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Effect of GnRH treatment as a potential solution for ovarian disorders in dairy cows infected with foot and mouth disease in Indonesian smallholder farms

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ABSTRACT

Background: The outbreak of foot and mouth disease (FMD) in Indonesia induces reproductive disorders in dairy cows that lead to economic losses to smallholder dairy farms.

Aim: The study was to assess the influence of FMD on reproductive traits and evaluate the effect of gonadotropin hormone-releasing hormone (GnRH) administrations on the reproductive performance in FMD-infected dairy cows.

Methods: The study was conducted in Jemowo village, Taman Sari sub-district, Boyolali district, Central Java, Indonesia. A total of 155 cows were used to identify the reproductive disorders on FMD-infected dairy cows aged 2–10 years old. Cows were raised in similar conditions and fed diets. A single dose of 2 ml GnRH was injected intramuscularly into 96 ovarian disorder cows. Reproductive performance was measured by service per conception (S/C), conception rate (CR), and pregnancy rate (PR). A descriptive study was conducted to demonstrate the results.

Results: The study showed that 61.9% of FMD-infected cows had reproductive disorders, whereby 53.5% ovarian hypofunction, 4.52% silent heat, 1.94% repeat breeder, 1.29% ovarian atrophy, and 0.65% endometritis. FMD-infected cows injected with GnRH had a 98% reproductive recovery rate. Moreover, the S/C, CR, and PR of cows injected with GnRH were 2.02%, 51%, and 85%.

Conclusion: GnRH administrations enhanced the reproductive traits of FMD-infected dairy cows indicated by the improvement of CR and PR.

Keywords: Dairy cow, Foot and mouth disease, Gonadotropin-releasing hormone, Indonesia, Reproductive disorder.

Introduction

Foot and mouth disease (FMD) is an acute and rapidly spreading disease that leads to significant financial losses (Grubman and Baxt, 2004). Attribute to the Aphovirus genus in the Picornaviridae family (MacLachlan and Dubovi, 2011), it presents an incubation period of 2–14 days, with mortality rates varying from 1% to 5% in adult cattle to surpassing 20% in calves (WOAH, 2022). Clinical symptoms of FMD encompass anorexia, fever, and lesions on the mouth, hooves, and udder (Knipe and Howely, 2001), along with diminished milk production (Adjid, 2020; Sudarsono, 2022). Moreover, FMD inhibits growth, reduces milk yield, impairs fertility, and elevates mortality in dairy cattle (Paton, 2018).

FMD is classified as a strategic infectious animal disease in Indonesia (MARI, 2013). Although Indonesia attained

FMD-free status in 1986, the disease re-emerged in 2022, swiftly spreading to 22 provinces and resulting in significant economic loss. The outbreak affected 570,137 cattle, with a morbidity rate of 1.04% and a mortality rate of 0.02%. Additionally, it necessitated the forced slaughter of 12,650 cattle by November 2022 (MARI, 2022). However, there is no data on the impact of FMD on reproductive performance, and no strategy for the recovery of reproductive performance in smallholder dairy cattle has been implemented in Indonesia to date.

Moreover, gonadotropin-releasing hormone (GnRH) is a neuropeptide that plays a pivotal role in regulating vertebrate reproduction (Mohammadzadeh, 2019). Administration of GnRH induces the activation of GnRH receptors in the pituitary, leading to the release of LH and the initiation of luteinization (Schneider *et*

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al., 2006). Also, GnRH administration facilitates the luteinization process of the corpus luteum (Besbaci et al., 2020; López-Gatius and Garcia-Ispuerto, 2020; García-Guerra et al., 2020) and enhances progesterone levels post-ovulation (Roth et al., 2021). These result in normal reproductive function in cows indicated by the estrus cycle within 18–21 days (Crowe et al., 2018). Based on the aforementioned, we hypothesized that GnRH administrations have potential effects to enhance the reproductive performance of FMD-infected dairy cows. Thus, the study was to assess the influence of FMD on the reproductive traits in dairy cows and to examine the impact of GnRH injections on the ovarian disorder of FMD-infected dairy cows.

Materials and Methods

Animals and location

All subjects in the study were dairy cows that had been infected with foot-and-mouth disease (FMD) 1 month prior, aged from 2 to 10 years old, and owned by smallholder farmers in Jemowo village, Tamansari, Boyolali district, Central Java. All cows were reared under identical conditions. The research was performed from October 2022 to March 2023.

Identification of reproductive disorders

A total of 155 head dairy cows were used for the identification of ovarian disorders during and one month after FMD infection. The assessments were conducted through farmer interviews and rectal palpation. No signs of estrus behaviour as reported by farmers were used as indicators of potential reproductive disorders. Furthermore, no follicular activity in the ovaries detected by rectal palpation confirmed the irregular reproductive cycle.

Experimental treatment

GnRH treatments were administered to 96 ovarian disorders FMD-infected dairy cows at 1 month after FMD infection with some cows showed recovery signs and others still displaying mild clinical symptoms. The GnRH was Gonasyl, a commercial product from Agroveta, Kalbe Co., Indonesia, containing gonadorelin (acetate) at a concentration of 50 mg/ml. All cows received a single intramuscular injection of 2 ml GnRH in accordance with the manufacturer's instructions.

Estrus detection and artificial insemination

Estrus signs were observed after the treatment (Fig. 1). Visual assessments were conducted to identify estrus signs, including the presence of a reddish and enlarged vulva, warm palpability, restlessness, engagement in mounting behavior with other cows, and remaining silent when mounted by others. Cows displaying signs of estrus were subjected to artificial insemination at the optimal time.

Pregnancy evaluation

The assessment of pregnancy was performed at 60 days using ultrasound. Service per conception (S/C), conception rate (CR), and pregnancy rate (PR) were indicators to measure artificial insemination (AI)

success. S/C was derived from the ratio of artificial inseminations to successfully pregnant cows. CR represented the proportion of cows achieving pregnancy with a single artificial insemination. PR was determined by dividing the number of pregnant cows by the total number of inseminated cows.

Statistical analysis

Descriptive analysis was used in this study. Data were presented in numbers and percentages.

Ethical approval

All protocols followed the ethical procedure approved by the Ethics Committee of the Faculty of Veterinary Medicine, Gadjah Mada University, Indonesia (71/EC-FKH/Int./2023).

Results and Discussion

Reproductive disorders of FMD-infected cows

The present study showed that clinical symptoms of foot-and-mouth disease (FMD) in dairy cattle included fever, low appetite, lameness, hypersalivation, and the presence of lesions in the mouth, tongue, and hooves. Reproductive disorders were identified in 96 out of 155 (61.9 %) FMD-infected cows including ovarian hypofunction (53.5%), silent heat (4.52%), repeat breeder (1.94%), ovarian atrophy (1.29%), and endometritis (0.65%) (Table 1). Based on farmer interviews, all of the sampled cows had no these reproductive disorders before FMD infection. Thus, we suggest that FMD infection was the primary factor of reproductive disorders in cows in the present study.

In this investigation, the prevalence of reproductive disorders was notably high. It is higher than previous studies, whereby the studies of Khan et al. (2016) and Hadush et al. (2016) found that FMD induces reproductive abnormalities in cattle with incident rates at 33.85% and 37.85%. Moreover, Tesfaye and Shamble (2013) discovered that 40.25% of cows have reproductive disorders attributed to the effects of FMD. Anoestrus emerged as the primary reproductive abnormality observed in FMD-infected cows in the present study. The incidence of anoestrus was 57.4% in FMD-infected cows with conditions such as

Table 1. Reproductive status of FMD-infected cows.

Reproduction status	Head	Frequency (%)
Normal (pregnant, follicular, and luteal phases)	59	38.1
Reproductive disorder:		
• Ovarian hypofunction	83	53.5
• Silent heat	7	4.52
• Repeat breeder	3	1.94
• Ovarian atrophy	2	1.29
• Endometritis	1	0.65
Total	155	100

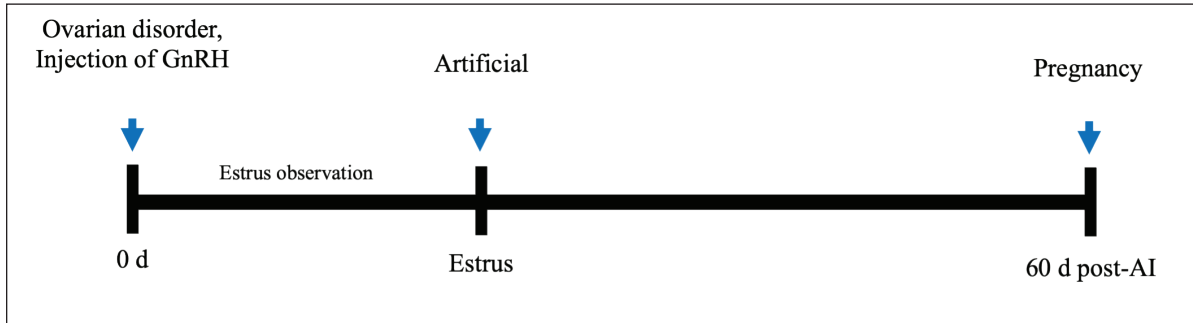


Fig. 1. Illustration of the study of GnRH injection on reproductive performance in FMD-infected cows.

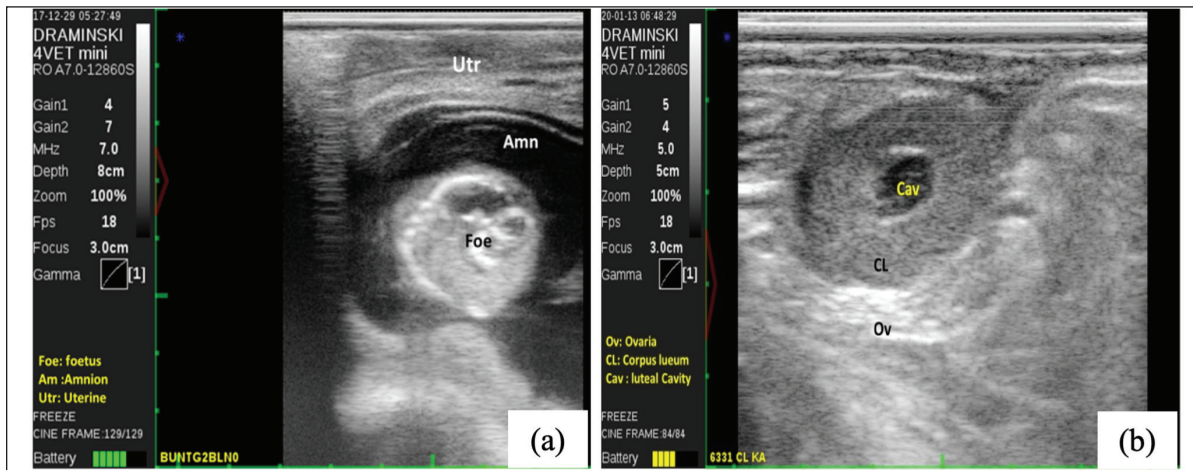


Fig. 2. Displaying pregnancy test using ultrasound (USG) at 60 days post-AI in FMD-infected cows (Foe: Foetus, Amn: amnion, Utr: Uterine) (a); depicting corpus luteum (CL) at normal oestrus cycle (Cav: luteal cavity, Ov: ovarium) (b).

ovarian hypofunction, silent heat, ovarian atrophy, and endometritis. Our result was higher than the finding of Sarder *et al.* (2010), which revealed that the prevalence of anoestrus crossbred dairy cows infected by FMD in Bangladesh is 20.4%. Similarly, Khan *et al.* (2016) reported the incidence of anoestrus dairy cows infected by FMD in India is 31.79%.

The prevalence of inactive ovaries (ovarian hypofunction and ovarian atrophy) was recorded at 54.84% in the present study. This incidence was higher than the research of Zaher and Ahmed (2008) conducted on FMD-affected buffaloes in Egypt, whereby the incidence of inactive ovaries was 31.89%. The inactive ovarian incidence in FMD-infected dairy cows was attributed to low nutritional intake during the infection. Low body condition scores and inadequate nutritional intake cause hypofunction and ovarian atrophy. Hermadi *et al.* (2017) found that ovarian atrophy was prolonged ovarian hypofunction. FMD reduces the appetite of cows because of the lesions in the mouth and tongue resulting in a negative energy balance (NEB). Furthermore, NEB leads to a decrease

in the reproductive performance and the fertility of cows (Roche *et al.*, 2017; Bisinotto *et al.*, 2018; Đuričić *et al.*, 2019). Likewise, Ahmed *et al.* (2006) found that NEB affected by inadequate nutritional intake caused inactive ovaries in FMD-affected Egyptian buffaloes.

Effect of treatment on reproductive performance of FMD-infected cows

Administrations of gonadotropin hormone-releasing hormone (GnRH) effectively induced estrus in all cows with ovarian hypofunction and silent heat in this study. A total of 94 heads of cows (97.9%) showed normal estrus after the treatment. However, estrus signs were not present in cows with ovarian atrophy. No prior research has documented the optimal timing for GnRH injection post-FMD infection. Therefore, our findings suggest that administering GnRH one month after FMD infection is an effective strategy for restoring reproductive function in cows.

The pregnancy test was performed at 60 days post artificial insemination with ultrasound to show the fetus and amnion (Fig. 2). Our study revealed that the S/C in FMD-infected cows post-treatment was 2.02 (Table 2).

Table 2. Effect of GnRH administrations on reproductive performance of FMD-infected cows.

Parameters	Total
Pregnant cows (head)	82
Service per conception (S/C)	2.02
Conception rate (%)	51%
Pregnancy rate (%)	85%

Moreover, CR and PR were 51 % and 85 % in FMD-infected cows post-treatment.

The present investigation showed that GnRH administration successfully triggers estrus activity, resulting in an 85% PR. Our study is in line with the finding of Burnett *et al.* (2019), where GnRH administration in low-estrus cows results in a 40.0% PR, compared to 30.8% in untreated cows. Likewise, Roth *et al.* (2021) reported that GnRH treatment during the dry season, especially in the fall, increases the PRs of cows. Moreover, the administration of 200- μ g GnRH increases the ovulatory response, leading to a 54.6% PR in cows (Ariciniega *et al.*, 2020). López-Gatius and Garcia-Ispuerto (2020) demonstrated that GnRH treatment effectively maintains pregnancy in sub-fertile cows. Furthermore, Besbaci *et al.* (2020) documented GnRH-treated cows group has higher PRs than the untreated group. In addition, GnRH injection in Ovsynch protocol, combined with split-time artificial insemination, increases total estrus response and PRs in cows (Bishop *et al.*, 2017). Thus, our study confirms the finding of Long *et al.* (2022) study, whereby GnRH administration is an effective method for managing cows with ovarian disorders. Furthermore, it contributes to the normalization of the ovarian cycle (Jeengar *et al.*, 2014).

GnRH treatment proves very effective for treating ovarian disorders in cows (Ari *et al.*, 2017; Naglis, 2019). GnRH, a neuropeptide produced by the hypothalamus, is a preeminent regulator for physiological processes and reproductive functions in mammals (Mohammadzadeh, 2019). It stimulates the synthesis and release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary (Kadokawa *et al.*, 2014). Moreover, GnRH also acts as a regulator of gonadotropin secretion and LH/FSH-releasing hormone (Hafez *et al.*, 2000). It is well-documented that GnRH effectively induces estrus in cows, whereby its actions are facilitated by GnRH receptors in follicular and corpus luteum tissues (Ramakrishna *et al.*, 2005). Exogenous GnRH injections activate pituitary GnRH receptors, triggering the release of LH (Schneider *et al.*, 2006). Thus, we suggest that GnRH administration effectively induced normal estrus in FMD-infected cows by modulating LH secretion.

The S/C of FMD-infected cows post-treatment in this study was 2.02. Our finding was similar to the study of Pramono *et al.* (2010) found that the S/C of dairy cows in Yogyakarta is 1.98 ± 0.91 . Similarly, Kusmayadi and Hadist (2023) discovered that S/C was 1.8 ± 0.85 for dairy cows in Pengalengan and Kertasari, West Java. Wirando *et al.* (2023) also recorded that the S/C of dairy cows in Banyuwangi, East Java is 2.15 ± 0.28 . In contrast, Setyorini *et al.* (2022) reported that S/C is 1.4–1.7 for dairy cows in the Baturraden and Sleman regencies, Indonesia. Moreover, the present found that the CR of FMD-infected cows post-treatment was 51 %. It is better than the report of Yekti *et al.* (2019), whereby the CR of crossbred Ongole cows is 43.75%.

Conclusion

The study revealed that 98% of FMD-infected cows had normal estrus after the injection of GnRH. The treatments resulted in a CR (51 %) and PR (85 %) in FMD-infected cows. Thus, the administration of GnRH effectively improves the reproductive performance of FMD-infected cows. However, a larger sample is necessary in further investigation to validate our results.

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Conflict of interest

The authors declare that there is no conflict of interest.

Authors' contributions

JS designed and conducted the research, analyzed the data, and wrote the manuscript. EMNS, MHW, and AB supervised the research. SH and AB reviewed and revised the manuscript.

Data availability

All data are provided in the manuscript.

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