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PROFILE OF PROPHYLACTIC ANTIBIOTICS IN CESAREAN SECTIONS WITH OCCURRENCE OF INFECTION: LITERATURE REVIEW

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ABSTRACT

Caesarean section is a surgical procedure that requires the use of prophylactic antibiotics throughout its implementation. Providing prophylactic antibiotics before surgery can reduce the risk of postoperative infections. The most common short-term complications of a caesarean section are wound infections. This research aims to ascertain the profile of prophylactic antibiotic use in caesarean section patients and to review the incidence of infections. The method used is a literature review. A total of eleven papers met the inclusion criteria for review. Based on the results of the article review, all of the research conducted were randomised controlled trial (RCT) studies. Randomised controlled trials (RCTs) are the gold standard for assessing the benefits of a treatment. Cefazolin, the first-generation cephalosporin antibiotic, is the most commonly used antibiotic for patients undergoing caesarean section. This aligns with the recommendations in the guideline. The highest prevalence of post-cesarean section infections is wound infections, with a percentage of 11.8% or 437 caesarean section patients. The most common microbiological pattern causing these infections is Staphylococcus aureus.

KEYWORDS

prophylactic antibotics, caesarean section, wound infection



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INTRODUCTION

Caesarean section (SC) is the most frequently performed operation in the field of obstetrics and gynecology, and the trend continues to increase every year. According to the WHO, the number of caesarean sections performed throughout the world is increasing and now reaches more than 1 in 5 (21%) deliveries. Meanwhile, according to 2018 riskesdas data in Indonesia, the number of births by caesarean section was 17.6% of the total number of births. Childbirth by caesarean section carries a risk of short-term and long-term complications. The most common short-term complications are bleeding and wound infection. Caesarean section is a type of clean, contaminated surgery that carries a risk of post-operative complications with a risk level of around 3-15% (Aljohani et al., 2021). Complications of post-cesarean section infection are an important and significant cause of maternal mortality and increased hospital and medical costs. Complications of this infection range from mild to severe and can be fatal (Mohamed et al., 2023).

One effort that can be taken to prevent infection after a *cesarean section* is to administer prophylactic antibiotics. Prophylactic antibiotics are antibiotics given in the short term, namely 30-60 minutes before surgery (Organization, 2021). Based on the *Guideline for the Prevention of Surgical Site Infection* (2017), up to 50% of infections can be prevented by selecting appropriate and effective prophylactic antibiotics. Improper use of antibiotics can cause antibiotic resistance. Antibiotic resistance occurs when bacteria, viruses, fungi, and parasites

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are able to develop and destroy antibiotics, thereby reducing their effectiveness (Taylor et al., 2024). Prophylactic antibiotic administration has been shown to reduce maternal morbidity, healthcare costs, and antibiotic overuse. The aim of antibiotic prophylaxis in surgery is not to sterilize tissue, but rather to reduce the pressure of microorganism colonization (Mohamed et al., 2023). WHO recommends the use of prophylactic antibiotics for caesarean sections, namely a single dose of first-generation cephalosporin or penicillin. It is necessary to consider choosing the right antibiotic in terms of drug selection and administration time, dose, and duration.

Previous studies have shown that the use of prophylactic antibiotics in *caesarean sections* plays a crucial role in reducing the risk of post-operative infections. A study by Aljohani et al. (2021) found that antibiotic prophylaxis significantly decreased the rate of post-*caesarean* infections, emphasizing the importance of appropriate antibiotic selection. In another study, Mohamed et al. (2023) highlighted that proper prophylactic antibiotic administration reduced maternal morbidity and healthcare costs by minimizing infections like endometritis and wound infections. These studies suggest the importance of timely and appropriate antibiotic administration, but there is still a gap in understanding the full scope of antibiotic use patterns and their effectiveness in preventing post-*caesarean* infections, especially in diverse settings like Indonesia.

This study aims to determine the profile of prophylactic antibiotic use in *caesarean* section patients and review the incidence of infection after caesarean section in the form of wound infections, fever, endometritis, open wounds, and urinary tract infections. The findings could help inform hospital protocols and public health policies aimed at reducing maternal morbidity and enhancing the cost-effectiveness of caesarean section procedures.

RESEARCH METHOD

This research is a literature study or literature review, which was carried out by collecting data through four databases, namely *PubMed*, *BMC*, *Cochrane*, and *ResearchGate*. The research results or journals that will be reviewed in this study are articles published between 2015 and 2024. These articles are identified by the search keywords, namely (antibiotic OR antimicrobial) AND (fever OR surgical site infection OR urinary tract infection OR endometritis OR separation wound) AND caesarean section.

Article Selection

The article selection process aims to assess the relevance of research identified in the search according to the characteristics of the research articles used. From searches using the four journal databases, 191 articles were found. From the articles found, selection was then carried out based on the inclusion criteria, and ultimately, 11 articles were selected (Table 1).

Table 1. Article Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria				
• The articles obtained are in accordance with the predetermined keywords	Systematic review article				
All articles with a maximum search between 2015 and 2024	Not accessible full-text				
Articles with Randomized Controlled Trial (RCT) research design	• The language used in the article is other than English.				
 Articles are sourced from database sources namely pubmed, Cochrane, BMC and Researchgate 					
 Article with the subject: women with sectio cesarean delivery who get prophylactic antibiotics 					
 Results: surgical wound infection, fever, endometritis, open wound and urinary tract infection 					

Data Extraction

The author extracted journal data that met the inclusion criteria by reading and understanding all journals and then comparing each journal. Next, the data were entered into the results, with several points, namely in *Table 2*, consisting of the name of the drug and the percentage of prophylactic antibiotic use. *Table 3* consists of the author, year of research, antibiotics used, and the number of patients included in the research for each journal. In *Table 1*, data extraction is in the form of the author's name, antibiotics used in both the intervention group and the control group, as well as the incidence of infection after *caesarean section* contained in the journal in the form of wound infections, fever, endometritis, open wounds, and urinary tract infections. Next, data analysis, compilation of results, and research discussion will be carried out.

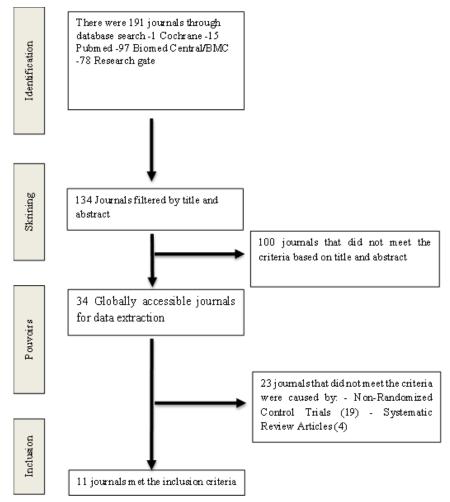


Figure 1. Literature Review Flow Diagram

RESULT AND DISCUSSION

Research Design

Almost all research articles used in this literature review are randomized controlled trials (RCT). *RCT* is the gold standard for assessing the benefits of a treatment (Kabisch et al., 2011). *RCT* research is usually used as a basis for decision-making or drug policy. One example is the preparation of drugs that will be included in the national formulary.

Selection of Prophylactic Antibiotics

Of the 11 studies, 6 studies had a percentage of antibiotic use above five percent, namely *Cefazolin* (30.34%), *Cefazolin* 1g followed by *Cefalexin* + *Metronidazole* 500 mg (18.21%), intravenous *Ceftriaxone* (1g) and *Metronidazole* 500 mg (9.06%), *Amoxicillin-clavulanate* 1.2g (8.93%), *Ceftriaxone* 2g (7.62%), and *Cefazolin* 1g followed by *Cephalexin* (5.28%) (*Table 2*).

Table 2. Description of Prophylactic Antibiotic Use in Cesarean Surgery

Antibiotics used	% Usage
Sefazolin 1gr	30,34
Sefazolin 1gr diikuti Cephalexin+Metronidazole 500mg	18,21
Intravenous sephtriaxone 1 gr and Metronidazole 500mg	9,06
Amoxicillin-clavulanate 1,2 g	8,93
Seftriakson 2 gr	7,62
Sefazolin 1gr diikuti Sephalekin	5,28
Sefazolin 2gr	5,08
Sefazoline+Azitromisin	5,03
Intravenous Sephtriaxone 1 g and Metronidazole 500mg+ Sefuroxim 500mg	5,03
Intravenous Sephtriaxone 1 g and Metronidazole 500mg followed by Sefurroxim+Metrodinazole	4,03
Amoxicillin-clavulanate 1.2 g + Metronidazole 500mg	3,90

The prophylactic antibiotic most often chosen for *caesarean section* is *Cefazolin*. *Cefazolin* is a first-generation *cephalosporin* that has a spectrum of activity against organisms commonly encountered during *cesarean section* surgery. *Cefazolin* is very active against *grampositive* bacteria and less active against *gram-negative* bacteria and has a longer half-life, approximately 2-3 hours. *Cefazolin* has greater protein binding, around 80% compared to other first-generation *cephalosporin* antibiotics, so blood levels are high. *Cefazolin* can reach peak concentrations within 40 minutes after parenteral administration and has a half-life of 42 minutes (Almuhtarihan et al., 2022).

The distribution volume of *Cefazolin* is 9.44 liters/hour. The clearance from using *Cefazolin* as a prophylactic antibiotic increases during pregnancy, so administration of larger doses is recommended to obtain the same antibacterial effect as in non-pregnant women. Maternal administration of the prophylactic antibiotic *Cefazolin* up to 2 g is effective and results in exposure within clinically approved limits (Elkomy et al., 2014). Based on the Guideline, *WHO* recommends the use of prophylactic antibiotics for *cesarean sections*, namely a single dose of first-generation *cephalosporin* or *penicillin* antibiotics compared to other classes of antibiotics (WHO, 2021). In this study, the profile of prophylactic antibiotic use for *cesarean section* was in accordance with that recommended by the guideline.

Of the 11 studies, there were 3 studies, namely by Valent et al. (2017), Jyothi et al. (2019), and Tara et al. (2022), who used a double dose of prophylactic antibiotics in conditions of obesity, namely *Cefazolin* 1 g followed by *Cephalexin* 500 mg and *Metronidazole* 500 mg, involving 823 pregnant women with obesity, and the use of a double dose of antibiotics, *Cefazolin* 2 g followed by *Azithromycin* 500 mg, involving 200 pregnant women with obesity (Table 3). Based on the results of these three studies, the use of double-dose prophylactic antibiotics can reduce the occurrence of surgical wound infections in obesity conditions. Surgical wound infections observed in the three studies included *endometritis*, open wounds, and fever. Obesity during pregnancy can be associated with various negative impacts on the condition of the mother and fetus, one of which is that the mother is at risk of experiencing a

cesarean delivery (Valent et al., 2017). Complications of cesarean delivery have a higher rate of surgical wound infections compared to vaginal delivery.

Table 3. Profile of Prophylactic Antibiotic Use in Cesarean Sections and Number of Patients in Each Article

Number of Patients in Each Article													
N o	Auth or's nam e and year	Penis ilin Amo xicilli n- clavu lanat e 1,2 g	Sefal Sefa zoli n 2g	Sefa zoli n 1g	Sefa zolin 1gr diiku ti Seph aleki n	Sefal ospor in gen 3 Seftri axone 2 g	Sefazoline +Azitromi sin	Intrav enous Sephtr iaxone (1 g) and Metro nidazo le (500m g) + Sefuro xym	Intrav enous ceptri axone (1 g) and Metro nidazo le (500m g)	Intravenous sephtriaxon e (1 g) and Metronidaz ole 500mg followed by Sefuroxim+ Metrodinaz ole	Amoxi cillin- clavul anate 1.2 g + Metro nidazo le 500mg	Sefazo lin 1gr diikuti Sefale xin + Metro nidazo le 500mg	Tot al pat ient s
1	Dlam ini et al. (201 5)					464		500mg					464
2	Vale nt et al. (201 7)		202									201	403
3	Jyotir mayi Eight Al. (201 7)			110 6									110 6
4	Rai et al. (201 8)	200											200
5	Jyoth i et al. (201 9)			100			100						200
6	Moh amm ed et al. (202 0)	80									80		160
7	Pal & Dasg upta (202	75									75		150
8	Pooja et al. (202								160	160			320
9	Igwe madu et al. (202					81						81	162
1	2) Tara et al.				210							210	420

	Number of Patients in Each Article												
-	(202 2)												
1 1	Agar wal & Lam ba (202 3)							200	200				400
	otal tibiotic e	355	202	120 6	210	545	100	200	360	160	155	492	398 5

Table 4. Incidence of Infection in Surgery

			abic 4. Incidence	Incidence of Infection						
No	Author's name and year	Types of	`Antibiotics	Wound Infection n=473 (11.8 %)	Fever n=218 (5,5%)	Endometritis n=169 (4,2%)	ISK n=81 (2%)	Open wounds n=38 (0.9%)		
1	Dlamini et al.	Intervention	Seftriaxson 2 g before incision	108 (22,8)	-	31 (18,3)	-	-		
1	(2015)	Control	Seftriaxone 2 g after clamping	138 (29,1)	-	52 (30,7)	-	-		
2	Valent et al. (2017)	Intervention	Sefazolin 2g followed by Cephalexin, 500mg, and Metronidazole, 500mg	13 (2,7)	9 (4,1)	2 (1,2)	-	16 (42)		
		Control	Sefazolin 2g + Plasebo	31 (6,5)	10 (4,6)	8 (4,7)		22 (57,8)		
3	Jyotirmayi Eight Al. (2017)	Intervention	Sefazolin 1g before the incision	2 (0,4)	11 (5)	5 (2,9)	16 (9,7)	-		
		Control	Sefazolin 1g after clamping	25 (5,3)	32 (14,6)	14 (8,3)	21 (25,9)	-		
4	Rai et al. (2018)	Intervention	Amoxicillin Clavulanate 1,2g before incision	2 (0,4)	-	-	-	-		
4		Control	Amoxicillin Clavulanate 1.2gr after clamping	7 (1,5)	-	-	-	-		
-	Jyothi et al.	Intervention	Sefazolin 2gr + Azitromisin	15 (3,1)	17 (7,8)	10 (5,9)	12 (14,8)	-		
5	(2019)	•	Control	Sefazolin 2gr	3 (0,6)	3 (1,4)	2 (1,2)	3 (3,7)	-	

	Author's name and year			Incidence of Infection						
No		Types of Antibiotics		Wound Infection n=473 (11.8 %)	Fever n=218 (5,5%)	Endometritis n=169 (4,2%)	ISK n=81 (2%)	Open wounds n=38 (0.9%)		
		Intervention	Amoxicillin Clavulanate 1,2gr	5 (1,05)	10 (4,6)	6 (3,5)	5 (6,2)	-		
6	Mohammed et al. (2020)	Control	Amoxicillin Clavulanate 1,2gr + Metronidazole 500mg	8 (1,69)	12 (5,5)	9 (5,3)	4 (4,9)	-		

The presence of surgical wound infections can increase the duration of hospitalization and healthcare costs (Tara et al., 2022). Giving a double dose as a prophylactic antibiotic for *caesarean section* is reported to reduce the incidence of surgical wound infections, thereby reducing post-*caesarean section* complications. This is beneficial for mothers in the process of breastfeeding newborns directly (Valent et al., 2017).

Apart from the three studies that discussed double doses in mothers with obesity, there were five studies, namely by Mohammed et al. (2020), Pal et al. (2021), Pooja et al. (2021), Igwemadu et al. (2022), and Agarwal & Lamba (2023), who looked at the effectiveness of prophylactic antibiotics by administering a double dose vs a single dose in pregnant women without obesity (Table 3).

Prophylactic antibiotic administration with a double dose in *caesarean section* patients without obesity is as effective as a single dose. This therapy can be used as a reference in reducing the cost of using antibiotics and preventing resistance (Pooja et al., 2021).

Incidence of Wound Infections in *Cesarean Sections* and Timing of Prophylactic Antibiotics

Based on the results of an analysis of 11 studies involving 3,985 patients with *caesarean section*, it shows that the most common incidence of infection after *caesarean section* was wound infection at 11.8% or 437 *caesarean section* patients, fever at 5.5% or 218 *caesarean section* patients, *endometritis* by 4.2% or 169 *caesarean section* patients, urinary tract infection (UTI) by 2% or 81 *caesarean section* patients, and the last surgical wound infection, namely an open wound, amounted to 0.9% or 38 *caesarean section* patients (Table 4).

Of the 11 research journals, there were 9 studies that monitored the incidence of infection after *caesarean section*. Based on research conducted by Dlamini et al. (2015), involving 464 patients, the highest incidence of infection was wound infections, with 108 (22.8%) in the intervention group and 138 (29.1%) in the control group (Table 4). Wound infection was defined as palpable induration and local pain of a serous nature or purulent presence in the wound. The incidence of wound infection according to research by Mohammed et al. (2020) shows that the most common microbiological pattern that causes wound infections is *Staphylococcus aureus*, apart from *Escherichia coli*, *Klebsiella*, and *Pseudomonas*.

Of the 11 research journals, almost all journals monitored the incidence of infection after another *caesarean section*, namely the presence of fever. Based on research by Pooja et al. (Pooja et al., 2021) involving 320 pregnant women with *caesarean section*, the incidence of fever after surgery increased in the control group compared to the intervention group, namely 8 patients (3.6%) and 3 patients (1.4%). The control group received *Ceftriaxone* 1 g intravenously 30-40 minutes before surgery, while the intervention group received *cefotaxime* + *sulbactam* and *Metronidazole* intravenously for the first 3 days after surgery, followed by oral *cefixime* for the next 5 days. The result was a higher incidence of phlebitis, which can cause morbidity due to the presence of fever. The longer the IV cannula is used, the greater the risk of infection. The occurrence of fever was defined as an oral temperature of >38°C in the first 10 days postpartum.

Of the 11 research journals, almost all journals monitored the incidence of infection after caesarean section, namely the presence of endometritis. Based on research conducted by Dlamini et al. (2015) involving 464 pregnant women with caesarean section, the incidence of endometritis increased in the control group compared to the intervention group, occurring in 52 patients and 31 patients, with an increase percentage of 9%. Endometritis is described as marked uterine tenderness and/or annoying vaginal discharge accompanied by fever. This is similar to the research of Mohammed et al. (2020), where the incidence of endometritis in the study and control groups was 3.5% and 5.3%, respectively. The large number of endometritis cases in the control group could be due to the effect of antibiotic administration time. The timing of the administration of prophylactic antibiotics is more important than extended prophylaxis. During labor, the endometrium and peritoneal cavity can become contaminated with a number of highly pathogenic aerobic and anaerobic bacteria. Therefore, high plasma concentrations of antibiotics can reduce the incidence of endometritis.

Urinary tract infection (UTI) is defined as a positive urine culture result, whether accompanied by dysuria or not and can be accompanied by fever (2023). The incidence of urinary tract infections according to research by Mohammed et al. (2020) shows that the most common microbiological pattern that causes UTI is the organism *Escherichia coli*. Based on research by Jyothirmayi et al. (2017), involving 1,106 pregnant women with *caesarean section*, the incidence of UTI in the intervention group was 16 (9.7%) and in the control group was 21 (25.9%).

Of the 11 studies, there were 3 studies that examined the timing of prophylactic antibiotic administration during *caesarean section*, namely the study by Dlamini et al. (2015), Jyothirmayi et al. (2017), and Rai et al. (2018), who reported that administering antibiotics before skin incision was better in reducing the incidence of infection in the mother than administering them after umbilical cord clamping (Table 4). This is in accordance with the recommendation from the *WHO* guideline that prophylactic antibiotics are recommended to be given 30-60 minutes before the incision for both emergency and elective *caesarean sections*. High concentrations of prophylactic antibiotics in the blood during microbial contamination can reduce the incidence of surgical wound infections (Mohammed et al., 2020). Infections here can be prevented by selecting appropriate prophylactic antibiotics.

CONCLUSION

Based on the results of this article review, all research articles are RCT studies. *RCTs* are the gold standard for assessing the benefits of a treatment. Providing additional therapy with *Cephalexin* and *Metronidazole* as prophylactic antibiotics to obese pregnant women who will undergo *caesarean section* can significantly reduce the incidence of infection. The first-generation *cephalosporin* class of antibiotics, namely *Cefazolin*, is the antibiotic most widely used in patients undergoing *caesarean section*, and this is in accordance with the recommendations in the guideline. The prevalence of infection after *caesarean section* was the highest, namely infection in the surgical wound, which occurred in 11.8% or 437 *caesarean section* patients, with the most common microbiological pattern causing wound infection being *Staphylococcus aureus*.

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