Rational use of Antibiotic Prophylaxis during Childbirth: A Case of Community Hospital in Northeastern Thailand

Punnawadee Upanan* Waraporn Juntarat** Suthan Chanthawong*** Dr.Cheardchai Soontornpas[1]****

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ABSTRACT

Irrational antibiotic use has become the national agenda both in Thailand and other countries worldwide. This prospective cohort study was conducted to determine the prevalence and the rational use of antibiotic prophylaxis during childbirth among pregnant women who were admitted to Yangtalat Hospital, Kalasin Province between 1 January and 30 June 2020. Data were collected from medical records and patient interviews during hospitalization and after hospital discharge. A total of 270 participants were recruited in the study. There were 127 and 143 women with vaginal delivery and caesarean section, respectively. Antibiotic prophylaxis was prescribed in 139 participants (51.5%). The percentage of appropriateness of prescribing antibiotic prophylaxis was 97.8%. Peripartum infections were presented in 8.9%. In conclusion, most of antibiotic prophylaxis is rational with low incidence of complications.

Keywords: Childbirth, Delivery, Antibiotic prophylaxis, Rational use

[1]*Corresponding author: chesoo@kku.ac.th*

**Student, Master of Pharmacy Program in Clinical Pharmacy, Faculty of Pharmaceutical Sciences, Khon Kaen University, Thailand*

***Obstetrician, Department of Medicine, Yangtalat Hospital, Kalasin, Thailan*

****Assistant Professor, Division of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, Khon Kaen University, Thailand*

*****Associate Professor, Division of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, Khon Kaen University, Thailand*

Introduction

According to the World Health Organization (WHO) data, the global maternal mortality ratio (MMR) decreased by 48% from 442 per 100,000 live births in 1980 to 216 per 100,000 live births in 2015. However, infection was still a leading cause of maternal mortality and accounted for 11% of deaths. [1] Maternal peripartum infection was defined as bacterial infection of the genital tract or its surrounding tissues occurring at any time between the onset of membrane rupture or laboring and the 42nd day postpartum such as puerperal sepsis, endometritis, myometritis, salpingitis, chorioamnionitis, wound infection, urinary tract infection, etc. [1] In caesarean section, the incidences of surgical site infection and endometritis were reported as 2–7 % and 2-16%, respectively. [2] The incidence of sepsis was about 0.8%. [3] One strategy to reduce maternal mortality is the use of antibiotics to prevent infection during childbirth delivery. Antibiotic prophylaxis in caesarean section could significantly reduce maternal morbidity and infectious complications including endometritis, wound infections and urinary tract infections. [1] However, antibiotic prophylaxis is unnecessary in vaginal delivery with a mild perineal tear resulting in low risk of infection but may be necessary in the case of severe perineal tear with higher risk of infection. A previous systematic review reported that antibiotic prophylaxis in vaginal delivery could only lower the rate of endometritis with statistically significance but the rate of urinary tract infections, perineal wound infections, and the durations of mothers' hospitalization were not significant difference. [4] As a result, the rational use of antibiotic prophylaxis during laboring should focus on providing suitable treatment while reducing the risk of antibiotic resistance. [5] Currently, the rational drug use (RDU) hospital policy in Thailand also emphasizes the antibiotic usage in all public hospitals including the avoidance of antibiotic prophylaxis in pregnant women undergo vaginal delivery except for case with 3rd or 4th degree of perineal tear. [1] However, antibiotics were still used routinely in some hospitals including the tertiary care hospitals. A study at Maharaj Nakorn Chiang Mai Hospital reported that antibiotic prophylaxis was prescribed in 9.4% of women with vaginal delivery in which 72.3% were inappropriately. [6] A study at Mahasarakham Hospital reported that antibiotic prophylaxis was prescribed in 6.2% of pregnant women with vaginal delivery in which 31.1% were prescribed with 3rd or 4th degree of perineal tears indications. But amoxicillin oral form was most frequently prescribed. However, prescribing amoxicillin was considered as inappropriate use when prescribed for prophylaxis in vaginal delivery of normal term labor (APL) in RDU hospital. [7-8] A study at Ramathibodi Hospital reported that antibiotic prophylaxis in vaginal delivery was reduced from 25.4% (2016) to 9.9% (2017), rational drug use was increased from 12.4% to 34.4%. But the prevalence of episiotomy wound infection was not significant difference (P = 0.96). [9] However, research studies in hospitals in lower level with inadequate facility should be performed to evaluate whether the antibiotic prophylaxis during laboring are rational and can prevent infections.

Yangtalat hospital is a secondary care and community hospital in Kalasin province with a capacity of 120 beds and has conformed to the RDU hospital policy since 2017. Although the threshold of antibiotic prophylaxis for normal vaginal delivery is set to not exceed 10%, the rates of antibiotic prophylaxis in normal vaginal delivery were 21.7% and 12.0% in 2017 and 2018, respectively, that meant failure to meet the

indicator's requirements but had a good trend. [8] Therefore, this study was performed to assess the use of antibiotic prophylaxis for childbirth delivery, indicate whether the antibiotic utilization in the vaginal delivery met the requirements. Moreover, antibiotic prophylaxis in caesarean section and following up of peripartum complications were also investigated.

Objectives

This study aimed to determine the prevalence and rational use of prophylactic antibiotics during childbirth at Yangtalat Hospital, Kalasin Province. In addition, the peripartum complications were determined.

Methodology

Study design

This study was a prospective cohort study. It was approved and permitted to perform by the Ethic Committee for Human Research Khon Kaen University (No. HE 622225).

Study sample

The target population were pregnant women who were admitted to Yangtalat Hospital, for childbirth in 2020. The inclusion criteria were all pregnant women aged 18 years old or older, agreed to participate in the study, gave permission by signing the consent form and were able to communicate with the researcher. Pregnant women who were referred to other hospitals, who had incomplete information in medical records, who lost to follow up twice and who did not receive follow-up calls were excluded.

Sample size

Sample size was calculated using the formular as shown below.

Sample size (n) = $Z^2_{\alpha/2}\ \pi\ (1-\pi)/\varepsilon^2$.

The expected proportion of peripartum complications after vaginal delivery and caesarean section (π) were 0.02 and 0.08, respectively. [10] When type I error was set at 0.05, $Z_{\alpha/2}$ was 1.96 and precision (ε) was 0.05, the sample size of pregnant women with vaginal delivery and caesarean section should be 30 and 113 cases, respectively, and were rounded to totally at least 160 patients to compensate for 5% of dropout cases. If sample size was calculated based on the non-rational drug use of antibiotic prophylaxis 65.6% in previous study [9], the number of participants with normal vaginal delivery would be 125 cases. Finally, this study recruited all women with childbirth delivery during the first 6 months of 2020 or until the required number of participants had been reached because the rate of admission for childbirth in our hospital was regular throughout the year.

Rational use of prophylactic antibiotics

There is no Yangtalat Hospital guideline for antibiotics prophylaxis in childbirth delivery. However, the use of antibiotic prophylaxis in vaginal delivery of normal term labor is followed the APL in Thailand RDU hospital manual. Briefly, antibiotic prophylaxis is not recommended in normal cases but may be used in abnormal cases with 3rd or 4th degree perineal tear (cefazolin or clindamycin were recommended). For caesarean section, the physician adopted the antibiotic prophylaxis guideline belonged to the ACOG and ASHP and selected the drug available in hospital formulary (cefazolin, clindamycin or a aminoglycoside are recommended by ACOG and cefazolin, ampicillin, piperacillin/tazobactam or metronidazole are recommended by ASHP).

Appropriateness of antibiotic prophylaxis, in terms of indication, drug, and regimen, during childbirth was determined. The use of antibiotic prophylaxis in vaginal delivery of normal term labor should follow the APL in Thailand RDU hospital manual. [8] Briefly, antibiotic prophylaxis was not recommended in vaginal delivery for participants with 1st or 2nd degree perineal tear. For the 3rd or 4th degree perineal tear, the recommended antibiotics were cefazolin 1-2 g for non-penicillin allergic case and clindamycin 600-900 mg for penicillin allergic case given by single dose intravenous injection. For all participants with caesarean section, the physician adopted the antibiotic prophylaxis guidelines belonging to the American College of Obstetricians and Gynecologists (ACOG) [11] and the American Society of Health-System Pharmacists (ASHP) [12] and selected the drug available in the hospital formulary. The recommended intravenous antibiotics were cefazolin 1-2 g, ampicillin 2 g or piperacillin-tazobactam 3.375 mg for non-penicillin allergic case and metronidazole 500 mg or clindamycin 900 mg plus gentamicin 5 mg/kg for penicillin allergic case.

Data collection

Data were obtained from medical records and patient interviews including (1) recruitment data, (2) hospitalization data (general information, past medical history, current medical history, and postpartum information) and (3) follow up data at 2nd and 6th weeks after hospital discharge. Maternal peripartum infections were diagnosed by obstetrician if patients had at least two conditions as following: pelvic pain, fever, abnormal vaginal discharge, abnormal smell/foul odor discharge or delay in uterine involution. Data collector was a pharmacist with 5 years' experience in hospital pharmacy.

Statistical analysis

All data were analyzed using descriptive statistics and presented as mean and standard deviation or frequency and percentage. Data were analyzed by using STATA version 14.

Results

Characteristics of participants

A total of 270 participants were recruited in the study and the average age was 26.8 ± 0.37 years old. Most of them aged 20-29 years (67.4%), graduated from middle high school (35.9%), the body

mass index at admission date 25.0-29.9 kg/m^2 (41.5%) and incomes less than 7,000 bath/month. Universal coverage was the major health benefit scheme (54.8%). There were 4 participants who had allergic history to amoxycillin, ampicillin, dicloxacillin, and ceftriaxone (1 person per each antibiotic). The major number of pregnancies was the second pregnancy (45.6%). All of participant's medical conditions during pregnancy had recruit in study. The common medical condition during pregnancy was gestational diabetes (4.8%) as shown in Table 1.

Table 1 Demographic characteristics of participants (n=270)

Characteristics	Number of participants (%)
Age (years)	
< 20	1 (0.4)
20 - 29	182 (67.4)
30 - 39	78 (28.9)
≥ 40	9 (3.3)
Body mass index (kg/m^2)	
< 18.5	3 (1.1)
18.5-24.9	82 (30.4)
25.0-29.9	112 (41.5)
30.0-34.9	49 (18.1)
35-39.9	21 (7.8)
> 40.0	3 (1.1)
Health benefit scheme	
Universal coverage	148 (54.8)
Social security scheme	82 (30.4)
Others (Self-payment, Non-Thai Resident)	40 (14.8)
Drugs allergy history	
Allergy	4 (1.5)
No allergy	266 (98.5)
Education level	
Elementary School	26 (9.6)
Middle High school	97 (35.9)
Junior High school	87 (32.2)
Diploma	39 (14.5)
Bachelor's degree or higher	21 (7.8)
Incomes (bath/month)	
No incomes	73 (27.0)
< 7000	112 (41.5)

Table 1 Demographic characteristics of participants (n=270) (Cont.)

Characteristics	Number of participants (%)
7001 - 30000	65 (24.1)
> 30000	20 (7.4)
Type of delivery	
Vaginal delivery	127 (47.0)
Caesarean section delivery	143 (53.0)
Number of pregnancies	
1	105 (38.9)
2	123 (45.6)
3	29 (10.7)
4	10 (3.7)
5 or higher	3 (1.1)
Attending to Antenatal care (ANC) program	
Yes	267 (98.9)
No	3 (1.1)
Medical conditions during pregnancy	
Gestational diabetes	13 (4.8)
Hypertensions	3 (1.1)
Late latent syphilis	1 (0.4)
Hyperthyroidism	2 (0.7)
Human Immunodeficiency Virus	1 (0.4)

Use of prophylactic antibiotics during childbirth delivery

From 127 participants with vaginal delivery, 124 participants had 1st or 2nd degree perineal tear and all of them did not receive antibiotic prophylaxis. (Table 2) Only 3 participants had 3rd and 4th degree perineal tear and all of them received amoxicillin capsules as antibiotic prophylaxis. (Table 3) Therefore, the appropriateness in term of indication was 100%. Meanwhile the appropriateness in terms of prophylactic antibiotics were 0%. For 136 participants with caesarian section, all of them received antibiotic prophylaxis as shown in Table 2. The other seven participants in caesarean section group were continued intravenous antibiotics for treatment of other conditions, therefore antibiotic prophylaxis was not prescribed. Cefazolin injection was the most used antibiotics (97.1%) followed by ampicillin injection (2.2%) and metronidazole injection (0.7%) (Table 3). Dosage regimens of all prophylactic antibiotics were in accordance with the guidelines, therefore, the appropriateness in term of indication and prophylactic antibiotic were 100%. Finally, the overall appropriateness of antibiotic prophylaxis in both vaginal delivery and caesarean section was 97.8 %. (Table 4)

Table 2 Use of prophylactic antibiotics during childbirth (n=263)

Type of childbirth delivery	Number of participants (%)		
	ATB prophylaxis	No ATB prophylaxis	Total
Vaginal delivery (n=127)	**3 (2.4)**	**124 (97.6)**	**127(100.0)**
1st degree perineal laceration	0	84	84
2nd degree perineal laceration	0	40	40
3rd and 4th degree perineal laceration	3	0	3
Caesarean section (n=136)	**136 (100.0)**	**0**	**136(100.0)**

Table 3 Types of prophylactic antibiotics prescribed for childbirth delivery (n=139)

Antibiotic	Number of participants (%)
Vaginal delivery (n=3)	
Amoxicillin capsule	3 (100.0)
Caesarean section (n=136)	
Cefazolin injection	132 (97.1)
Ampicillin injection	3 (2.2)
Metronidazole injection	1 (0.7)

Table 4 Appropriateness of antibiotic prophylaxis during childbirth

Type of delivery	Number of participants with appropriate antibiotic prophylaxis (%)[a]			
	Indications	Drug	Regimens	All category
Vaginal delivery	**127 (100.0)**	**N/A**	**N/A**	**100.0**
1st degree perineal tear	84 (100.0)	N/A	N/A	100.0
2nd degree perineal tear	40 (100.0)	N/A	N/A	100.0
3rd and 4th degree perineal tear	3 (100.0)	0	0	0
Caesarean section[b]	**136 (100.0)**	**136 (100.0)**	**136 (100.0)**	**136 (100.0)**
Total	263 (100)	136 (97.8)	136 (97.8)	136 (97.8)

[a]N/A or no assessment in participants without indication and did not receive antibiotic prophylaxis.

[b]the appropriateness was evaluated only in participants receiving antibiotic prophylaxis.

Peripartum complications

Peripartum infections and other complications were assessed during hospitalization and after hospital discharge for 6 weeks. Infections were found in 24 of 270 participants (8.9%), 16 participants (5.9%) during hospitalization, 2 participants (0.7%) in the 2nd week and 6 participants (2.2%) in the 6th

week after hospital discharge. Participants with caesarean section had higher infection rate than participants with vaginal delivery which were 13 of 143 (9.1%) and 11 of 127 participants (8.7%), respectively. Infections occurred in 12 participants with antibiotic prophylaxis and 12 participants without antibiotic prophylaxis as shown in Table 5. In addition, anemia was found in 5 of 270 participants (1.9%), 3 participants with caesarean section, 1 participant with 1st degree perineal tear and 1 participant with 2nd degree perineal tear.

Table 5 Peripartum complications during hospitalization and after hospital discharge (n=24)

Complications	Number of participants (%)			
	Endometritis	Puerperal sepsis	Vaginosis	Urinary tract infection
Receiving antibiotic prophylaxis				
1st degree perineal tear	-	-	-	-
2nd degree perineal tear	-	-	-	-
3rd and 4th degree perineal tear	-	-	-	1 (4.2)
Caesarean section	4 (16.7)	1 (4.2)	3 (12.5)	3 (12.5)
Not receiving antibiotic prophylaxis				
1st degree perineal tear	-	-	2 (8.3)	5 (20.8)
2nd degree perineal tear	1 (4.2)	1 (4.2)	-	1 (4.2)
3rd and 4th degree perineal tear	-	-	-	-
Caesarean section	-	-	2* (8.3)	-
Total	5 (20.8)	2 (8.3)	7 (29.2)	10 (41.7)

*Not receiving antibiotic prophylaxis for caesarean section but ongoing antibiotic use for other infection

Discussion and Conclusions

Most of participants in this study were aged between 20-29 years old with the average age of 26.8 $\pm$ 0.37 years old. The gestational age of patients with vaginal delivery and caesarean section were 38.3 $\pm$ 2.9 and 38.2 $\pm$ 2.4 weeks, respectively. Previous study at Maharaj Nakorn Chiang Mai hospital reported that the average age of women giving childbirth was 27.3 $\pm$ 4.8 years old and the average gestational age of women with vaginal delivery and caesarian section delivery were 38.7 $\pm$ 1.2 and 38.7 $\pm$ 1.1 weeks, respectively. [6] Similarly in study participants may result from that both studies were performed in reproductive period (15-49 years) of Thai women. [13] Most of them married and became pregnant after finishing their compulsory graduation courses and having work with stable incomes. [14] Gestation age was usually full-term delivery and the second pregnancy which were associated with the best outcomes for pregnancy. However, 20 of 270 participants (7.4%) had medical conditions during pregnancy. Gestational diabetes mellitus was found in 4.8% of participants which was slightly higher

than 3.9% in previous study. [6] Most of participants (41.5%) had BMI 25.0-29.9 kg/m^2 which were categorized as overweight according to WHO criteria. Moreover, 27.0% of participants had BMI over 30 kg/m^2 which were classified as obesity. [15] Higher BMI is related to glucose intolerance in pregnant women.

For women with caesarean section, the infectious complications are surgical site infection, wound infection and endometritis which are the major causes of prolonged hospital stay and pose a burden to the healthcare system. Therefore, all pregnant women with caesarean section should receive prophylactic antibiotics. [2-3] In this study, all participants with caesarean section received prophylactic antibiotics in accordance with ASHP [12] and ACOG [11] recommendations, therefore, use of antibiotic prophylaxis was 100% appropriate in terms of indication and prophylactic antibiotics. In contrast, antibiotic prophylaxis in women with vaginal delivery was usually unnecessary and recommended only in vaginal delivery with 3rd or 4th degree perineal tear. [1-8] In this study, participants with vaginal delivery and 1st or 2nd degree perineal tear did not receive antibiotic prophylaxis and participants with 3rd and 4th degree perineal tear received antibiotic prophylaxis so that the appropriate rate in terms of indication was 100%. However, improper prophylactic antibiotics were belonged to use of oral amoxicillin over 1 day instead of parenteral antibiotic given as single dose according to the guidelines. [8] Finally, the overall antibiotic prophylaxis for normal vaginal delivery in our hospital during the study period was 3 of 127 participants (2.4%) which was less than the threshold of antibiotic prophylaxis in RDU hospital policy.

The overall rate of peripartum infections was 8.9%. The rate of infection in participants with vaginal delivery was 8.7% which was lower than 9.1% of participants with caesarean section. The rate of infection in women with normal delivery in this study was higher than 3.5% reported by previous study in Ramathibodi hospital. [9] The difference in the results between hospitals may be resulted from vary or different type of emergency delivery and capacity of hospital. Ramathibodi hospital is a university hospital and medical school, therefore, both personnel and facilities are ready for infection control than the study hospital. In addition, the rate of infection in pregnant women with vaginal delivery in our study was higher than the report in the previous study which conducted in seven secondary care hospital at Chiang Mai province (1.5%). [16] This may be caused by the different frequency of times to participants following up. This study had 2 times follow-up, at the 2nd and 6th weeks after hospital discharge.

However, the infection rate in caesarean section in the present study was less than 27% reported in a study in tertiary care hospital in China [17] This finding reflected the quality of infection control in government hospital in Thailand. Anemia related with maternal blood loss and required blood transfusions was found in 5 women (1.9%) but was less than 8.5% in the study in Maharaj Nakorn Chiang Mai hospital. [6] The results in each hospital were different because of different capacities, type of populations and patient-specific factors.

In conclusion, use of antibiotic prophylaxis during childbirth is rational. The antibiotic prophylaxis prescribed in normal vaginal delivery was less than the threshold indicated in RDU hospital policy. A low incidence of complications was found.

Limitations of the study

This study conducted in one secondary care and community hospital in northeastern of Thailand. This limits the generalization of the study.

Recommendations

The future studies should be conducted as multicenter composed of many community hospitals in different levels to represent a wider population. In addition, the safety of drug use and complications in infants should be further investigated.

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