MSSA cohort. A comprehensive breakdown of antibiotic utilization during the empiric and definitive phases of treatment, after susceptibility results were reviewed, is presented in **Table 3.**

Table 3. De-escalation of antibiotics.

Antibiotics	**Total**			***MSSA***			***E. coli***		
	Before	**After**	**% Change**	**Before**	**After**	**% Change**	**Before**	**After**	**% Change**
Inj. Cefoperazone+Sulbactam[a]	151	41	**↓73**	98	16	**↓84**	53	25	**↓53**
Inj. Amikacin[a]	149	49	**↓67**	95	15	↓84	54	34	**↓37**
Inj. Ceftriaxone[a]	33	15	**↓55**	14	8	**↓43**	19	7	**↓63**
Inj. Metronidazole[b]	30	10	*↑67*	9	4	**↓56**	21	6	**↓71**
Inj. Piperacillin+Tazobactam[c]	22	19	**↓14**	0	0	0	22	19	**↓14**
Inj. Meropenem[c]	20	37	*↑85*	8	3	**↓63**	12	34	*↑183*
Inj. Vancomycin[d]	16	7	**↓56**	9	7	**↓22**	7	0	**↓100**
Inj. Ciprofloxacin[a]	14	11	**↓21**	5	3	**↓40**	9	8	**↓11**
Tab. Co-amoxiclav[a]	13	7	**↓46**	11	5	**↓55**	2	2	0
Inj. Moxifloxacin[a]	13	3	**↓77**	5	1	**↓80**	8	2	**↓75**
Tab.Ciprofloxacin[a]	11	32	*↑191*	8	11	*↑38*	3	21	*↑600*
Inj. Cefotaxime[a]	10	1	**↓90**	0	0	0	10	1	**↓90**
Inj. Linezolid[d]	7	9	*↑29*	5	9	*↑80*	2	0	**↓100**
Inj. Co-amoxiclav[a]	6	4	**↓33**	2	3	*↑50*	4	1	**↓75**
Inj. Ampicillin[a]	6	0	**↓100**	2	0	**↓100**	4	0	**↓100**
Tab. Linezolid[d]	6	39	*↑550*	4	39	*↑875*	2	0	**↓100**
Inj. Clindamycin[a]	6	6	0	4	6	*↑50*	2	0	**↓100**
Inj. Imipenem + Cilastatin[c]	5	7	*↑40*	2	2	0	3	5	*↑67*
Inj. Levofloxacin[a]	3	15	*↑400*	1	6	*↑500*	2	9	*↑350*
Tab. Clindamycin[a]	3	24	**↓700**	3	24	*↑700*	0	0	0
Fosfomycin Sachet[a]	2	12	*↑500*	1	1	0	1	11	**↑1000**
Total	526	348	**↓34%**	286	163	**↓43**	240	185	**↓23**

Notes: [a]: Broad Spectrum, [b]: Narrow Spectrum, [c]: Extended Spectrum, [d]: Broad Spectrum only for Gram Positive microbes, otherwise Narrow Spectrum; ↓Reduce, ↑; Increase, Bold; Reduce, Italic; Increase.

Early pathogen identification, paired with proper antibiotic delivery, is vital to reducing the toll of infectious illnesses in terms of both illness and death [40]. Even with established recommendations, the regularity with which clinicians request culture reports remains suboptimal, a reality worsened by customary prescribing routines, reliance on personal clinical assessment, staffing limitations, laboratory capacity, and expense—challenges most acutely felt across low- and middle-income countries [41-44]. This deficit is consequential, as misuse of antimicrobials accelerates the propagation of resistant organisms and drives up associated illness, fatalities, and economic burden [45-47]. In addition, mounting resistance has shifted prescribing toward broader-spectrum agents even when a definitive pathogen is known [48]. Yet this is not an invariable rule; a report from South Africa noted that, when culture-sensitivity data were incorporated, 83% of antibiotic courses underwent subsequent modification [49]. The rollout of antimicrobial stewardship programs is now broadly advocated as a critical strategy to rein in inappropriate antibiotic consumption [50, 51]. A corresponding imperative thus exists to operationalize stewardship initiatives across Pakistan [52], in alignment with the ambitions of the country's National Action Plan (NAP) [38].

As far as we are aware, this is the first study originating in Pakistan to assess how positive culture-sensitivity results for *E. coli* or MSSA translate into antibiotic de-escalation. In our series, the majority of patients harbored *E. coli* and MSSA as causative agents of orthopedic infections. This pattern differs from findings in South India, where Methicillin-resistant Staphylococcus aureus (MRSA) prevailed in similar clinical settings [53]. Such regional discordance is likely due to differences in the distribution of pathogens and their distinct susceptibility profiles.

Our data revealed that fosfomycin retained complete (100%) activity against all *E. coli* isolates. By way of contrast, an Ethiopian investigation documented that *E. coli* showed the greatest sensitivity to nitrofurantoin (96.4%), norfloxacin (90.6%), and gentamicin (79.6%) [54]. Regarding MSSA, we observed excellent susceptibility to cefoxitin, oxacillin, fosfomycin, and colistin. Earlier national surveillance in Pakistan, however, had reported peak sensitivity of MSSA to vancomycin (100%), linezolid (98.9%), rifampicin (95.7%), and chloramphenicol (94.7%) [55]. The absolute (100%) oxacillin susceptibility we recorded, when juxtaposed with previously published national rates (91.7%) [55, 56], may reflect the progressively diminishing clinical use of this agent. Co-trimoxazole and nitrofurantoin, on the other hand, offered the weakest coverage against MSSA [57].

Turning to prescribing habits, the empirical landscape in our study was dominated by cefoperazone-sulbactam, amikacin, and ceftriaxone. Indian data, however, indicated that piperacillin/tazobactam was the leading empiric choice in orthopedic patients [41]. This variance may be attributable to the ample supply of cefoperazone + sulbactam within GTTH and its favorable local susceptibility profile, coupled with amikacin's robust anti-*E coli* spectrum. When transitioning to definitive treatment, meropenem and amikacin were the most frequently prescribed agents in our cohort, mirroring what has been reported elsewhere [41].

Several limitations of this work deserve mention. The observational framework meant that study pharmacists could not intervene to influence antibiotic selection by treating physicians. Additionally, our deliberate restriction to patients yielding cultures positive solely for MSSA or *E. coli* constrained the total sample size. Furthermore, Pakistan currently lacks nationally endorsed guidelines that explicitly link culture-sensitivity data to antibiotic prescribing decisions, which preclude comparison of our results against a domestic benchmark. Despite these caveats, we contend that our observations remain robust: the study demonstrated that culture-sensitivity reports can drive meaningful de-escalation while also curtailing antibiotic use and inpatient stays. Beyond this, the findings highlight an unequivocal need for formal antibiotic prescribing guidelines to promote effective therapy and reduce needless antibiotic exposure.

Conclusion

The evidence from this study underscores that susceptibility reports empower clinicians to streamline antibiotic therapy. Consequently, de-escalation practices merit wider adoption across both medical and surgical disciplines to combat antibiotic overuse and restrain the spread of resistance. Parallel efforts are needed to develop clear guidance on proper antibiotic use and to define which healthcare cadres may prescribe, topics we intend to explore in forthcoming investigations.

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Conflict of Interest: None

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