Original Article

Pattern of Empiric Antibiotic Use in Surgical Site Infection According to World Health Organization Access, Watch, Reserve Classification

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ABSTRACT

Surgical site infection (SSI) is a type of healthcare associated infection that may occur in any part of the body following any surgical procedure. The duration varies from 30 days for simple procedure to 1 year for any implant in situ. SSI increases patient mortality risk ranging from 2 to 11 times. The World Health Organization (WHO) developed the Access, Watch, Reserve (AWaRe) classification of antibiotics in 2019 to streamlining the use of antibiotics and thus contain antimicrobial resistance. The objective of this study is to identify and analyses pattern of the empirical antibiotic use in patients with surgical site infection based on the AWaRe classification. This prospective, observational study was conducted from July 2022 to June 2023 in Dhaka Medical College Hospital and Mugda Medical College Hospital, Dhaka, Bangladesh, among 186 patients with surgical site infections. Wound infection with cellulitis and suture abscesses were excluded. Pattern of empiric antibiotic use was recorded. Among the total of 186 patients, 88(47.3%) were males and 98(52.7%) were females; male-female ratio was 1:1.1. Out of 186 samples, 117 tested positive for bacterial culture that including 12 Gram-positive and 105 Gram-negative bacteria. Among SSI patients, 53(34.2%) received one antibiotic, while 95(61.3%) and 7(4.5%) received two and three antibiotics respectively. Distribution of prescribed empiric antibiotics was 30(57%), 18(34%) and 5(9%) from Watch, Access and Reserve respectively. However, when combination of antibiotics was used, the most common combination was Access with Watch group (93.1%). Among all the empiric antibiotics, resistance to cefixime (97.4%) was highest among the isolated bacteria, whereas antibiotic resistance to other agents showed cefuroxime (96.6%), ceftriaxone (94.7%), amoxiclav (85%) and ciprofloxacin (72%), clindamycin (66.7%). Linezolid was 100% sensitive to isolated gram-positive bacteria whereas colistin was 91.3% to gram-negative bacteria. Resistance to Access group of antibiotics was found 83%, followed by Watch and Reserve group of antibiotics 77% and 21.3% respectively.

Keywords: *Surgical site infection, empiric antibiotic, AWaRe classification, antimicrobial resistance*

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INTRODUCTION

Surgical site infection (SSI) is the most frequent health care associated infection (HAI) in low- and middle-income countries according to the World Health Organization (WHO). It can affect up to 1/3 of the surgical patients. The increasing rate of SSI affects all types of procedure, including clean surgery. Among the common type of nosocomial infections in surgical patients, SSI is the 2nd most common hospital acquired infection in Europe and the United States.[1] The rate of SSI ranges between 2.5 to 41.9% globally.[2] SSI is defined as the wound created by an invasive

surgical procedure. It can occur 1 month after a surgical operation or a procedure, either at or near the incisional site.[3] The most common causes of SSI are inadequate supply of personal protective equipment, lack of training on infection control measures, absence of hospital policy on infection control and inadequate hand washing practices. Excessive nursing workload is also responsible for SSI.[4] The host factors including patient's age, length of surgery, preoperative shaving of operation site, hypothermia & comorbidities e.g., diabetes, obesity etc. affect SSI.[5] Many exogenous and endogenous microorganisms that enter into the operative wound during the surgery are responsible for SSI. The most common identified organisms are *Staphylococcus aureus, Streptococci, Enterococci, E. coli, Klebsiella, Enterobacter, Citrobacter, Acinetobacter, Proteus* etc.[6] The incidence of SSI is increasing due to some multidrug-resistant organisms like *methicillin* resistant *Staphylococcus aureus* (MRSA), coagulase negative *Staphylococcus*, vancomycin resistant *Enterococci* (VRE), *Escherichia coli, Acinetobacter baumanii, Pseudomonas aeruginosa etc*.[7]

Antibiotics have the potential impact on SSI as it reduces the incidence of SSIs.[8] Use of inappropriate and unnecessary antibacterial agent causes resistance and increase hospital stay, economic burden to patients and family also.[9] The World Health Organization (WHO) developed the AWaRe classification of antibiotics in 2019 and classified 180 antimicrobials on the WHO Essential Medicines List (EML) using the Access, Watch, and Reserve (AWaRe) category. In 2019, WHO also set a specific target of at least 60% of antibiotic consumption being from Access group.[10] It is used as a tool to guide safe and effective prescription of antimicrobials. The drugs in the 'Access' (green) group of antimicrobials are first- or second-line agents meant to be widely available, as they are recommended in the empiric treatment of several common infectious diseases. The antibiotics in the Watch (amber) group, such as carbapenems, have shown a greater risk of selecting for resistance and so are recommended as first or second line drugs for a limited number of indications. The third Reserve (red) group comprises antibiotics of last resort that should only be used in specific life-threatening clinical scenarios.[11] Inappropriate or over prescription of antibiotics are greatly increasing worldwide and associated with the increasing prevalence of antimicrobial resistant (AMR) strains.[12] This study aimed to observe the usage pattern of empirical antibiotics based on the WHO AWaRe classification in surgical site infection. This study would also guide the selection of the most effective empirical antibiotic and thus help to reduce unnecessary use of broad spectrum antibiotics and also reduction in the selection pressure of antibiotic resistance.

METHODS

This prospective, observational study was conducted among 186 admitted patients with SSIs in Obstetrics & Gynaecology, Surgery and Orthopaedics Departments of Dhaka Medical College Hospital and Mugda Medical College Hospital, Dhaka, Bangladesh, between June 2022 and July 2023. Patients above 18 years and any surgical operation done within last 30 days were included in the study. Wound infections with cellulitis or suture abscesses were excluded. Data were collected through a face-to-face interview by using a previously designed semi-structured questionnaire. Pus/wound swabs collection was done before starting of the empiric antibiotic therapy.

Wound/pus samples were collected from patient with the help of a sterile swab stick. Normal saline was used to wash the wound prior to collection of pus to remove contaminating materials like debris, dried exudates and dressing residue. In case of dry wound, the swab was moistened with sterile saline. Strict precaution was taken to prevent the swab being contaminated from the surrounding skin. Tip of the swab was applied to wound with gentle pressure and rotated between fingers in a zig-zag pattern across the entire wound. In case of a large wound at least 1 to 2 cm area was sampled and materials from both the wound bed and wound margin were collected. It was then transferred to the specimen container. The specimen was transported to the Microbiology laboratory of the respective institute for processing as soon as possible.

The pus samples were inoculated onto blood agar, MacConkey agar & chocolate agar media immediately and were incubated at 35 ± 2^0C aerobically for 24 hours. The isolated organisms were recognized by standard methods after incubation, preliminary

detection of bacteria was based on colony characteristics such as hemolysis on blood agar, pink color production for lactose fermentation and other physical characteristics of the colony. Gram-negative rods were recognized by performing a battery of biochemical tests, namely: oxidase, indole production, urease production, Simon's citrate agar and motility. Gram-positive cocci were recognized based on their hemolytic properties, gram reaction, catalase and coagulase test results.[3] Antibiotic susceptibility testing was done by the Kirby Bauer disc diffusion method.

Data was collected, scrutinized, compiled and analyzed. Statistical analysis was carried out by using MS-Excel and Statistical Package for Social Science (SPSS) software version 26.0 for Windows. Data was expressed as frequency and percentage.

The study study was approved by the Institutional Review Board (IRB) of Mugda Medical College, Dhaka, Bangladesh.

RESULTS

Among the total of 186 patients, 88(47.3%) were males and 98(52.7%) were females; male-female ratio was 1:1.1. Among SSI patients, 53(34.2%) received one antibiotic, while 95(61.3%) and 7(4.5%) received two and three antibiotics respectively (Table-I). Distribution of prescribed empiric antibiotics was 30(57%), 18(34%) and 5(9%) from Watch, Access and Reserve respectively (Table-II). However, when combination of antibiotics was used, the most common combination was Access with Watch group (93.1%) (Fig. 1). Among all the empiric antibiotics, resistance to cefixime (97.4%) was highest among the isolated bacteria, whereas antibiotic resistance to other agents showed cefuroxime (96.6%), ceftriaxone (94.7%), amoxiclav (85%) and ciprofloxacin (72%), clindamycin (66.7%). Linezolid was 100% sensitive to isolated gram-positive bacteria whereas colistin was 91.3% to gram-negative bacteria (Table-III). Resistance to Access group of antibiotics was found 83%, followed by Watch and Reserve group of antibiotics (77% and 21.3% respectively) (Table-IV).

Table-I: *Distribution of prescribed empiric antibiotics according to number (n=155)*

Number of antibiotics used	n (%)
One	53 (34.2)
Two	95 (61.3)
Three	7(4.5)

Table-II: *Distribution of empiric antibiotics according to AWaRe classification in patients receiving monotherapy (n=53)*

Empiric antibiotics	Access n (%)	Watch n (%)	Reserve n (%)
Amoxiclav	1 (1.9)	-	-
Cefuroxime	-	8 (15.1)	-
Ceftriaxone	-	9 (17.0)	-
Cefixime	-	4 (7.5)	-
Ciprofloxacin	-	4 (7.5)	-
Flucloxacillin	16 (30.2)	-	-
Linezolid	-	-	2 (3.8)
Meropenem	-	5 (9.4)	-
Clindamycin	1 (1.9)	-	-
Colistin	-	-	2 (3.8)
Tigecycline	-	-	1 (1.9)
Total	18 (34)	30 (56.5)	5 (9.5)

Table-III: *Pattern of antimicrobial susceptibility of empiric antibiotics among culture positive samples*

Empiric Antibiotic	Number of tested antibiotics	Sensitive n (%)	Intermediate n (%)	Resistant n (%)
Amoxiclav	60	7 (11.7)	2 (3.3)	51 (85.0)
Clindamycin	6	2 (33.3)	-	4 (66.7)
Cefuroxime	29	1 (3.4)	-	28 (96.6)
Ceftriaxone	75	4 (5.3)	-	71 (94.7)
Cefixime	39	1 (2.6)	-	38 (97.4)
Ciprofloxacin	83	23 (28)	-	60 (72.0)
Meropenem	79	38 (48)	2 (2.5)	39 (49.5)
Colistin	69	63 (91.3)	-	6 (8.7)
Linezolid	12	12 (100)	-	-
Tigecycline	46	22 (47.8)	3 (6.5)	21 (45.7)

Different panels of antibiotics are tested against different organisms according to the standard protocol.

Table-IV: *Comparison of susceptibility pattern of empiric antibiotics according to WHO AWaRe classification of antibiotics with antibiogram of isolated bacteria*

Empiric Antibiotic	Number of tested antibiotics	Sensitive n (%)	Intermediate n (%)	Resistant n (%)
Access	66	9 (14.0)	2 (3.0)	55 (83.0)
Watch	305	67 (22.0)	2 (1.0)	236 (77.0)
Reserve	127	96 (75.5)	3 (2.4)	27 (21.3)

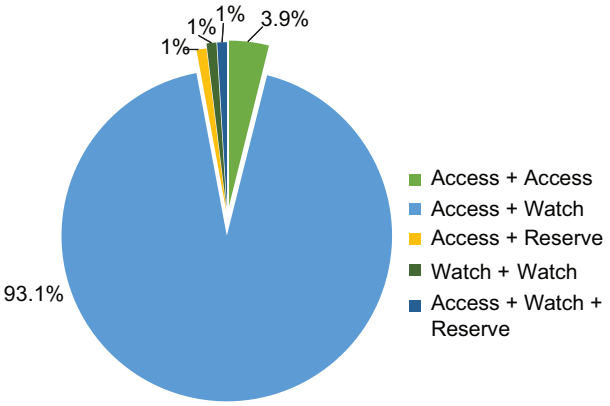

Fig. 1: *Pattern of combination therapy of empiric antibiotics according to AwaRe classification by WHO (n=102)*

DISCUSSION

This study was done to observe the pattern of empiric antibiotic usage in surgical site infections. Distribution of empiric antibiotics reflects the antibiotics chosen for empiric treatment in SSI cases based on their accessibility, resistance potential, and effectiveness. In this study, distribution of prescribed empiric antibiotics was 30(57%), 18(34%) and 5(9%) from Watch, Access and Reserve respectively. Another study done by Rashid et al. reported that about 62.9%(382), 36.4%(221), and 0.2%(1) of patients were treated with Watch, Access, and Reserve group of antibiotics respectively, in hospital surgery wards. Among the patients of obstetrics & gynaecology wards, 55.4%(265), 44.4%(212), and 0.2%(1) patients were treated with Watch, Access, and Reserve antibiotics, respectively. Watch group of antibiotics were used in 64%(1352) of patients followed by 35.6%(752) of Access and 0.1%(2) of Reserve group of antibiotics, which supports the findings of present study.[13] In contrast, reported distribution of antibiotics was found 246(55.5%), 191(43.1%) and 6(1.4%) from Access, Watch and Reserve respectively in a study done by Mudenda et al.[14]

In our study, we also found that most of the SSI patients received two antibiotics 95(61.3%), followed by one antibiotic 53(34.2%) and three antibiotics

7(4.5%). Dissimilar findings were reported by Mudenda et al.[14] The current study showed that gram-positive bacteria were found to be 100% sensitive to linezolid, which was similar to the results observed by Hubab et al.[15]

In the present study, most common combination of drug group was Access with Watch group (93.1%). Watch group was more commonly used and more resistant (77%). While the Watch group antibiotics were frequently used, they were associated with a higher resistance rate compared to the Reserve group antibiotics. This finding highlights the importance of considering both the prevalence of usage and the resistance patterns when selecting empiric antibiotics for treating infections. It also underscores the need for judicious antibiotic prescribing practices to combat antibiotic resistance effectively. Gandra & Kotwani suggested that Watch group should be reserved for very sick patients or patients admitted to intensive care units or when there is a clinical deterioration on first line agents of Access group.[16]

The present study has some limitations. The sample size was relatively small; hence, the results of this study may not reflect the exact picture of the whole country. Due to the limitation of resources, anaerobic culture could not be done.

CONCLUSION

Among SSI patients, 34.2% received one antibiotic, while 61.3% and 4.5% received two and three antibiotics respectively. Distribution of prescribed empiric antibiotics was 57%, 34% and 9% from Watch, Access and Reserve respectively. The most common (93.1%) combination was Access with Watch group. Resistance to Access group of antibiotics was found 83%, followed by Watch and Reserve group of antibiotics (77% and 21.3% respectively). Antibiotics having efficacy against Gram-negative organisms should be empirically selected for surgical site infections. Our results are of great concern and highlight the need for strengthened antimicrobial stewardship in all hospitals of the country. AWaRe classification should be followed meticulously while selecting antibiotics in all hospitals especially prior and after surgical operations.

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