

Antibiotic Use in Caesarean Section and Hysterectomy Procedure : Qualitative and Quantitative Assessment

Andika Dwi Mahendra^{1}, Yovita Dwi Arini¹, Lusia Rubi Astuti¹, Annie Rahmatillah²*

¹Department of Pharmacy, SMC Telogorejo Hospital, Semarang, Indonesia

²Faculty of Pharmacy, Universitas Muhammadiyah Surakarta, Surakarta, Indonesia

Abstract. Antibiotic resistance is a global issue and its incidence is increasing. Resistance occurs because of the use of antibiotics that are not wise and appropriate so causing a decrease in the antibiotic effectiveness. The aim of this study was to evaluate the choice of antibiotics in caesarean section and hysterectomy. A retrospective study was conducted from September 2016 - January 2017 in obstetrics and gynecology ward in a private hospital. Data were analyzed quantitatively using the ATC/DDD method and qualitatively based on The guidelines of The American College of Obstetricians and Gynecologists (ACOG): Antibiotic Prophylaxis for Gynecologic Procedures and The American Society of Health-System Pharmacists (ASHP): Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery. Overall, 90 of the 95 patients were given prophylactic antibiotics. The most commonly used antibiotics are ceftriaxone and ceftazidime. The suitability of the selection of antibiotics based on the guidelines for caesarean section was 1.75% and hysterectomy was 6.1%. The use of antibiotics in the procedure is very high but it is not appropriate in its selection. It is necessary to evaluate and assess periodically the use of antibiotics. so that the increase in antibiotic resistance is reduced

Keywords: ATC-DDD index, Antibiotic Evaluation, Antibiotic Prophylaxis, Obstetrics and Gynecology

Abstrak. Resistensi antibiotik merupakan masalah global dan insidennya terus meningkat. Resistensi terjadi karena penggunaan antibiotik yang tidak bijak dan tepat sehingga menyebabkan penurunan efektivitas antibiotik. Tujuan dari penelitian ini adalah untuk mengevaluasi pilihan antibiotik pada operasi caesar dan histerektomi. Penelitian retrospektif dilakukan pada bulan September 2016 – Januari 2017 di bangsal obstetri dan ginekologi di rumah sakit swasta. Data dianalisis secara kuantitatif menggunakan metode ATC/DDD dan kualitatif berdasarkan The American College of Obstetricians and Gynecologists (ACOG): Antibiotic Prophylaxis for Gynecologic Procedures dan The American Society of Health-System Pharmacists (ASHP): Clinical Practice Guidelines for Profilaksis Antimikroba dalam Pembedahan. Secara keseluruhan, 90 dari 95 pasien diberi antibiotik profilaksis. Antibiotik yang paling umum digunakan adalah ceftriaxone dan ceftazidime. Kesesuaian pemilihan antibiotik berdasarkan pedoman seksio sesarea sebesar 1,75% dan histerektomi sebesar 6,1%. Penggunaan antibiotik dalam prosedur sangat tinggi tetapi tidak tepat dalam pemilihannya. Untuk itu perlu dilakukan evaluasi dan penilaian secara berkala terhadap penggunaan antibiotik. sehingga peningkatan resistensi antibiotik berkurang

Kata kunci: Indeks ATC-DDD, Evaluasi Antibiotik, Antibiotik Profilaksis, Obstetri dan Ginekologi

*Corresponding author at: Department of Pharmacy, SMC Telogorejo Hospital, Semarang, Indonesia

E-mail address: andikadwimahendra@gmail.com

Received 28 July 2021 | Revised 30 August 2021 | Accepted 8 September 2021

1 Introduction

Suitable of antibiotic prophylactic have presented to be fairly effective in diminishing the occurrence of Surgical Site Infections (SSIs) (1). Antibiotic prophylaxis is aimed to drop amount of bacteria contamination which are cause infections during surgery (2). However, inappropriate use of prophylactic antibiotics will lead to an increase in the rate of antibiotic resistance (3) and ultimately SSI (1).

SSIs usually occur to patients who undergo operative procedures (2). Development of SSI elevated up to 10% in gynecologic surgical (4). SSI is directly proportional to mortality, length of hospital, and re-admission rate to hospital (5). Research at Soetomo hospital Surabaya showed that there were postoperative infections as many as 53 cases out of 2106 obstetrical surgeries (6). At Cipto Mangunkusumo Hospital, there were 85 cases of surgical infection from 2052 (4.41%) (7). This incidence is not much different in North America and Israel with an incidence of 2.7% and 3.7% (8,9). Another study in Southeast Asia (Thailand) showed that 5.9% of patients had an obstetrical surgery infection (10). Another study that compared the incidence of infection after caesarean section showed that in developed countries the incidence was 1.5-7.0% and in developing countries it was 6% (8,11). Some of these infections can be triggered due to inappropriate use of antibiotics and the occurrence of antibiotic resistance (12). Although the principle of using prophylactic antibiotics has been applied, there is still inappropriate use of antibiotics (13).

Postoperative infection is the most common occurrence in hospital (14). Risk factors that influence the high incidence of infection are dose of antibiotics related to body mass index and the selection of appropriate prophylactic antibiotics (8). The aim of the study is to describe and evaluate quantitatively and qualitatively of prophylactic antibiotics selection based on Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) and the guidelines of antibiotic prophylactic on Obstetrics and Gynecology procedures.

2 Methods

This study was conducted at a private hospital in Semarang in the period September 2016 - January 2017. Data were collected retrospectively from patients' medical records. The subjects were all patients in the obstetrics and gynecology department who underwent caesarean section and hysterectomy.

Data analysis was carried out quantitatively using the ATC/DDD method, namely a drug classification system based on ATC (Anatomical Therapeutic Chemical). The use of the ATC (Anatomical Therapeutic Chemical) method will classify drugs based on therapeutic purposes,

pharmacology, and chemical structure of drugs. DDD (Defined Daily Dose) is the assumption of the average maintenance dose per day in adult patients with certain indications. Measurement of drug use using Defined Daily Dose based on guidelines issued by the WHO Collaborating Center for Drug Statistics Methodology with units of DDD/100 patients/day. The ATC code and standard antibiotic DDD (grams) from the World Health Organization (WHO) index are recorded, then the number of antibiotics used by the patient (grams) is calculated which is obtained from calculating the dose multiplied by the number antibiotic unit. Then calculated the number of Length of Stay (LOS) obtained from the total days of care for each patient. From these data, a description of the use of antibiotics is calculated using DDD/100 patient-days units by dividing the number of grams of antibiotics used by the patient per WHO standard DDD multiplied by 100 per total LOS.

Qualitative analysis was carried out by assessing the selection of antibiotics based on the guidelines of The American College of Obstetricians and Gynecologists (ACOG): Antibiotic Prophylaxis for Gynecologic Procedures and The American Society of Health-System Pharmacists (ASHP): Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery.

3 Results And Discussion

The research involved 95 women (table 1) who underwent Hysterectomy and Cesarean Section. The number of patients who received antibiotic prophylactic before procedures were displayed on table 2. Quantitative calculation (figure 1) portrays antibiotics which were used in each month on the period. From September 2016 to January 2017, ceftriaxone usage on September was 16.18 and raised gradually from 7.43 (October) to 21.14 (January) DDD/100patient-days. Higher DDD/100 patient-days, the more patients who receive antibiotic for certain indication. On January, ceftriaxone had 21.14 DDD/100patient-days means there were 21-22 patients who received defined daily dose of ceftriaxone (2000mg) per day. In contrast, ceftazidime dropped gradually to 0.81 DDD/100patient-days (January). On the other hand, cefazolin use was the fewest and only used on September, December, and January. It was 0.49, 0.36, and 0.54 DDD/100patients-days, respectively.

Table 1. Number of patients over the five months

No. of patient	With antibiotic (%)	Without antibiotic (%)
95 patients	90 patients (94.74)	5 patients (5.26)
Procedures		
Hysterectomy	33 patients (34.74)	
Caesarean Section	57 patients (60.00)	5 patients (5.26)

Caesarean section was the procedure which frequently performed in the hospital (table 3). During the period, fifty-seven of sixty-two patients used antibiotic prophylaxis prior to the procedure. Ceftazidime was the most antibiotic used on cesarean section followed by ceftriaxone, cefotaxime, and cefazolin. The antibiotic use rate was 23.36%, 17.76%, 11.21%, and 0.93%, respectively. Next, all of patients on hysterectomy procedure received antibiotic prophylaxis. Kind of antibiotics were ceftriaxone (18.69%), ceftazidime (7.48%), cefotaxime (2.80%) and cefazolin (1.87%). On Cochrane's study which involved more than 13,000 mothers resulted antibiotic prophylaxis reduced occurrence of endometritis, complication of serious maternal infection, wound infection and fever on mother who undergoing obsgyn procedures (Schalkwyk & Eky, 2010; Smaill & Gyte, 2010;).

Principle of antibiotic prophylaxis should cover the narrowest organism or spectrum as can as possible to decline the progression of antibiotic resistance (15). It is crucial to consider the probable source of pathogens in a surgery. In obstetrics or gynecology, the most infections were caused by the endogenous flora of woman's vagina or skin such as *Staphylococcus spp*, *S. Pseudintermedius*, *Streptococcus aureus*, and *Escherichia coli* (16). Cefazolin is first generation of cephalosporin which is effective to kill the bacteria (17). The antibiotic has activity against *Staphylococcus spp.*, *Streptococcus spp.*, *Escherichia coli*, and *Klebsiella spp* which are flora normal infection-causing bacteria in cesarean section (18,19).

Table 2. Number of patients who attained antibiotic prophylactic in Caesarean Section and Hysterectomy procedure

Procedure	Antibiotics				Total
	Ceftriaxone	Ceftazidime	Cefotaxime	Cefazolin	
Hysterectomy	20	8	3	2	33
Cesarean section	19	25	12	1	57

A meta-analysis (81 randomized) involved 11,937 women who underwent elective and nonelective cesarean section by receiving antibiotic prophylaxis resulted a significant reduction in risk of fever, endometiosis, SSI, urinary tract infection, and serious infection (18). First-generation cephalosporins (specifically cefazolin) has been advocated by The American College of Obstetricians and Gynecologists (ACOG) due to its efficacy, narrow spectrum activity, and low cost (2,18). Appropriate antibiotic selection for reducing infection incidence after cesarean section is crucial, not only to decrease the incident but also to diminish antibiotic resistance. The American College of Obstetricians and Gynecologists (ACOG) explains that antibiotic recommendation in emergency or elective caesarean section (no labour no rupture membrane) suggests cefazolin 1-2 gram IV 15-60 minutes prior to skin incision (LoE I-A) (2). The American Society of Health-System Pharmacists (ASHP) recommends cefazolin or

clindamycin + aminoglycoside (if patient has beta-lactam allergy) (17). Based on the antibiotic recommendation guidelines, our finding was only 1.75% which appropriate selection of antibiotic prophylaxis in caesarean section procedure which the drug of choice should be cefazolin.

Table 3. The Number of Procedures at Department of Obstetrics and Gynecology

Procedures	Month (Number of Patients)					Total
	Sept.	Oct.	Nov.	Dec.	Jan.	
Hysterectomy	5	5	5	13	5	33 (34.74%)
Cesarean Section	8	15	10	14	15	62 (65.26%)

Antibiotic prophylactic substantially drops infection after surgery and diminishes length of stay of women who undergoing hysterectomy (20). This facts were supported and proven with more than 30 prospective randomized clinical trial and two meta-analyses in decrease infections (21). A double-blind RCT comparing the use of cefazolin in obstetric and gynecological surgery found that cefazolin was better at reducing the incidence of infection (22). Fourteen RCTs compared to antibiotic prophylactic in hysterectomy procedure that cefazolin had benefit to reduce incidence of infections than other beta lactam antibiotics (cefotetan, cefotaxime, ceftriaxone, ampicillin, amoxicillin/clavulanate, or penicillin) (23). A total of 320 patients RCT study (each group 160 patients) which compared the incidence of post-abdominal hysterectomy infection found that 14.4% of patients had infection in the ceftriaxone group and 13.1% in the cefazolin group (24).

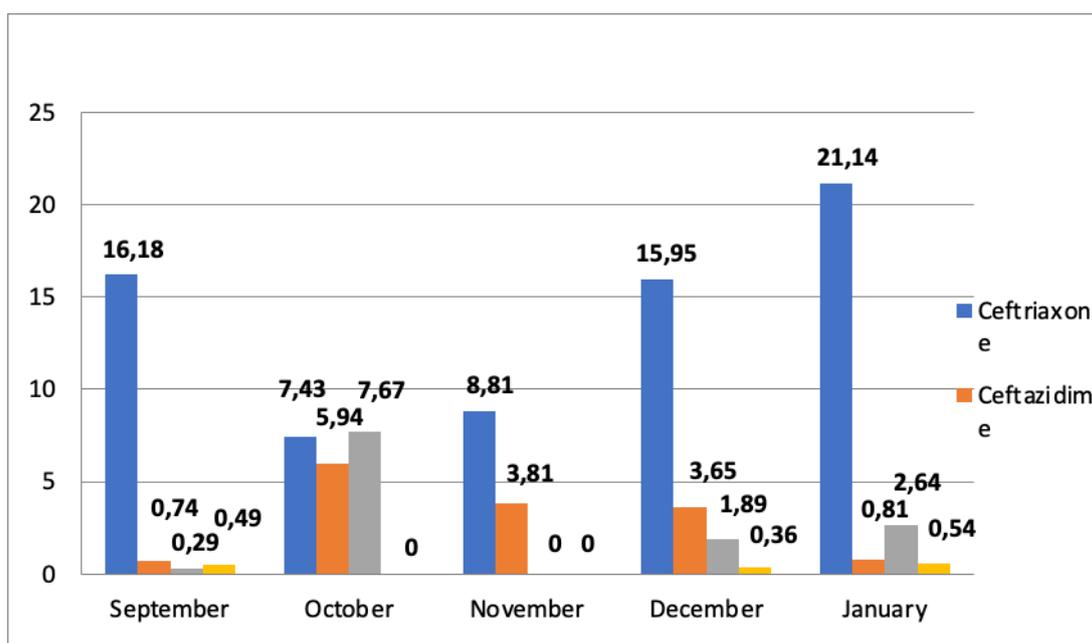


Figure 1 Defined Daily Dose (DDD)/100 patient-days Department Obstetrics and Gynecology during September 2016 – January 2017

As in caesarean section infection, infection during hysterectomy is caused by normal flora of the skin and from the vaginal canal (25) such as *Staphylococcus spp*, *S. Pseudintermedius*, *Streptococcus aureus*, and *Eschericia coli* (16). Therefore, it is recommended to use cefazolin as a antibiotic prophylactic (2,17,21,26). Based on the antibiotic prophylactic guideline of The American College of Obstetricians and Gynecologists (ACOG) for Hysterectomy procedure, drug of choice for this procedure is single dose cefazolin one hour before surgery. 2 grams or 3 grams are recommended for the patient weighing more than 120 kg (2). The American Society of Health-System Pharmacists (ASHP) also recommends cefazolin single dose for patient who undergoing vaginal or abdominal hysterectomy (using an open or laparoscopic approach) (17). The result of our study that almost patients were administered ceftriaxone and cefotaxime instead of cefazolin as drug of choice. Therefore, in our study only 6.1% which is appropriate antibiotic selection of 33 patients.

4 CONCLUSION

Antibiotic prophylaxis is a pace to prevent post-operative infection and also to diminish bacteria resistant. Before using antibiotic prophylaxis, we should consider and concern of its risks and benefits covering level of bacterial resistance, infection-causing bacteria, timing and antibiotic spectrum. This retrospective study reveals that the most widely prescribed antibiotic prophylactic was ceftriaxone and ceftazidime instead of first-generation cephalosporin. On quantitative measurement, the highest antibiotic used was ceftriaxone followed by ceftazidime and cefotaxime. For qualitative, only 1.75% correct selection of antibiotic prophylactic in cesarean section and 6.1% in Hysterectomy procedure. Less correct of antibiotic selection in these procedures, contribute to accelerate antibiotic resistance. Evaluation of antibiotic use is needed to be performed periodically to depict and assess quality of antibiotic use. For further evaluation of antibiotic prophylactic, researcher needs to come up with data such as timing and re-dosing of antibiotic prophylactic. Researcher also combines qualitative assessment through Gyssens flow chart by collaboration with the prescriber in order to provide significant and precision result to depict advanced antibiotic prophylactic evaluation.

ACKNOWLEDGEMENT

Authors are grateful to SMC Telogorejo Hospital for providing financial support to conduct the research.

REFERENCES

- [1] Hawn MT, Richman JS, Vick CC, Deierhoi RJ, Graham LA, Henderson WG, et al. Timing of Surgical Antibiotic Prophylaxis and the Risk of Surgical Site Infection. *JAMA Surg.* 2013 Jul 1;148(7):649.
- [2] ACOG Practice Bulletin No. 104: Antibiotic Prophylaxis for Gynecologic Procedures. *Obstetrics & Gynecology.* 2009 May;113(5):1180–9.
- [3] Zulfa IM. The Qualitative Evaluation Of Antibiotics Used In Pediatric Respiratory Tract Infection Treatments At A Primary Hospital In Surabaya. *Pharm : j farm Indones.* 2018 Dec 1;15(2):135.
- [4] Kamat AA, Brancazio L, Gibson M. Wound Infection in Gynecologic Surgery. :6.
- [5] Clifford V, Daley A. Antibiotic prophylaxis in obstetric and gynaecological procedures: A review. *Aust N Z J Obstet Gynaecol.* 2012 Oct;52(5):412–9.
- [6] Marsanto AE, Kuntaman K, Paraton H, Prasetyo B. Pattern of disease and type of operation of Surgical Site Infection in obstetrics and gynecology at Dr Soetomo Hospital, Surabaya, Indonesia. *MOG.* 2019 Sep 19;27(2):49.
- [7] Harzif AK, Wicaksono MD, Kallista A, Emeraldi M, Pratama G. Overview of risk factor and bacterial pattern in patient with surgical site infection after caesarean section in Ciptomangunkusumo Hospital from 2016 to 2018. *Infection Prevention in Practice.* 2020 Dec;2(4):100090.
- [8] Ketcheson F, Woolcott C, Allen V, Langley JM. Risk factors for surgical site infection following cesarean delivery: a retrospective cohort study. *CMAJ Open.* 2017 Jul 11;5(3):E546–56.
- [9] Saeed KBM, Greene RA, Corcoran P, O’Neill SM. Incidence of surgical site infection following caesarean section: a systematic review and meta-analysis protocol. *BMJ Open.* 2017 Jan;7(1):e013037.
- [10] Assawapalangool S, Kasatpibal N, Sirichotiyakul S, Arora R, Suntornlimsiri W. Risk factors for cesarean surgical site infections at a Thai-Myanmar border hospital. *American Journal of Infection Control.* 2016 Sep;44(9):990–5.
- [11] Edwards JR, Peterson KD, Mu Y, Banerjee S, Allen-Bridson K, Morrell G, et al. National Healthcare Safety Network (NHSN) report: Data summary for 2006 through 2008, issued December 2009. *American Journal of Infection Control.* 2009 Dec;37(10):783–805.

- [12] Kementerian Kesehatan Republik Indonesia. PMK No. 28 Th 2021 ttg Pedoman Penggunaan Antibiotik-signed.pdf. Kementerian Kesehatan Republik Indonesia; 2021.
- [13] Musmar SM, Ba`ba H, Owais A. Adherence to guidelines of antibiotic prophylactic use in surgery: a prospective cohort study in North West Bank, Palestine. *BMC Surg.* 2014 Dec;14(1):69.
- [14] Lewis SS, Moehring RW, Chen LF, Sexton DJ, Anderson DJ. Assessing the Relative Burden of Hospital-Acquired Infections in a Network of Community Hospitals. *Infect Control Hosp Epidemiol.* 2013 Nov;34(11):1229–30.
- [15] Friedman ND, Temkin E, Carmeli Y. The negative impact of antibiotic resistance. *Clinical Microbiology and Infection.* 2016 May;22(5):416–22.
- [16] Maksimović A, Filipović S, Rifatbegović M, Maksimović Z, Beširović H. Vaginal and uterine bacteria of healthy bitches during different stages of their reproductive cycle. *Veterinary Record.* 2012 Oct;171(15):375–375.
- [17] American Pharmacists Association. *Drug information handbook: a comprehensive resource for all clinicians and healthcare professionals.* Hudson, Ohio: Lexi-Comp; 2013.
- [18] Al Busaidi IH, Ilham HA, Dhar H, Rathi B, Nimre EA, Sachdeva V. A Study of Post-Caesarean Section Wound Infections in a Regional Referral Hospital, Oman. *Sultan Qaboos University medical journal.* 2014;14(2):211–7.
- [19] Kusaba T. Safety and Efficacy of Cefazolin Sodium in the Management of Bacterial Infection and in Surgical Prophylaxis. *Clinical Medicine Therapeutics.* 2009 Jan;1:CMT.S2096.
- [20] Akkour KM, Arafah MA, Alhulwah MM, Badaghish RS, Alhalal HA, Alayed NM, et al. A comparative study between a single-dose and 24-hour multiple-dose antibiotic prophylaxis for elective hysterectomy. *J Infect Dev Ctries.* 2020 Nov 30;14(11):1306–13.
- [21] Lachiewicz MP, Moulton LJ, Jaiyeoba O. Infection Prevention and Evaluation of Fever After Laparoscopic Hysterectomy. *JSLs.* 2015;19(3):e2015.00065.
- [22] Rahayu A, Rahmawati F, Andayani TM, Siradjuddin A. Uji Perbandingan Antibiotik Profilaksis Ceftriaxone versus Cefazolin pada Bedah Obstetri dan Ginekologi. *J Manaj dan Pelayanan Farm* [Internet]. 2021 Jan 5 [cited 2021 Nov 27];10(4). Available from: <https://jurnal.ugm.ac.id/jmpf/article/view/59779>

- [23] Pop-Vicas A, Johnson S, Safdar N. Should Cefazolin Be the First-line Antimicrobial Prophylaxis Choice in Patients Undergoing Hysterectomy? A Systematic Review and Meta-analysis. *Open Forum Infectious Diseases*. 2017;4(suppl_1):S650–S650.
- [24] Phoolcharoen N, Nilgate S, Rattanapuntamane O, Limpongsanurak S, Chaithongwongwatthana S. A randomized controlled trial comparing ceftriaxone with cefazolin for antibiotic prophylaxis in abdominal hysterectomy. *International Journal of Gynecology & Obstetrics*. 2012 Oct;119(1):11–3.
- [25] Burgess A, Fish M, Goldberg S, Summers K, Cornwell K, Lowe J. Surgical-Site Infection Prevention After Hysterectomy: Use of a Consensus Bundle to Guide Improvement. *J Healthc Qual*. 2020 Jul;42(4):188–94.
- [26] Salkind AR, Rao KC. Antibiotic Prophylaxis to Prevent Surgical Site Infections. *American Family Physician*. 2011;83(5):6.