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Original article

Impact of different antibiotic treatments on pregnancy maintenance in Holstein Friesian cows infected with foot-and-mouth disease

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ABSTRACT

This study was conducted at Setia Kawan dairy cattle farming cooperative in Nongkojajar, Pasuruan, East Java to evaluate the effects of different antibiotic treatments on pregnancy sustainability in Holstein Friesian (HF) dairy cows infected with foot and mouth disease (FMD). The objective was to identify which antibiotics have minimal impact on pregnancy outcomes in FMD infected cows. A total of 106 pregnant HF cows infected with FMD were included in this study. Samples were selected using a purposive sampling method with inclusion criteria of pregnant HF dairy cows that tested positive for FMD. Four types of antibiotics were assessed, including enrofloxacin, oxytetracycline, amoxicillin, and penicillin-streptomycin. The results showed that among cows treated with enrofloxacin, 88.46% maintained pregnancy while 11.54% experienced abortion. For oxytetracycline, 73.08% of cows did not abort, whereas 26.92% did. In the amoxicillin group, 61.54% maintained pregnancy and 38.46% aborted. For penicillin-streptomycin, only limited data were available, with 23.07% maintaining pregnancy and no recorded cases of abortion. In conclusion, while variations were observed among different antibiotic treatments, statistical analysis indicated no significant association between antibiotic type and abortion rate in HF cows infected with FMD. Further studies with larger sample sizes are recommended to confirm these findings.

Keywords: amoxicillin, enrofloxacin, oxytetracycline, penicillin, streptomycin

INTRODUCTION

Since 1887, Indonesia has experienced several outbreaks of foot and mouth disease (FMD) (Susila *et al*., 2023). The Directorate of Animal Health also stated that in 1887, the disease first entered the Malang region in East Java through the importation of cattle from the Netherlands. The last recorded outbreak of FMD on the island of Java occurred in 1983, which was subsequently eradicated through a mass vaccination program. However, to this day, several countries in Southeast Asia are still facing FMD outbreaks, which raises the possibility of the disease re-entering Indonesia. FMD re-emerged, affecting thousands of cattle in Indonesia, with the first case detected in Gresik regency on April 28, 2022, involving 402 cattle (Sutawi, 2022). Sutawi further reported that a second case was found involving 102

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cattle in Lamongan regency and 595 dairy cattle and buffalo in Sidoarjo regency infected with FMD on May 1, 2022. According to the PMK Alert website, as of July 11, 2022, there were 219,821 remaining FMD cases in Indonesia, along with additional data indicating 361,207 sick animals, 135,504 recoveries, and 2,342 deaths (FMD Alert, 2022).

The specific treatment for FMD remains unknown; however, supportive care might be administered to alleviate clinical symptoms and prevent secondary infections, including the use of antipyretics, antibiotics, and vitamins (Clemmons *et al*., 2021). The government, through the decision of the Director General of Livestock and Animal Health No. 5429 of 2022, had established protocols for managing sick animals affected by FMD, including the administration of antibiotics aimed at expediting the resolution of clinical signs and treating secondary infections. One consequence of antibiotic treatment in pregnant cows affected by FMD was the increased risk of abortion or premature birth.

Abortion is defined as the birth of a fetus that is dead or lacks the ability to survive outside of its mother's body. Generally, all types of livestock could experience abortion, which might occur during early, mid, or late pregnancy, or at any stage of gestation. Abortion cases were more frequently observed in dairy cattle than in beef cattle, attributed to two factors, the advanced selective breeding process and excessive milk extraction, which weakened physical condition and immune response (Albuja *et al*., 2019).

The spread of FMD had also impacted the population of dairy cattle at the Setia Kawan cooperative in Tutur district, Pasuruan regency, East Java, Indonesia. In managing FMD within the operational area of the cooperative, various types of medications are utilized for treatment. One of the medications employed is antibiotics; four types of antibiotics used include enrofloxacin, oxytetracycline, amoxicillin and penicillin-streptomycin. Therefore, this study aims to determine which antibiotic administration has the minimal side effects on pregnant Holstein Friesian (HF) dairy cows infected with FMD.

MATERIALS AND METHODS

Study design

This study employed a field survey approach. Both primary and secondary data were utilized. Primary data were collected through structured questionnaires distributed to local dairy farmers. Secondary data were obtained from veterinary service reports provided by the cooperative.

Sample selection

Secondary data were selected using purposive random sampling, with specific inclusion criteria of pregnant HF dairy cows that tested positive for FMD. All sampled cows were located within the Setia Kawan cooperative operational area, in Nongkojajar, Tutur district, Pasuruan regency. FMD diagnosis was conducted by veterinary officers based on clinical symptoms such as fever, reduced appetite, and visible lesions, including oral blisters on the tongue and mouth, as well as interdigital lesions.

According to official data submitted to the Ministry of Agriculture and Livestock through the website siagapmk.crisis-center.id, a total of 1,006 dairy cows tested positive for FMD in the Tutur district area under Setia Kawan cooperative between May 31, 2022, and February 7, 2023. Based on the recommendation for descriptive studies to include at least 10% of the target population (Gay *et al*., 2009), this study selected a sample size of 106 pregnant HF cows. The sample was allocated into four treatment groups, based on the type of antibiotic administered. The first group received enrofloxacin (Roxine® Inj by PT Sanbe Farma, Bandung, Indonesia), the second group received oxytetracycline (Oxy-kel 20® LA by Kela, Belgium), the third group received amoxicillin (Betamox® LA by Norbrook, Northern Ireland, UK), and the fourth group received penicillin-streptomycin (Pen & Strep® by Norbrook, Northern Ireland, UK), and a fifth group served

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as the control, consisting of cows that were not treated with antibiotics.

Research variables

The main variables observed were the occurrence of premature birth and abortion among the sampled cows.

Data analysis

Primary data were analyzed descriptively, based on responses to the farmer questionnaires. Secondary data were extracted from veterinary service reports provided by the cooperative. The results are presented using descriptive statistics.

RESULTS

In the control group, only three cows remained at the end of the observation period, while six cows remained in the penicillin-streptomycin group; the rest were culled or died during the study. Among the 87 cows analyzed, 20 (22.99%) experienced abortion (Table 1).

Table 1 Pregnancy outcomes in FMD-infected HF cows treated with various antibiotics

treatment group	abortion (%)
control	0/3 (0%)
enrofloxacin	3/26 (11.54%)
oxytetracycline	7/26 (26.92%)
amoxicillin	10/26 (38.46%)
pen-strep	0/6 (0%)

control: group consisted of pregnant HF cows infected with FMD that did not receive antibiotic treatment; pen-strep: refers to cows treated with a combination of penicillin and streptomycin; statistical analysis using the Chi-square test showed no significant differences between groups ($p > 0.05$).

DISCUSSION

The use of enrofloxacin, oxytetracycline, amoxicillin, and the penicillin-streptomycin combination in treating dairy cows was crucial for animal health; however, their potential impacts on reproductive outcomes, particularly abortion risks in pregnant cows, necessitated careful consideration. Veterinary professionals were urged to assess the individual benefits and risks associated with each antibiotic, particularly during critical stages of gestation.

Enrofloxacin, oxytetracycline, amoxicillin, and penicillin-streptomycin were important antibiotics used in veterinary medicine, particularly for treating bacterial infections in livestock, including dairy cows (Lianou and Fthenakis, 2022). Understanding their mechanisms of action, pharmacokinetics, and potential effects on reproductive health, especially in pregnant cows, was vital for safe and effective treatment practices. Enrofloxacin is a fluoroquinolone antibiotic that inhibits bacterial DNA gyrase and topoisomerase IV, enzymes critical for DNA replication, transcription, and repair. This mechanism of action effectively halted the growth of various Gram-negative and some Gram-positive bacteria (Grabowski *et al*., 2022). When administered, enrofloxacin was absorbed systemically, reaching various tissues, including the udder and uterus. While generally regarded as safe for lactating and non-pregnant cows, enrofloxacin's use during pregnancy raised concerns. It could cross the placenta, potentially exposing the fetus to therapeutic concentrations that might lead to developmental issues, particularly during critical stages of organ development (Ellerbrock *et al*., 2019). There had been no reports showing a relationship between enrofloxacin use and abortion in dairy cows, especially in early pregnancy.

Oxytetracycline, part of the tetracycline antibiotic class, inhibited bacterial protein synthesis by binding to the 30S ribosomal subunit, effectively stopping bacterial growth (Shutter and Akhondi, 2025). Its pharmacokinetics involved rapid absorption and distribution throughout a cow's body, including the placenta, raising concerns about fetal exposure and potential toxicity (Mileva *et al*., 2020). Oxytetracycline showed fast absorption and penetration in the uterine secretions and have a cross the placental barrier necessitated caution during use in pregnant cows. However, no well-documented links between oxytetracycline and

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abortion had been established.

Amoxicillin, a penicillin class antibiotic, functions by inhibiting bacterial cell wall synthesis through binding to penicillin-binding proteins (PBPs). This disruption led to bacterial cell lysis (Roney *et al*., 2023). Amoxicillin was typically well-absorbed and has a significant distribution within the cow's body, including the uterus, crossing the placental barrier. Although amoxicillin was considered safe when used appropriately, its use in pregnant cows must be approached cautiously (Wisher, 2012). Limited studies on its teratogenic effects existed, but anecdotal evidence and observations suggested possible links between antibiotic use, including amoxicillin, and abortion, although causation remains unassessed.

The combination of penicillin and streptomycin provided a dual approach to treating bacterial infections. Penicillin disrupted cell wall synthesis, while streptomycin inhibited protein synthesis, leading to bacterial death (Tufa *et al*., 2023). Both antibiotics penetrated various tissues, including the placenta (Pacifici, 2006; Waters and Tadi, 2023). While penicillin generally posed a low risk during pregnancy (Pacifici, 2006), streptomycin's safety profile was less clear, particularly concerning potential auditory effects on the developing fetus (Waters and Tadi, 2023). Factors such as dosage and timing could influence the risk of adverse outcomes, including abortion. Both antibiotics were essential for managing infections, which could pose greater risks if left untreated during pregnancy. Veterinary practitioners had to be diligently evaluate the necessity of antibiotic treatments in pregnant dairy cows against the backdrop of potential risks involved (Huber *et al*., 2024). Ongoing research was imperative to refine guidelines that ensure both effective infectious disease management and the health of pregnant cows and their calves. Overall, adhering to established practices in antibiotic administration, including proper dosing and withdrawal times, could promote food safety and animal welfare.

This study demonstrated that the use of enrofloxacin, oxytetracycline, amoxicillin, or the combination of penicillin-streptomycin to prevent secondary infections in pregnant cows infected with the FMD virus did not have a significant effect on pregnancy outcomes. The observed cases of abortion were likely due to nutritional deficiencies resulting from the clinical symptoms associated with FMD. Infected cows often experienced hyperthermia, which negatively impacted their appetite. Additionally, inflammation of the oral cavity and esophagus impaired the ability to chew and swallow forage, further contributing to reduced nutrient intake.

CONCLUSIONS

This study found no association between antibiotic use and abortion in pregnant HF cows infected with foot-and-mouth disease (FMD). The observed cases of abortion were not attributed to antibiotic treatment but were likely caused by non-infectious factors, particularly poor nutritional status resulting from limited access to feed due to the effects of FMD

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AUTHOR'S CONTRIBUTIONS

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VZDWP conceived the idea, designed the framework of the manuscript, and was responsible for data acquisition, analysis, interpretation, and drafting of the manuscript under the supervision of KR. JR, HAH, and NT critically reviewed and revised the manuscript for intellectual content. All authors read and approved the final version of the manuscript.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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