

Evaluation of Asymptomatic Bacteruria Management Before and After Antimicrobial Stewardship Program Implementation: Retrospective Study

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Research Article

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Abstract

Background

The Infectious Diseases Society of America (IDSA) recommends against screening for and/or treating asymptomatic bacteriuria (ASB). This study aims to evaluate the inappropriate use of antibiotics in ASB before and after Antimicrobial Stewardship Program implementation and advance towards its appropriate use.

Method

We performed a retrospective study of patients diagnosed with ASB from 2016 to 2019 at a tertiary hospital in Saudi Arabia. This study included hospitalized patients ≥ 18 years old who had a positive urine culture with no signs or symptoms of urinary tract infection and were on antibiotics for asymptomatic bacteriuria. We excluded pregnant women, solid organ transplant patients, patient on active chemotherapy, and patients about to undergo urological surgery.

Results

A total of 716 patients with a positive urine culture were screened . Among these, we identified 109 patients with ASB who were enrolled in our study. The rate of inappropriate antibiotic use was 95% during the study period. The implementation of the Antimicrobial Stewardship Program was associated with a significant reduction in the use of carbapenems ($P = 0.04$) and an increase in the use of cephalosporins ($P = .099687$). However, overprescribing antimicrobial agents was a concern in both eras. Approximately 90% of the microorganisms identified were gram-negative bacteria. Of those, 38.7% were multidrug-resistant strains.

Conclusion

The urine culture order in ASB is considered relatively small number; however, it showed a high rate of the inappropriate use of antibiotics when there is an order of urine culture in both era. ASP ought to focus on targeting the ordering physician, promoting awareness and/or organizational interventions that appear to reduce the incidence of overtreatment.

Introduction

Asymptomatic bacteriuria (ASB) refers to the isolation of $\geq 10^5$ colony-forming units [CFU]/mL or $\geq 10^8$ CFU/L of bacteria from an appropriately collected urine specimen in an individual with no signs or symptoms of urinary tract infection ^[1,2]. ASB is common, but its exact prevalence is highly variable. Patients with chronic indwelling catheters and spinal cord injuries have a very high prevalence of bacteriuria (100% and 50%, respectively) compared with that among healthy premenopausal women (1%) ^[1,2,10]. In 2019, the Infectious Diseases Society of America (IDSA) recommended against screening for and/or treating ASB with antibiotics unless patients are undergoing endoscopic urologic procedures

associated with mucosal trauma or are pregnant [1]. The inappropriate treatment of ASB has no positive impact on clinical outcomes and results in adverse events [1, 3, 7]. In recent years, the overprescribing of antibiotics for ASB has contributed to an increasing number of health care-related problems in clinical practice. A prospective study found that overtreatment of ASB was responsible for 17% of prescribed antimicrobials [9]. In fact, overtreatment of ASB led to several adverse effects, such as increased prevalence of multidrug-resistant (MDR) organisms, increased rates of *Clostridium difficile* infection (CDI) and long hospitalizations, all of which factors increase the costs of health care [2, 4, 5, 6]. In addition, previous studies have shown that MDR organisms are frequently found in ASB patients, with a prevalence of 16% [3, 4, 7]. These findings support the guideline recommendations against ASB treatment. ASB is a major concern worldwide, and few studies outline the types of antibiotics unnecessarily prescribed and the associated costs. The goal of our study was to evaluate the inappropriate use of antibiotics in ASB patients before and after the implementation of Antimicrobial Stewardship Program.

Methods

Study setting

We conducted a 4-year retrospective, descriptive study to determine the inappropriate use of antimicrobials in ASB patients at a tertiary hospital in Riyadh, Saudi Arabia. This study was approved by the institutional review board (IRB) of SFH.

Antimicrobial Stewardship Program implementation:

In 2018, Antimicrobial Stewardship Program (ASP) has been applied as one of the tools to fight microbial resistance and antimicrobial misuse. The aim was to focus on strategies that have most impact on decreasing antibiotics use and resistance such as antibiotics restriction and prospective audit and feedback. Logistics or supplemental strategies such as education and IV to oral switch are also assistants in achieving our ASP goals. We conduct annual infections control and antimicrobial stewardship symposium to educate clinician about appropriate use of antibiotics. In addition, several clinical guidelines were performed to and integrated in the system to help physicians choose the appropriate antimicrobial agents.

Data collection

The data were collected from January 2016 to December 2019. The list of patients who were diagnosed with a urinary tract infection (UTI) was obtained from the hospital information system (HIS) database. The data collected included patient name, medical record number (MRN), visit number, age, gender, drug name, dose, frequency, duration, date of treatment start and laboratory results. The criteria for selecting subjects were as follows: hospitalized patients age ≥ 18 years, with a positive urine culture and no signs or symptoms of urinary tract infection. The exclusion criteria included pregnancy, solid organ transplantation, active chemotherapy, and urological surgery.

Study Outcomes

This project sought to i) Evaluate the inappropriate use of antibiotics in ASB patients before and after Antimicrobial Stewardship Program implementation; ii) assess the gaps to reduce the incidence of overtreatment ; and iii) identify the type of unnecessarily prescribed antibiotics.

Statistical analysis

Descriptive included means and standard deviations or percentages as appropriate. The pharmacy intern group was compared to the standard of care using independent sample t-test for continuous variables and Fisher's exact test for categorical variables

Results

A total of 716 patients with a positive urine culture were screened. Among these, we identified 109 patients with ASB who were enrolled in our study. The median patient age was 65 years, and common comorbidities included hypertension (82%), diabetes myelitis (80%), and dyslipidemia (38%). (Table 1)

Table 1
Show characteristics of patients diagnosed with asymptomatic bacteriuria (ASB)

Patient characteristics	Total (N = 109)
Median age, in years, (range)	65 (11–98)
Female gender, n (%)	74 (68)
Urinary catheter, n (%)	64 (58.7)
Comorbidities	
Hypertension, n (%)	82 (75.2)
Diabetes mellitus, n (%)	80 (73.3)
Dyslipidemia, n (%)	38 (34.8)
Ischemic Heart Disease, n (%)	37 (33.9)
Neurological disease ^b , n (%)	32 (29.3)
Cerebrovascular Accident, n (%)	32 (29.3)
Chronic kidney disease, n (%)	25 (23)
Endocrine disease ^c , n (%)	13 (11.9)
Pulmonary disease ^d , n (%)	7 (6.4)
Urinalysis result	
Pyuria, n (%)	96 (88.0)
RBCs ^e in urine, n (%)	36 (33.02)
Leukocytes in urine, n (%)	100 (91.74)
^a ASB: Asymptomatic Bacteriuria;	
^b Neurological disease: Alzheimer's, Parkinson's, Dementia and Epilepsy.	
^c Endocrine disease: Hypothyroidism and Addison's disease.	
^d Pulmonary disease: Asthma and Chronic Obstructive Pulmonary Disease.	
^e RBCs= Red Blood Cell	

The most important clinically relevant finding was that 95% (n = 104) of ASB patients were inappropriately treated with antibiotics during the study period. Before ASP implementation, the rate was 96.6% (53/55) and after ASP was 94.4% (51/54). Approximately seventy-one patients (68%) were given

more than one unnecessary antibiotic either concomitantly or subsequently. Also, 59% of antibiotics were administered intravenously (IV), 30.4% were administered orally (PO) and 10.6% were converted from IV to PO.

The most commonly used class of antibiotics was cephalosporins (41.2%), followed by carbapenems (29%). (Table 2). Of the microorganisms identified in the urine, 90.20% were gram-negative bacteria, of those, 38.7% were MDR. The numbers of MDR cases from 2016–2018 and 2018–2019 were 27 (44%) and 18 (32%), respectively. (Table 3)

Table 2
 Evaluation of antimicrobial agents used, and microorganisms identified in ASB (N = 104)

Number of antimicrobial agents, n	151
Duration, mean	12 d
Route of administration, n (%)	89 (59)
IV ^a	46 (30.4)
PO ^b	16 (10.6)
IV to PO	
Type of antimicrobial agents, n (%)	
<i>Quinolones</i>	29 (19.2)
<i>β-lactam</i>	73 (48.3)
<i>Penicillin</i>	11 (7.28)
<i>Cephalosporin</i>	33 (21.85)
<i>2nd generation</i>	29 (19.21)
<i>3rd generation</i>	44 (29.14)
<i>Carbapenem</i>	1 (0.66)
<i>Vancomycin</i>	4 (2.65)
<i>Others</i>	
Microorganisms identified (N = 116)	

^aIV=intravenous; ^bPO= orally;

* Multidrug Resistance was 45 (38.7%) isolates in the urine

Number of antimicrobial agents, n	151
<i>Gram-positive, n (%)</i>	<i>11 (9.40)</i>
<i>Enterococcus</i>	7 (6.03)
<i>Coagulase negative staph</i>	2 (1.72)
<i>Streptococcus group B</i>	2 (1.72)
<i>Gram-negative, n (%)*</i>	<i>105 (90.2)</i>
<i>E. coli</i>	54 (46.55)
<i>K. pneumoniae</i>	23 (19.83)
<i>Pseudomonas</i>	13 (11.21)
<i>Citrobacter</i>	3 (2.59)
<i>others</i>	12 (10.35)
^a IV=intravenous; ^b PO= orally;	
* Multidrug Resistance was 45 (38.7%) isolates in the urine	

Table 3
Before and After Antimicrobial Stewardship Program Implementation

	Before ASPs (N = 53)	After ASPs (N = 51)	P Value
Number of antimicrobial agents per patient	1.3 (73/53)	1.5 (78/51)	NA
MDR, n (%)	27/61 (44%)	18/55 (32.7%)	0.20
Antimicrobial agents, n (%)			
Carbapenem	27/73 (40%)	17/78 (21.8%)	0.04
Cephalosporin	25/61 (37%)	37/78 (47.4%)	0.09
Quinolones	15/61 (20.5%)	14/78 (18%)	0.68
ASPs = Antimicrobial Stewardship			
MDR = Multi-drug Resistance			

Discussion

The mismanagement of ASB is a worldwide problem. Treatment of ASB is not only useless but also harmful [1, 3, 7, 8, 10]. We found that a small number of urine culture order was requested when the patient do not have signs and symptoms. This shows that the level of awareness in a physician is high and this practice complies with the stewardship.

Nevertheless, if the culture was requested, almost 95% of ASB cases were inappropriately treated with antibiotics, a finding that justifies this level of concern, and this rate remained alarmingly high even after the implementation of Antimicrobial Stewardship Program.

We found a relatively high proportion of ASB among patients who were female, of advanced age, diabetic, and who had hypertension. This is consistent with findings from other studies [2, 4, 3, 8].

A systematic review and meta-analysis concluded that female gender and the overinterpretation of some laboratory data (positive nitrites, pyuria, presence of gram-negative bacteria and cultures with higher microbial counts) are associated with inappropriate prescribing practices [3, 9]. In our analysis, we found a similar result.

E. coli, *Enterococcus* species, and *Candida* species are common bacterial and fungal colonizers of the urinary tract [16]. In our analysis, *E. coli* was the most common pathogen associated with ASB, followed by *K. pneumoniae* and *Pseudomonas*. Multidrug-resistant (MDR) bacteria are common in our patients (44% vs. 33% before and after ASP), a finding that could have an impact on the prescribing of antimicrobial agents for ASB.

Remarkably, cephalosporins was the most frequently used antibiotic class (41%), followed by carbapenems (29%) and quinolones. The inappropriate carbapenem prescribing practices might be affected by the high frequency of urine MDR isolates.

The implementation of the Antimicrobial Stewardship Program was associated with a significant reduction in the use of carbapenems ($P = 0.04$) and an increase in the use of cephalosporins ($P = .099687$). However, overprescribing antimicrobial agents was a concern in both eras.

Since the urine culture order for ASB is considered relatively small number, we aim to identify whom it was ordered by (eg., intern, resident) and target them in the stewardship. Furthermore, we plan to embed ASB educational lecture in our annual ASP conference to promote awareness among our healthcare providers and create an ASB protocol. Interestingly, the challenge of managing ASB appropriately may be surmountable with approaches such as identifying the ordering physician, promoting awareness and/or organizational interventions that appear to reduce the incidence of overtreatment.

The current study has some limitations. First, it was conducted in a single center with convenience sampling which may limit the generalizability of the findings.

Conclusion

The rate of inappropriate use of antibiotics in ASB is high in ordered urine culture. Targeting asymptomatic bacteruria management in Antimicrobial Stewardship Program might decrease the misuse of antibiotic, and we should focus on advocating awareness among healthcare providers and implementing stricter protocols.

List Of Abbreviations

CFU: colony-forming units

IDSA: Infectious Diseases Society of America

ASB: Asymptomatic Bacteruria

ASP: Antimicrobial Stewardship Program

MDR: Multidrug-resistant

Declarations

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by Security Forces Hospital Institutional Review Board.

Consent for publication: not applicable

Competing interests: The authors declare no conflict of interest. The funder had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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Informed Consent Statement: Informed consent was obtained from all participants

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