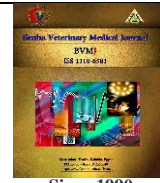




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A field investigation of the impact of the interaction between IBR vaccination and insemination time in cow herd: Reproductive and economic perspectives.

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ABSTRACT

Post-vaccination response could impair animal fertility and cause economic losses. To verify the possible consequences of IBR vaccination, Holstein cows (n= 840) from 1st-3rd lactations vaccinated with polyvalent modified-live viral vaccine were included in this investigation. Cows were allocated to Pre-vac. (n=82; inseminated Day-36 to Day-18), around vac. (n=133; inseminated Day-17 to Day+3) and post-vac. (n=363; inseminated from Day+4 to Day+60) groups according to insemination time related to the day of IBR vaccination (Zero day). The number of inseminations/conceptions, return to service rate, pregnancy rate, days return to service, and milk production were recorded. Results showed that 3-week return, and 90-day return rates were maximal in the around vac. (45%) and pre-vac. (50%) groups, respectively. At the 2nd insemination, the around-vac and post-vac inseminated animals decreased compared to pre-vac. The return to insemination in the around-vac, post-vac, and pre-vac groups was 69%, 63%, and 59%, respectively, during the first 45 days post-insemination. The service return (days) was 31.74±2.46, 23.61±1.87, and 27.10±1.39 in pre-vac, around-vac and post-vac groups, respectively. The synchronization and insemination extra cost/100 cows during the pregnancy period were maximal in the pre-vac. group (27590 & 17800 EGP, respectively), but least in the post-vac. group (22010 & 14200 EGP, respectively). In conclusion, MLV IBR vaccination showed a transit effect on fertility and resulted in economic losses. This study spotted the light to the interaction between IBR vaccination and insemination timing to avoid any conception failure and extra costs to dairy farm profitability.

1. INTRODUCTION

The reproductive efficiency is a key factor in determining the dairy farm profitability (Wang et al., 2021). Efficiency refers to the maximum average production input so that maximum profits are also obtained (Mandaka and Hutagaol, 2005). Using synchronization followed by artificial insemination with superior semen helps the cows to breed quickly, calving at regular intervals, and increasing the potential milk production (Rusdiana et al., 2020). Although early pregnancy loss is a primary reason that affects reproductive efficiency and possess severe economic losses, the early and accurate pregnancy loss diagnosis guide for estrus synchronization shortens day open and increases the overall conception rate of the dairy herd (Gui et al., 2024).

Approximately 50% of pregnancy losses in cattle are associated with infectious diseases (Khodakaram and Ikede, 2005; McEwan and Carman, 2005). Infectious bovine rhinotracheitis, caused by the Bovine Herpes virus 1 (BHV-1), negatively affects the productive and/or reproductive performances of infected cattle herds and results in considerable economic losses (Renault et al., 2018). Vaccination with either modified-live virus (MLV) or inactivated virus vaccines could impair fertility

through a systemic reaction due to the immunization (inducing hyperthermia) or stress (Kelling, 2007). Thermal stress can affect many reproductive parameters in cows including oocyte quality, conception failure, defective embryo development, and increased embryo mortality (Wolfenson et al., 2000; Hansen et al., 2001; Bridges et al., 2005).

Embryos are fragile before uterine implantation and sensitive to factors such as hyperthermia or stress (Hansen et al., 2001). Moreover, vaccinated animals around the time of insemination or before the implantation of the embryo show an increase in the return to estrus (Nusinovici et al., 2011). The time lag between the vaccination and the return to estrus may be long, frequent, or might not systematically expressed (Nusinovici et al., 2011). A decrease in the first service conception increases the number of inseminations, number of days open, feeding cost, culling loss, and replacement heifers cost (Chang et al., 2006). Therefore, the identification of factors that potentially limit the success or failure of first service/conception is useful for improving reproductive performance in dairy cows.

Generally, although live attenuated vaccines can generate strong protective immunity, they also are known to provoke side effects e.g., teratological effects, depress milk production, and abortion (Veronesi et al., 2005;

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Saegerman et al., 2007). Besides, some vaccines e.g., infectious bovine rhinotracheitis virus (IBR) carry the potential to revert to virulence and inflict the damage they are designed to prevent (Kelling, 2007). Because of the above mentioned, some practicing veterinarians resist the notion of vaccinating cows on the same day of artificial insemination arguing that this practice could cause pregnancy loss (Ferreira et al., 2018).

In the current research, we hypothesized that the cows are assumed to be exposed to a possible side effect of vaccination according to the interval between insemination and vaccination. Therefore, this study aimed to quantify possible side effects of vaccination against IBR using polyvalent MLV vaccines under field conditions on the fertility and extra costs of dairy cows.

2. MATERIAL AND METHODS

Ethical approval

The research protocol was approved by the Ethical Committee for Institutional Animal Use and Care of the Faculty of Veterinary Medicine, Benha University with the approval number (BUFVTM 44-06-23).

2.1. Animal groupings

The present investigation extended from Jan. 2020 to Dec. 2022 on Holstein cows (n= 840) from 1st to 3rd lactations, belonged to the private dairy farm located in North of Delta, Egypt. Animals were managed according to routine animal husbandry procedures, fed an age-appropriate balanced ration, and vaccinated with a comprehensive routine vaccination program against common viral (FMD, LSD, 3-day thickness) and bacterial (Colistredium, Brucella, Pastrella,..) diseases.

Vaccination against respiratory reproductive diseases (e.g., infectious bovine rhinotracheitis (IBR), bovine viral diarrhoea (BVD), bovine respiratory syncytial virus (BRSV), and parainfluenza 3 (PI3)) was adopted twice per year (in winter and summer seasons) using the commercially available, a polyvalent vaccine (Cattle Master GOLD FP 5 L5, Zoetis Inc.) by subcutaneous route.

All cows were routinely examined to ensure the soundness of the reproductive and general health aspects, and any cows that showed any pathological conditions were excluded.

Cows were allocated to three study groups according to insemination time and coincident with the day of IBR vaccination (Zero-day) as follows: Pre-vac. group (n=82) in which cows inseminated from 36 to 18 days before the day of vaccination (day -36 to day -18). The around vac. group (n=133) were inseminated during the period from 17 days before vaccination to day 3 after vaccination (day -17: day +3). The post-vac. group (n=363) was inseminated from Day 4 to Day 60 after vaccination (day + 4: day +60).

All cows were observed daily after vaccination for post-vaccine-adverse-response. Estrus detection was done routinely through a skilled farm team on a 24/7 basis and accordingly, insemination was accomplished either relying on the detection of the standing heat (non-synchronized animals) or at a fixed time after Ovsynch protocol (synchronized animals) (Pursley et al., 1995).

2.2 Vaccine:

Polyvalent vaccine (Cattle Master GOLD FP 5 L5, Zoetis Inc.) was used. It is a combined freeze-dried preparation of chemically altered strains of IBR and PI3 viruses and modified live BRSV, plus a liquid adjuvanted preparation of inactivated BVDV (types 1 and 2) and inactivated cultures of the 5 Leptospira serovars.

2.3. Reproductive data collection and handling

Data were collected from the farm recording system during the study period, for tracing the reproductive parameters (Nusinovici et al., 2011) including:

2.3.1. The number of inseminations/cow after vaccination till conception.

2.3.2. Indices of pregnancy failure

a) 3-week return to service rate (%).

b) Return rate < 90-day (%).

c) Return rate >90-day post artificial insemination (AI) (%)

d) Embryonic/fetal loss rate (%).

2.3.3. Indices of pregnancy success

a) 3-week nonreturn (i.e. Conception) rate (%)

b) Pregnancy rate (%)

c) Days return to service. (Aono et al., 2013).

2.3.4. The productive index e.g., average milk production per cow during the study period.

2.4. Economic losses calculations

The extra costs were estimated descriptively per 100 cows. The costs calculated included feeding costs for cows returned to service (EGP), costs of one extra AI dose per 100 cows returned 45 days post-breeding (EGP), insemination cost per 100 cows for one extra AI dose at the least for the failed pregnant cows (EGP), and cost of synchronization/100 cows.

2.4.1. The AI cost/100 cows= mean number of inseminations per conception \times 100 cows \times cost of AI dose (\approx 200 EGP).

2.4.2. Costs of feed/cow returned to service= days to return service \times feed cost/day (\approx 300 EGP).

2.4.3. Cost of synchronization/100 cows= cow% \times number of synchronization dose(s) \times dose cost (\approx 310 EGP).

2.5. Statistical analysis

Data obtained were tabulated with Microsoft Excel, and statically analyzed with the *Chi*-square analysis and One-way ANOVA according to data type using statistical tests using SPSS (ver. 23) program (Arkkelin, 2014). The setting of the P value was at 0.05 to mark the significant differences.

3. RESULTS

As shown in Table (1) there were numerical differences in the fertility indices as affected by the period related to the time of vaccination. The mean number of inseminations in pre-vac, around vac, and post-vac groups was 2.40 ± 0.15 , 2.64 ± 0.13 , and 2.77 ± 0.09 , respectively. The 3-week return rate was the highest in the around vac. group (45%), and the 90-day return rate was the highest in pre-vac. group (50%). The conception rate was the highest for the post-vac. group (67%), within the first 3 weeks of pregnancy, while it was the lowest for the pre-vac group (50%) within the period from 22 to 90 days of pregnancy. The percentage of returned cows all over the pregnancy period was the highest for the pre-vac. group (89%) when compared with around vac and post-vac groups (78 and 71%, respectively). There were extra costs from additional synchronization and insemination doses among different groups as shown in Tables (2 and 4), as every 100 pregnant-failed cows costs were (27590&17800, 24180 &15600, and 22010&14200 EGP, respectively) for at least one extra synchronization and AI dosage. Fig. (1) showed the distribution of cows inseminated after vaccination. At the 1st insemination, there was a numerical similarity between pre-vac., around-vac., and post-vac. groups. However, at the 2nd insemination, the around-vac and post-vac groups showed a decrease in the

cows presented to insemination compared to the pre-vac group.

As shown in Fig. (2) during the first 45 days post-insemination, the rate of cows showing a return to insemination was the highest in around vac group (69%), followed by the post-vac group (63%) and pre-vac group (59%), that reflected on increasing the extra costs for synchronization, and insemination in around-vac. group rather than other groups. As shown in Table (3) the average days to return to service were the shortest in the around-vac. group (23.61±1.87 d) than in pre-vac. (31.74±2.46 d) and post-vac groups (27.10±1.39 d). Regarding the feed cost during the return time, it was 7083 EGP for a cow inside the

around-vac., while it was 9522 and 8130 EGP for pre-vac and post-vac ones. The gap in 3 weeks non-return to service (rate %) between groups was high between post-vac. and around-vac. groups in non-synchronized animals (59 vs. 51%) inseminated after heat detection and synchronized animals (79.5 vs.62%) inseminated at a fixed time. The Pre-vac. group showed a low overall pregnancy rate (11%) and high overall embryonic/ fetal losses (51%), in the meantime the corresponding values were improved (i.e. pregnancy rate was comparatively high, and embryonic/fetal loss was low) in the post-vac group. The overall mean milk production was nearly similar in the three studied groups (37.00±0.66, 36.91±0.56, and 36.39±0.34 kg/day, respectively).

Table 1 Return-to-service rates and distribution of cows and AI according to the IBR vaccination status

Item	Pre-vac. (-18 to -36 day)	Around vac. (-17 to +3 day)	Post vac. (+4 to +60 day)
No. of cows	82	133	363
Total number of inseminations	197	351	1007
Mean no. of insemination/animal	2.40±0.15	2.64±0.13	2.77±0.09
Form of pregnancy failure	3-weeks return rate	31 (38%)	60 (45%)
	90 days return rate	41 (50%)	41 (31%)
	> 90 days return rate	1 (1%)	3 (2%)
Form of pregnancy success	3-weeks non-return rate	51 (62%)	73 (55%)
	Rate of returned cows all over the pregnancy	89%	78%

Day 0 is a day of vaccination.

Table 2 Impact of IBR vaccination timing related to insemination on the extra costs of insemination/feeding in dairy herd.

Item	Pre-vac. (-18 to -36 day)	Around vac. (-17 to +3 day)	Post-vac. (+4 to +60 day)
AI cost/100 cows (EGP)	48000	52800	55400
Feeding costs for cows returned to service (EGP)	9522	7083	8130
Costs of one extra AI dose per 100 cows returned 45 days post breeding (EGP)	11800	13800	12600
Cost of at least one extra AI dose per 100 cows returned pregnant cows (EGP)	17800	15600	14200
Costs of several AI doses per 100 cows returned pregnant cows (EGP)	42720	41184	39334

Day 0 is a day of vaccination. The AI cost/100 cows= mean number of inseminations per conception × 100 cows × cost of AI dose (~ 200 EGP). Costs of feed/cow returned to service days to return service × feed cost/day (~ 300 EGP).

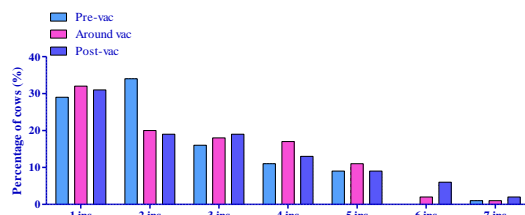


Fig. 1 Distribution of inseminated cows at 1st to 7th insemination post-vaccination

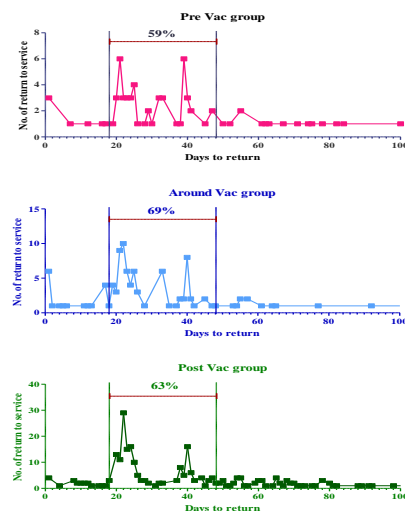


Fig. 2. Distribution of the time interval between AI and return-to-service in dairy cows during pre-vaccination (-18 days: -36 days), around vaccination (-17days, vac, +3), and post-vaccination (+4 days post vac.: +60) in unexposed to IBR virus.

4. DISCUSSION

Booster immunization with the polyvalent vaccine including MLV IBR vaccine showed a slight impact on the vaccinated

dairy cow fertility. The effect was found in the around vac. group (which inseminated 17 days before to 3 days after vaccination) through the increase in the 3 weeks return to service rate either in non-synchronized or synchronized animals compared to other groups. In addition, the rate of cows returning to service during the first 45 days post insemination was higher (69%) in the around vac group compared to the other groups. However, the impact on fertility disappeared in 90 or more days to return to service, overall pregnancy rate, and overall late embryonic loss. It was also noticed that the mean days to return to service were lower (23.61±1.87 days) than the other groups. These results may indicate short-term side effects of vaccination on cows' fertility which is likely to be due to early embryonic death. Nusinovici et al. (2011) speculated that hyperthermia and stress factors could be involved in fertility decrease following vaccination. Hyperthermia very often is observed after vaccination (Martinod, 1995) and an increase of ≥ 1 °C in body temperature can compromise reproductive functions (Hansen et al., 2001) and lead to reduced embryonic development (Putney et al., 1988). A slight transient rise in temperature (1° C) after vaccination is mentioned in some MLV IBR commercial vaccines leaflet e.g., Bovilis IBR Marker Live (MSD Animal Health) and in Hiprabovis IBR Marker Live (Hipra Animal Health). This temperature rise may also accompany other IBR vaccines even if it isn't observable as it is slight and transient. Slight hyperthermia might integrate the effect of vaccination on fertility when administered around the time of insemination. The fragility of embryos before uterine implantation and their sensitivity to factors such as hyperthermia or stress (Hansen et al., 2001) may point to vaccine consequences on early embryonic death.

As MLV vaccines carry with them the potential to revert to virulence and inflict the damage they are designed to prevent (Kelling, 2007), no signals of MLV IBR vaccine were used in our study to revert to IBR virulence. Our results concluded

that the mean days to return to service were numerically lower (23.61 ± 1.87 d) in the inseminated around-vac. group than the other groups, which slightly matches the behavior of IBR virus in inducing short estrous cycles (Kendrick and McEntee, 1967). This result is very critical from the economic point of view, as the shorter days to return the less additional feed cost because it reduces the calving interval. These findings were in the same line with Albaaj et al. (2023), who found that early abortion leads to an increased calving interval. The rate of returned cows all over the pregnancy period was the greatest in the pre-vac. group (89%) when compared with around vac and post-vac groups (78 and 71%, respectively). This result accused the extra costs needed for synchronization and insemination, which came in agreement with Ealy and Seekford (2019), who showed that abortion harmed cow productivity and increased feeding and reproduction costs, besides the veterinary and labor costs.

Generally, the interaction between the timing of IBR vaccination and conception is poorly studied and seems variable (Walz et al., 2015b; Ferreira et al., 2018). Our study disagreed with old studies (Van der Maaten et al., 1985; Chiang et al., 1990; Smith et al., 1990) which concluded an aggressive side effect of MLV IBR vaccination on cows' fertility. Our study relatively agreed with Walz et al. (2015a), who showed that there is no hindrance to fertility when the vaccine is given at 10 or 31 preceding synchronized natural insemination. A single field study can't prove a causal relation between vaccination and a decrease in fertility (Nusinovici et al., 2011). So, to specify and clarify the relation between IBR vaccination and cow insemination, it needs further studies to focus on the direct effect of the vaccine on the reproductive tract and its related hormones.

Table 3 Effect of infectious bovine rhinotracheitis virus vaccination on the reproductive and productive performance of cows

Item	Pre-vac. (-18 to -36 d)	Around vac. (-17 to +3 d)	Post vac. (+4 to +60 d)
Investigation period (Day 0 is day of vaccination)			
No. of Cows	82	133	363
Days to return to service	31.74±2.46a	23.61±1.87b	27.10±1.39ab
Summary of Repro. Protocols			
	No.		
Non-Synchronized	51	88	212
3-Week non-return to service rate	28/51 (55%)	45/88 (51%)	125/212 (59%)
3-Week-return-to service rates	23/51 (45%)	43/88 (49%)	87/212 (41%)
	No.		
Synchronized	31	45	151
3-Week non-return to service rate	23/31 (74%)	28/45 (62%)	120/151 (79.5%)
3-Week-return-to service rates	8/31 (26%)	17/45 (38%)	31/151 (20.5%)
Overall pregnancy rate	11%	22%	29%
Overall embryonic/fetal loss	51%	33%	38%
Overall average milk production (kg)	37.00±0.66	36.91±0.56	36.39±0.34

Data (Mean ±SEM) with different letters in the same column were significantly differed at $P < 0.05$.

Table 4 Impact of IBR vaccination timing related to insemination on the extra costs of medication/synchronization in dairy herd.

Item (per EGP)	Pre-vac.	Around-vac.	Post-vac.	Total
Synchronization costs in case of conception [1]				
% of cow conceived at 2 nd AI	34.15	20.3	19.28	73.73
Cost of one extra-synchronization dose	(34.15*1*310)=10586.5	(20.30*1*310)=6293.0	(19.28*1*310)=5976.8	22856.3
% of cow conceived at 3 rd AI	15.85	18.05	19.28	53.18
Cost of two extra-synchronization doses	(15.85*2*310)=9827.0	(18.05*2*310)=11191.0	(19.28*2*310)=11953.6	32971.6
Synchronization costs in case of pregnancy failure				
Cows returned 3-weeks post AI	(38*1*310)=11780.0	(45*1*310)=13950.0	(33*1*310)=10230.0	35960
Cows returned within 90 days post AI	(50*1*310)=15500.0	(31*1*310)=9610.0	(36*1*310)=11160.0	36270
Cows returned > 90 days post AI	(1*1*310)=310.0	(2*1*310)=620	(2*1*310)=620	1550
Total extra costs /100 cows/group in pregnancy failure (EGP) [2]	27590	24180	22010	73780
Sum of extra costs/ 100/cows/group (sum of [1] and [2])	48003.5	41664	39940.4	129607.9

EGP: Egyptian Pound. Total no. of synchronized cows=578 cows. Cost of synchronization dose=310 EGP. The number of cows conceived at the 1st AI=178 cows. Cost of synchronization/100 cows= cow% × no. of synchronization dose(s) × dose cost

5. CONCLUSIONS

This study highlighted the effect of MLV IBR vaccination on cows' fertility and money matters. The effect was largely transit and restricted to the increase in the 3-week return to service rate but minimally affected the overall pregnancy rates. This side effect thus likely passes undetectable in farms, though it harbors extra costs that affect the dairy farm's profitability. That is why we recommend avoidance of interaction between IBR vaccination and insemination days, to avoid any conception losses and economic drawbacks.

CONFLICT OF INTEREST

No conflict of interests.

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