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Research Article

Antibiotic overuse in obstetric and gynecologic procedures at Zagazig university hospitals: A prospective observational study

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Abstract

Surgical site infection (SSI) constitutes a major problem in healthcare in terms of healthcare cost, morbidity and mortality. Surgical antibiotic prophylaxis (SAP) is one of the effective strategies for SSI prevention. Poor adherence to SAP guidelines across different countries has been observed. Misuse of prophylactic antibiotics threatens patient safety and leads to an increase in the acquisition of antibiotic resistance. The aim of this study was to assess the utilization of SAP in obstetric and gynecologic procedures in terms of indication for prophylaxis, antibiotic selection, timing of administration and prophylaxis duration. A prospective observational study was conducted at the obstetrics and gynecology department of Zagazig University Hospital during the period from January 2020 to June 2020. Medical records of 264 women were recorded and evaluated. The American Society of Health-System Pharmacists (ASHP) therapeutic guidelines, World Health Organization (WHO) recommendations and The American College of Obstetricians and Gynecologists (ACOG) practice bulletin were used for data evaluation and hence women were stratified into two groups. For women who underwent procedures in which guidelines recommended the use of SAP (200 patients; 75.75%), 198 women (99%) received propperative prophylaxis. None of women (0%) received the recommended first line antibiotic by guidelines while the most commonly used prophylactic antibiotics were Cefotaxime (86 patients; 43.43%) and Ampicillin-sulbactam (62 patients; 31.31%). Preoperative antibiotic prophylaxis timing was 0-60 minutes before skin incision. All women received postoperative prophylaxis that extended to an average of 7 days. Regarding the other group who underwent procedures in which prophylactic antibiotics weren't recommended by guidelines (64 patients; 24.24%), 37 women (57.81%) followed the guidelines and didn't receive SAP while 27 women (42.18%) received SAP. Poor adherence to guidelines recommendations regarding prophylactic antibiotic selection and prophylaxis duration was observed. High utilization rate of prophylactic antibiotics in procedures that didn't require their use was reported..

Keywords

antibiotic prophylaxis, cesarean delivery, surgical site infection

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Introduction

Surgical antibiotic prophylaxis (SAP) is the rational, effective and safe use of antibiotic agents for reducing the risk of surgical site infection (SSI) (Bratzler et al. 2013). SSIs are caused mainly by microorganisms that come from the patient's own body and invade through surgical incision, some affect only skin and subcutaneous tissue while others are more serious and affect fascia, muscle or organ spaces (Anderson et al. 2008, National Institute of Health and care Excellence 2020). The gynecologic and obstetric procedures that carry a high risk for SSI include cesarean section and vaginal and abdominal hysterectomy (Guaschino et al. 2002). SSIs are associated with an increase in healthcare cost, morbidity and mortality (de Lissovoy et al. 2009, Cassini et al. 2016). Guidelines showed that appropriate SAP is one of the effective strategies for SSI prevention (Bratzler et al. 2013, WHO 2019). For optimal outcomes; SAP should be used when indicated, the selected prophylactic antibiotics should cover the likely pathogens on the operative site and the choice of antibiotic should consider the local pattern of antibiotic resistance (SIGN 2014). Poor adherence to SAP guidelines constitutes a significant problem, particularly in: antibiotic selection, timing of prophylaxis administration and duration of prophylaxis (Ng and Chong 2012). WHO reported that misuse of SAP threatens patients safety and leads to an increase in the acquisition and spread of antibiotic resistance (WHO 2019).

Aim of the study

Evaluate the utilization of prophylactic antibiotics in obstetric and gynecologic procedures in terms of: indication for prophylaxis, antibiotic selection, timing of administration and prophylaxis duration.

Set appropriate recommendations to optimize SAP utilization in the future.

Material and methods

Study setting and period

This prospective observational study was conducted at the obstetrics and gynecology department of Zagazig University Hospital during the period from January 2020 to June 2020, Zagazig University Hospital is a large tertiary hospital in Egypt and is the reference hospital to the Sinai and Qana provinces in addition to the populated Sharkia province.

Study design

A 6-month observational cross-sectional study was conducted to assess the use of prophylactic antibiotics in obstetric and gynecologic procedures. Patients attending the obstetrics and gynecologic ward during the study period who fulfilled the inclusion criteria were considered as the study population. Using a convenient sampling method, 264 women who underwent obstetric and gynecologic procedures during the study period were included based on the following inclusion criteria; adult patients, prophylactic antibiotic use and clean, clean-contaminated and contaminated procedures. Exclusion criteria included pediatrics (<18 years old), dirty procedures, presence of preoperative infectious disease and therapeutic uses of antibiotics. Assessment of prophylactic antibiotics utilization against the recommendations published by The American Society of Health-System Pharmacists (ASHP) therapeutic guidelines, World Health Organization (WHO) and The American College of Obstetricians and Gynecologists (ACOG) practice bulletin was performed with regard to the indication for prophylaxis, choice of antibiotic, timing of administration and duration of prophylaxis.

Data collection

Data was collected from medical records of the patients. Data collected included age in years, diagnosis, type of operation, length of hospital stay, names of prophylactic antibiotics, timing of preoperative prophylaxis administration relative to skin incision, duration of prophylaxis and oral antibiotic regimen given after hospital discharge.

Statistical analysis

Data were collected, entered and analyzed using Microsoft Office Excel 2010.

Ethical approval

Ethical approval for the study was obtained from the Institutional Review Board at the faculty of Medicine, Zagazig University (ZU-IRB#:5074-26-12-2019).

Results and discussion

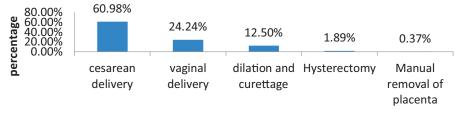
Medical records of 264 women admitted to the department of obstetrics and gynecology over a six month period were collected and evaluated. The average age of the study participants was 28.1 years with a standard deviation of 17.88. The average hospitalization period was 1 day. The most common procedures performed were Cesarean Delivery (CD) (161 procedures; 60.98%), Vaginal Delivery (VD) (64 procedures; 24.24%) and Dilation and Curettage (D&C) (33 procedures; 12.5%). Other procedures were Hysterectomy (5 procedures: 1.89%) and Manual Removal of Placenta (1 procedure; 0.37%). Percentage of performed procedures is illustrated in (Figure1).

Regarding the indication for prophylactic antibiotics, women were stratified into two groups based on recommendations of ASHP, WHO and ACOG guidelines. The first group included 200 women (75.75%) who underwent procedures in which prophylactic antibiotics were recommended by guidelines. The second group included 64 women (24.24%) who underwent procedures in which prophylactic antibiotics weren't recommended by guidelines. A diagram showing percentage adherence to ASHP, WHO and ACOG guidelines regarding prophylactic antibiotics utilization is illustrated in (Figure 2).

For the first group in which guidelines recommended use of prophylactic antibiotics according to ASHP, WHO, ACOG Guidelines: 198 women (99%) received preoperative prophylaxis in which 150 patients (75.75%) received a single prophylactic antibiotic, 46 patients (23.23%) received a combination of two prophylactic antibiotics and 2 patients (1.01%) received a combination of three prophylactic antibiotics. Percentage stratification of women in this group according to the number of administered antibiotics for prophylaxis is illustrated in (Figure 3). This reflects an awareness of preoperative antibiotic prophylaxis role in reducing the risk of postoperative infection and duration of hospitalization. Similar results were reported in previous studies in different countries including: a study in a Sudanese hospital which showed that 98.8% of the cases received antibiotic prophylaxis in the operation room (Elbur et al. 2014), a study in Midwestern Teaching

Hospital which showed a high rate of compliance (98.7%) to guideline-based recommendations for the use of prophylactic antibiotics (Uppendahl et al. 2018) and a study in the United States which showed a high rate of prophylactic antibiotics utilization (87%) in women who underwent procedures that require preoperative antibiotic prophylaxis use (Wright et al. 2013).

Regarding the antibiotic selection, none of women (0%) received the recommended first line antibiotic (Cefazolin) for CD and hysterectomy, (Doxycycline) for D&C or (1st generation cephalosporins or ampicillin) for manual removal of placenta while the most commonly used prophylactic antibiotics were Cefotaxime (86 patients; 43.43%) and Ampicillin-sulbactam (62 patients; 31.31%). Percentage stratification of women in this group according to the prophylactic antibiotics selected is presented in (Table 1). In this study 100% of prophylactic antibiotics selection was inconsistent with recommendations of ASHP, WHO, ACOG guidelines that recommended use of a single dose



procedures

Figure 1. Percentage of performed procedures at the department of obstetrics and gynecology over six months.

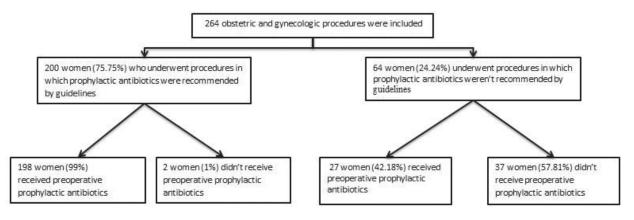


Figure 2. A diagram showing percentage adherence to ASHP, WHO and ACOG guidelines regarding prophylactic antibiotics utilization.

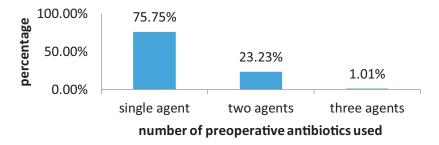


Figure 3. Percentage stratification of women underwent procedures in which guidelines recommended use of SAP according to the number of preoperative antibiotics used.

Table 1. Percentage stratification of women underwent procedures in which guidelines recommended use of SAP according to the prophylactic antibiotics selected.

Antibiotics used	No of cases	Percentage
Cefotaxime	86	43.43%
Ampicillin-sulbactam	62	31.31%
combination of Cefotaxime and Metronidazole	21	10.6%
combination of Ampicillin-sulbactam and	17	8.58%
Metronidazole		
combination of Cefotaxime and Gentamicin	6	3.03%
Gentamicin	2	1.01%
combination of Ampicillin-sulbactam and	1	0.5%
Gentamicin		
combination of Cefotaxime, Metronidazole and	1	0.5%
Gentamicin		
combination of Cefotaxime and Ampicillin-	1	0.5%
sulbactam		
combination of Ampicillin-sulbactam,	1	0.5%
Cefotaxime and Metronidazole		

of (Cefazolin) for CD and hysterectomy, (Doxycycline) for D&C or 1st generation cephalosporins or ampicillin for manual removal of placenta (Bratzler et al. 2013, World Health Organization 2015, The American College of Obstetricians and Gynecologists 2018). The most commonly used preoperative antibiotic was the third generation cephalosporin (Cefotaxime) (43.43%) followed by Ampicillin-sulbactam (31.31%) and unnecessary combination was used in 24.24% of the cases. The high rate of utilization of third generation cephalosporins leads to the development of new strains of clostridium difficile, extended spectrum beta lactamases (ESBLs), methicillin-resistant staphylococcus aureus (MRSA) and vancomycin resistant enterococci (Dancer 2001). low adherence to international guidelines was reported in previous studies including: a study in Nekemte referral hospital in Ethiopia showed that 89.4% of prophylactic antibiotics selection was inappropriate and the most commonly used prophylactic antibiotic was Ceftriaxone (84.3%) (Alemkere 2018), a study in Ayder referral hospital showed that 89.5% of prophylactic antibiotics selection was inappropriate and the most commonly used prophylactic antibiotic was Ceftriaxone (85.2%) (Mohamoud and Aklilu Yesuf 2016), a study in Iran showed that 92.5% of prophylactic antibiotics selection was inappropriate and the commonest administered regimen was a combination of Cefazolin plus Gentamicin (47.6%) ((Vessal et al. 2011), a study in Qatar showed that 31.5% of prophylactic antibiotics selection was inappropriate and the most commonly used prophylactic antibiotic was Cefazolin (44.6%) (Abdel-Aziz et al. 2013), a study in Sudan showed that 56.3% of prophylactic antibiotics selection was inappropriate and the most commonly used prophylactic antibiotic was Cefuroxime (92.6%) (Elbur et al. 2013), a study in Greece showed that 30% of prophylactic antibiotics selections was inappropriate and Ceforanide was the most frequently used prophylactic antibiotic (31.2%) (Tourmousoglou et al. 2008) and a study in Nicaragua showed that 66.8% of prophylactic antibiotics selection was inappropriate and the most commonly used prophylactic antibiotic was Ampicillin (58.3%) (van Disseldorp et al. 2006).

Regarding timing of prophylaxis administration, preoperative antibiotic prophylaxis timing for all women was 0-60 minutes before skin incision and this was consistent with recommendations of ASHP, WHO, ACOG guidelines. This finding is comparable with a study in India reported that timing of prophylaxis administration was appropriate in 89% of cases (Parulekar et al. 2009), a study in Abu Dhabi reported that timing of prophylaxis administration was appropriate in only 30.5% of cases (El Hassan et al. 2015) and a study in South West Ethiopia reported that timing of prophylaxis administration was appropriate in only 56% of cases (Jisha 2016).

Regarding duration of prophylaxis, postoperatively; all patients (100%) received additional antibiotic prophylaxis as following; 179 patients (89.5 %) received a combination of three antibiotics, 20 patients (10%) received a combination of two antibiotics and one patient (0.5%) received a single antibiotic. Percentage stratification of women in this group according to the number of postoperative antibiotics used is presented in (Figure 4). Percentage stratification of women in this group according to the postoperative prophylactic antibiotics selected is presented in (Table 2). Most patients were prescribed oral antibiotic prophylaxis after discharge; the most common regimen was a combination of Amoxicillin-clavulanic acid, Clindamycin and Metronidazole. The average duration of antibiotic prophylaxis was 7 days. Duration of antibiotic prophylaxis in this study was inconsistent with ASHP, WHO, ACOG guidelines that recommended a single dose of prophylactic antibiotic before skin incision (Bratzler et al. 2013, World Health Organization 2015, The American College of Obstetricians and Gynecologists 2018). A meta-analysis of 51 studies reported that there was no apparent benefit of using multi-dose regimens over single dose regimens (Hopkins and Smaill 2003). Prolonged antibiotic prophylaxis is associated with a high risk of acquiring antibiotic resistance (Harbarth et al. 2000). Prolongation of prophylaxis was also reported in a number of studies including: a study in Iran reported that unnecessary prophylaxis continuation occurred in 55% of the surgeries (Vessal et al. 2011), a study in Sudanese hospital reported that duration of prophylaxis was extended to an average of 8 days in 100% of the cases (Elbur et al. 2014), a study in South West Ethiopia reported that duration of prophylaxis was extended in 95% of the cases (Jisha 2016), a study in Ethiopia reported that 44.4% of the prophylaxis administration was extended for up to 5 days (Alemkere 2018) and a study in Saudi hospital reported that only 18.2% of the cases received antibiotic prophylaxis for an appropriate duration (Alahmadi et al. 2020).

For the second group who underwent procedures in which prophylactic antibiotics weren't recommended by guidelines: 37 patients (57.81%) followed the guidelines and didn't receive SAP while 27 women (42.18%) received SAP. Percentage of preoperative antibiotics prescription in this group is illustrated in (Figure 5). Regarding the antibiotic selection, Of the cases (27 women; 42.18%) who received prophylactic antibiotics without indication, 14 women (51.58%) received Cefotaxime, 10 women (37.03%) received

Table 2. Percentage stratification of women underwent procedures in which guidelines recommended use of SAP according to the postoperative prophylactic antibiotics selected.

Antibiotic	No of	Percent-
	cases	age
Combination of Ampicillin-sulbactam, Cefotaxime and Metronidazole	33	51.56%
Combination of Ampicillin-sulbactam and Metroni- dazole	12	18.75%
Combination of Cefotaxime and Metronidazole	8	12.50%
Combination of Cefotaxime, Metronidazole and Gentamicin	5	7.81%
Combination of Ampicillin-sulbactam, Gentamicin and Metronidazole	2	3.12%
Combination of Amoxicillin and Flucloxacillin	2	3.12%
Combination of Cefotaxime and Ampicillin-sulbactam	1	1.56%
Combination of Cefotaxime and Gentamicin	1	1.56%

Table 3. Percentage stratification of women underwent procedures in which guidelines didn't recommend use of SAP according to the preoperative prophylactic antibiotics selected.

Antibiotic	No of	Percentage
	cases	
Cefotaxime	14	51.85%
Ampicillin-sulbactam	10	37.03%
Combination of Ampicillin-sulbactam and	2	7.4%
Metronidazole		
Combination of Cefotaxime and Metronidazole	1	3.7%

Ampicillin-sulbactam, 2 women (7.4%) received a combination of Ampicillin-sulbactam and Metronidazole and 1 woman (3.7%) received a combination of Cefotaxime and Metronidazole. Percentage stratification of women in this group according to the preoperative prophylactic antibiotics selected is presented in (Table 3). Regarding timing of prophylaxis, preoperative antibiotic prophylaxis timing was 0-60 minutes before skin incision. Regarding duration of prophylaxis, postoperatively; all women (100%) received additional antibiotic prophylaxis as follows; 40 women (62.5 %) received a combination of three antibiotics, 24 patients (37.5%) received a combination of two antibiotics. All women were prescribed oral antibiotic prophylaxis after discharge; the most common regimen was a combination of Amoxicillin-clavulanic acid, Clindamycin and Metronidazole. The study revealed that prophylactic antibiotics were administered without indication to 42.18% of the cases. This finding is consistent with a study in the United States which reported that prophylactic antibiotics were administered without indication to 40.2% of the cases (Wright et al. 2013). Prophylactic antibiotics use without indication was also seen in number of studies: a study at a Midwestern hospital which reported that prophylactic antibiotics were administered without indication to 57.1% of the cases (Uppendahl et al. 2018), a study in Ethiopia which reported that prophylactic antibiotics were administered without indication to 19.6% of the cases (Alemkere 2018) and a study in Texas which reported that prophylactic antibiotics were administered without indication to 54% of the cases (Joyce et al. 2017). The irrational use of prophylactic antibiotics, along with the great ability of adaptation of microorganisms, leads to the development of

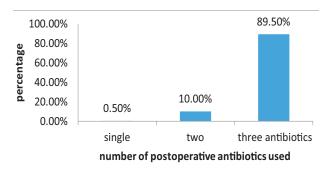


Figure 4. Percentage stratification of women underwent procedures in which guidelines recommended use of SAP according to the number of postoperative antibiotics used.

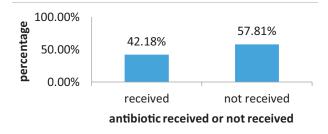


Figure 5. Percentage of preoperative antibiotics prescription in procedures in which guidelines didn't recommend their use.

new resistant strains with subsequent need for development of new antimicrobial agents and hence significant increase in the cost of healthcare service (E. Abbas et al. 2017).

Among the causes of non-adherence to SAP guidelines are the false generalization that using broad spectrum or combined prophylactic antibiotics and prolonged duration of prophylaxis are more effective in preventing SSIs and complications postoperatively than using narrow spectrum prophylactic antibiotics for short duration, easy accessibility to many antibiotics that weren't mentioned in guidelines and unawareness of SAP guidelines (Parulekar et al. 2009, Alahmadi et al. 2020). Improving availability of the recommended prophylactic antibiotics in hospitals is of great importance to improve adherence to SAP guidelines, a study in Jordan reported that 61.8% of improper SAP selection is due to drug unavailability (Al-Azzam et al. 2012).

Study limitations

This study encountered some limitations as most of the data were obtained from medical records so the data accuracy depended on the quality of recording system and some baseline characteristics of women weren't reported such as body mass index, medications (like immunosuppressant drugs, steroids), comorbidities (like obesity, diabetes) and nutritional status due to lacking of these data from medical records, these factors could affect decision making regarding regimen of antibiotic prophylaxis as they may increase the risk of infection. This study is a mono-center study with a relatively small sample size so this would restrict generalization of the study findings to other areas.

Conclusion

The selection of prophylactic antibiotics and the duration of prophylaxis were inconsistent with the recommendations of ASHP, WHO and ACOG guidelines. The use of broad spectrum prophylactic antibiotics and multidrug regimen were common practices identified in this study. This study reported a high rate of prophylactic antibiotics utilization in procedures that didn't require their uses. There is an urgent need for implementation of an antimicrobial stewardship program to optimize antibiotics use, reduce risk of resistance, improve clinical outcomes and reduce the cost of health care service. Moreover, there is an urgent need for establishment of an infection control committee to ensure implementation of infection control policies. Pharmacists must be given a central role in the selection, administration, monitoring of prophylactic antibiotics. Clinical pharmacist must promote optimal use of SAP by establishing and implementation of evidence based SAP guidelines for local setting based on international recommendations, monitor adherence to SAP guideline, ensure availability of the recommended first line prophylactic antibiotics and spread awareness among healthcare professionals about benefits of rational use of SAP through newsletters, clinical conferences and other types of educational tools. Future research is needed for performing outcomes based assessment of prophylactic antibiotics utilization after implementation of an antimicrobial stewardship program.

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