IRANIAN JOURNAL OF RUMINANTS HEALTH RESEARCH 2017, 2(2):31-40
Doi: 10.22055/ijrhr.2019.28584.1023

Determinants of foot-and-mouth disease in industrial dairy farms of Qazvin province: a case-control study

Kamalidoost, Y[1]., Bokaie, S[2*]., Nadalian, M[3]., Rahmanian`, V[4]., Mirzaie, K[5].

1- Graduated in Veterinary Faculty of University of Tehran, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran
2- Epidemiology and zoonosis division department of food hygiene, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran
3- The academy of Sciences Islamic Republic of Iran
4- Ph.D Candidate in Epidemiology, Epidemiology and zoonosis division department of food hygiene, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran
5- Ph.D in Epidemiology, Iran Veterinary Organization , Qazvin , Iran

[*]Corresponding author: sbokaie@ut.ac.ir

ABSTRACT

Foot-and-mouth disease (FMD) is a highly contagious viral disease of ruminants, which causes fever and blisters in their mouth and feet. This study, as a case- study design, was conducted to determine the factors related to FMD occurrence in the industrial dairy farms of Qazvin Province, Iran. The case unit was referred to any industrial dairy farms that had at least one cow or calf with clinical signs of FMD within the past three years. The control unit included industrial dairy farms that had a cow without a history of FMD in the same district where the case occurred within the past three years. Determinants of the disease were collected using a questionnaire. The incidence of FMD had a significant correlation with the new livestock arrival (OR=5.91 95% CI=1.54-22.5, P=0.009), vaccination (OR=0.054 95% CI=0.012-0.344, P <0.001), health status of animal husbandry (OR=0.17 95% CI=0.048-0.584, P=0.005) and livestock population unit (OR=0.22 95% CI=0.062-0.79, P=.021). Regarding the identified risk factors in the present study, it seems necessary to hold training sessions for owners and workers working in livestock farms as well as livestock traders and drovers about the epidemiology of FMD to increase their awareness, attitude and practice in the prevention of the disease and to improve the implementation of disease control programs.

Keywords: Foot-and-mouth disease, dairy farms, risk factors, case-control, Qazvin

Introduction

Foot-and-mouth disease (FMD) is a highly contagious viral disease among domesticated cloven-hoofed animals, such as cattle, sheep, goat and pig, as well as wild cloven-hoofed animals, such as gazelle and deer, characterized by fever and blisters in the mouth and hoof, (Hordofa *et al.* 2018).

The pathogenic agent of FMD is a RNA virus, called FMD Virus (FMDV), belonging to Aphthovirus genus in the family Picornaviridae. The virus has a wide range of hosts with rapid proliferation, high levels of transmission and

multiple transmission routes. These features make it harder to control and eradicate the virus (Alexandersen *et al.* 2003; Ramirez-Carvajal & Rodriguez, 2015).

On the other hand, the disease case fatality rate is about 5%, but it is important because of the adverse impact on the economy through the reduction of the production and development of the global trade prohibition for exports of livestock and animal products (Longjam *et al*. 2011).

FMD appears in dairy cattle with fever and reduced milk production during lactation. Disease-induced mastitis often causes a permanent reduction in milk production by 15%, and stops the growth of fattening calves (Lyons *et al*. 2015).

The most important routes of transmission are direct contact and virus entry through ulcers or mucous membranes. Some of the indirect transmission routes include mechanical transmission by humans, workers of animal husbandry, veterinarians, veterinary technicians, milking machines, forage, food and airborne transmission. Gastrointestinal transmission is more important in FMD free countries. The consumption of contaminated milk by non-immune calves is another transmission route. On the other hand, the virus has a high persistence in semen and therefore there is the possibility of virus entry and disease development through vitro fertilization (Paton, *et al.* 2018; Yoon *et al*. 2015).

The disease is endemic in 102 out of 194 countries of the world (Depa *et al.* 2012), including Iran, and imposes heavy losses on the livestock industry, especially the dairy industry, through successive outbreaks (Jemberu *et al.* 2014; Perez, *et al*. 2005).

According to a classification in terms of the prevalence of FMD, the universe is divided into seven domains. The third area includes Central Asia and the Middle East. Based on the roadmap in this region, the emergence of clinical signs in livestock should be discontinued by the year 2020. Countries in this area are classified into five positions and Iran is in the position of 2 that is, the control and prevention program has been implemented and the incidence of the disease has decreased (Abbas *et al*. 2014). According to the Iran Veterinary Organization (IVO), the mass vaccination of susceptible animals (at least every four months), the implementation of quarantine, sanitary measures, and clinical and serological surveillance in order to understand the changes in the disease and the nature of circulating circulating virus strains are some ways of FMD prevention and control (Rezaie et al., 2014). The cost of the first part of these preventive measures, namely vaccination, is estimated at an average of 210 billion Rials per year (Rasouli *et al*. 2010). This cost is imposed on the national economy of endemic countries,

including Iran, not only through direct economic losses such as young livestock losses, reduced milk production, abortions in pregnant animals, reduced livestock productivity, reduced quality and quantity of livestock, reduced fertility and economic losses, but also through indirect losses due to export prohibitions (Belton, 2004; Depa *et al*. 2012).

According to the studies conducted in Iran, several factors such as the arrival of new animals, the movement of nomadic livestock from farms, the history of vaccination, livestock capacity, age composition of livestock population and the lack of an appropriate distance (one kilometer) between cultivating units has influenced the prevalence of the disease in terms of the studied area (Bagheri Amiri *et al*. 2016; Enjili, 2010). Based on the results of these studies, the population of cattle in the country is at a higher risk than sheep. Therefore, an assessment of the determinants of the effects of the disease should be done routinely in each area so that it can target the control and prevention programs. The present study was carried out using case-control design with the aim of determining the factors affecting the incidence of FMD in dairy farms of Qazvin province.

Materials and methods

This case-control study was carried out in Qazvin Province of Iran, during year 2014. Based on the 95% confidence interval(α=0.05), 80% test power(B=0.2), 59% prediction interval for some risk factors in the case group (P1) and 19% prediction interval in the control group (P2), the minimum sample size was calculated to be 24 livestock farms in each of both the case and control groups (Enjili, 2010).

$$\bar{p} = \frac{P1 + P2}{2}$$

$$n \geq \frac{\left(Z_{1-\frac{\alpha}{2}}\sqrt{2\bar{P}(1-\bar{P})} + Z_{1-\beta}\sqrt{P_1(1-P_1)+P_2(1-P_2)}\right)^2}{(P_1 - P_2)^2}$$

The case unit was referred to any industrial dairy farms that had at least one cow or calf with clinical signs of FMD within the past three years. The control unit included industrial dairy farms that had a cow without a history of FMD in the same district where the case occurred within the past three years. This information was obtained from the data recorded in the GIS system of the Veterinary Organization and interviewed with Farmer. Controls were followed up by two weeks (maximum incubation period of the disease). In the event of the disease up to two weeks after the questioning of control livestock, the controls were classified into the case groups.

The industrial dairy farm was defined as keeping and breeding cattle based on the routine and advanced methods of animal husbandry, along with the principles of nutrition, health, breeding and management by employing the latest relevant methods (Statistical Center of Iran, 2014).

Data collection was done by a questionnaire designed by the research team and

field method by interviewing the farmer. The questionnaire contained the general information section of the livestock and animal husbandry department (Hedge type around farm, livestock other than cattle, male livestock in unit, livestock input supply, livestock population unit, elimination method, borrow equipment from other units, quarantine when buying, the distance between the nearest livestock unit, distance from the nearest village, distance from the nearest fattening farm, information on the incidence of disease in affected units, information on the entry of people of different kinds, equipment, new animals and other risk factors and information on vaccination (Booster vaccination, Suitable vaccine fence, Vaccination of new livestock). The health status of the farm in this study included cleaning the farmyard and other dairy farms, having number and cartex for each livestock with the exact date of arrival and vaccination of the livestock, the use of disinfection ponds in proper locations, appropriate implementation of quarantine measures regarding the arrival and departure of livestock, means of transport, the veterinarian and other people, and the correct and timely implementation of vaccinations in the herd.

Data were recorded by SPSS version 17 software (SPSS Inc., Chicago, IL, USA). To analyze the data, the relationship between the dependent variable and independent qualitative variables, the Chi-square test was first used; then, the logistic regression by calculating odds ratios and 95% confidence interval was used to investigate the factors associated with FMD occurrence by modulating variables. Variables in the univariate analysis of the P-value of less than or equal to 0.2 were selected to enter the multivariate analysis. The population attributable fraction (PAF) is estimated as a proportional reduction in population disease or mortality for each factor that was significant in the multivariate model. (Johnston *et al.* 2005).

Results

The present study, carried out in the industrial dairy farms of Qazvin Province, evaluated and questioned 24 case dairy farms compared with 24 control dairy farms. Based on the univariate analysis in Table 1, the incidence of FMD had a significant correlation with the new livestock arrival (OR=5.91, 95% CI=1.54-22.5, P=0.009), vaccination (OR=0.054, 95% CI=0.012-0.344, P <0.001), health status of animal husbandry (OR=0.17, 95% CI=0.048-0.584, P=0.005) and livestock population unit (OR=0.22, 95% CI=0.062-0.79, P=.021). In the next stage, variables with $p \leq 0.2$ were enrolled in the multivariate model. Only the livestock population

Table 1. Univariate analysis of foot-and-mouth disease-related factors in industrial dairy farms of Qazvin province based on logistic regression

Variables	Classification	Frequency		Odds ratio	95% confidence interval	P *value
		Case (percentage)	Control (percentage)			
Animal health	Desirable	8 (33.3)	18 (75)	0.17	0.048-0.584	0.005
	Undesirable	16 (66.7)	6 (25)	1	1	
Distance from the nearest dairy farm	Less than 1 km	18 (75)	12 (50)	3	0.65-13.88	0.16
	More than 1 km	6 (25)	12 (50)	1	1	
Distance from the nearest village	Less than 1 km	15 (62.5)	10 (41.7)	2.33	0.679-6.989	0.191
	More than 1 km	9 (37.5)	14 (58.3)	1	1	
Distance from the nearest fattening farm	Less than 1 km	22(91.7)	18 (75)	3.66	0.63-20.155	0.151
	More than 1 km	2 (8.3)	6 (25)	1	1	
Booster vaccination	Yes	9 (37.5)	22 (91.6)	0.054	0.012-0.344	<0.001
	No	15 (62.5)	2 (8.4)	1	1	
FMD vaccination interval in farm	<4 months	18 (75)	19 (79.2)	0.95	0.234-3.831	0.94
	≥4 months	6 (25)	5 (20.8)	1	1	
New livestock arrival	Yes	20 (83.3)	11 (45.8)	5.91	1.546-22.58	0.009
	No	4 (16.7)	13 (54.2)	1	1	
Worker communication with livestock outside the farm	Yes	15 (62.5)	15 (62.5)	1	0.311-3.218	0.89
	No	9 (37.5)	9 (37.5)	1	1	
Hedge type around farm	Wall	22 (91.7)	23 (95.83)	0.47	0.06-2.71	0.999
	Fence	2 (8.3)	1 (4.17)	1	1	
Livestock other than cattle	Yes	12 (50)	10 (41.7)	1.4	0.448-4.376	0.563
	No	12 (50)	14 (58.3)	1	1	
Male livestock in unit	Yes	20 (83.3)	14 (58.3)	3.57	0.93-13.718	0.064
	No	4 (16.7)	10 (41.7)	1	1	
Livestock input supply	Industrial	20 (83.3)	15 (62.5)	3	0.353-17.082	0.364
	Local	4 (16.7)	9 (37.5)	1	1	
Livestock population unit	<200	5 (20.8)	13 (54.2)	0.22	0.062—0.794	0.021
	>200	19 (79.2)	11 (45.8)	1	1	
Elimination method	Carcass well	4 (16.7)	5 (20.83)	0.76	0.167-3.103	0.659
	Others	20 (83.3)	19 (79.17)	1	1	
Borrow equipment from other units	Yes	6 (25)	3 (12.5)	2.33	0.509-10.692	0.275
	No	18 (75)	21 (87.5)	1	1	
Suitable vaccine fence	Yes	16 (66.7)	17 (70.8)	0.82	0.242-2.797	0.756
	No	8 (33.3)	7 (29.2)	1	1	
Quarantine when buying	Yes	3 (12.5)	7 (29.2)	0.35	0.078-1.549	0.165
	No	21 (87.5)	17 (70.8)	1	1	
Vaccination of new livestock	Observing conventional principles	7 (29.2)	9 (40.9)	0.68	0.175-2.022	0.405
	Without observing conventional principles	17 (70.8)	15 (59.1)	1		

* chi-square

Table 2. Multivariate analysis of factors related to foot-and-mouth disease and population attributable fraction in industrial dairy farms of Qazvin province

Variables	Classification	Odds ratio	95% confidence interval	p- value	Population attributable fraction (%)
Livestock population unit	<200	0.67	0.005-0.97	0.047	73.91
	>200	1	1		

unit was significant, so that farms with a livestock population of less than 200 were 33% less susceptible to the outbreak of FMD disease (p=0.047). On the other hand, calculating population PAF showed that 73.91% of the incidence rate of FMD in the whole population could be attributed to the livestock population unit (Table 2).

Discussion

Based on the results of this study, the new livestock arrival, the inappropriate health status of animal husbandry, non-vaccination, and livestock population of more than 200 were identified as risk factors for FMD events in the industrial dairy farms of Qazvin Province. Therefore, it seems that the proper management and decrease exposures of these risk factors can be made to reduce the incidence of the disease.

Ellis-Iversen *et al.* (2011) recorded the health and management status of livestock farms as risk factors of the FMD outbreak in southern England in 2007.

In this study, the farms with a history of FMD vaccination inoculation were 94.6% less likely to be infected with FMDV (p <0.001). Also, the farms with a vaccinator entry less than once a month had 4.49 times more odds ratio of developing FMD (p=0.021). According to the IVO, the mass vaccination of susceptible animals should be done at least once every four months (Rezaie *et al*. 2014). Two other studies in Iran showed the protective effect of vaccination (Emami *et al.* 2015; Enjili, 2010), but this relationship was insignificant in the study of Bagheri et al. (Bagheri Amiri *et al.* 2016).

In countries that, according to their national and regional circumstances, choose the vaccination strategy as a way to control the FMD, it is essential to have accurate information on vaccine performance during the executive program.

Moreover, a poor vaccination program using low quality or inappropriate virus strain or immunizing only a part of sensitive livestock will spread the disease slowly and silently. Thus, the disease cases in the care program are not easily

identified, increasing the likelihood of becoming endemic disease (Emami *et al*. 2015; Gullberg *et al*. 2016). It seems that type of FMD vaccines can have an important role in FMD outbreak in Iran.

In the present study, farms far away less than 1 km from dairy farms and less than 1 km from fattening farms had the odds ratio of FMD, respectively, 3 and 3.66 times higher, but not significant ($p> 0.05$). However, another study carried out in 18 provinces showed that failure to observe the appropriate distance (1 km) between breeding units could be considered as a risk factor for an outbreak (Enjili, 2010).

The airborne transmission of the FMD virus has been proven (Abbas *et al.* 2014; Colenutt *et al.* 2016), so that the virus was transmitted to the radius of 20 km by air during 2001 United Kingdom foot-and-mouth outbreak (Ellis-Iversen *et al.* 2011). The virus needs to have a moisture content of 60% or more to survive and have airborne infection capability. The lower temperature is also effective in increasing the survival of the virus (Bagheri Amiri *et al.* 2016).

Other results of the present study showed that the dairy farms with new livestock arrival in the past three years were 5.91 times higher at risk of FMD. In Baghiri *et al*.'s study, the new livestock arrival in the case dairy farms was nearly 15 times higher than the control dairy farms (Bagheri Amiri *et al*. 2016). This finding was also obtained in the studies conducted in Iran (Enjili, 2010; Ilbeigi, K. 2014) and Ecuador (Lindholm *et al*. 2007). The new livestock input supply has not been meaningful as a risk factor for FMD. However, it is necessary to note the presence of traders and drovers in the livestock market of Iran, who, as intermediaries, transport livestock from one place to another. Moreover, they may choose local and industrial farms, various places, and livestock smuggled from neighbouring countries as a source of purchase to obtain more profits from buying or selling livestock due to the wide and unlimited range of work and may transfer livestock for sale to other parts of the country and even abroad. Obviously, if a cow is infected with the FMD virus in a farm, the transfer of infected cow to another farm or livestock market will transmit the virus and infect other animals. In the 2001 FMD outbreak in the United Kingdom, the animal transfer was considered as one of the major risk factors for the disease (Ellis-Iversen *et al*. 2011).

The results of multivariate analysis indicated that the livestock population in the unit could be effective in predisposing the herd for disease, so that farms with a livestock population of less than 200 were 33% less susceptible to the outbreak of FMD ($p=0.047$). Meanswhile, calculating the population PAF showed that 73.91% of the incidence of FMD in the whole community could be attributed to the variable of the livestock population unit. Wada *et al.* (2017) in examining the FMD outbreak strategies in Japan and Ellis-Iversen *et al.* (2011) in an investigation into the risk factors for FMD

outbreaks in southern England in 2007 showed that the herd size could increase odds ratio for FMD (Ellis-Iversen *et al,* 2011; Wada, *et al.* 2017).

Conclusion

The results obtained from the present study introduced the new livestock arrival as the risk factors for disease occurrence, as well as livestock health, vaccination, and livestock population of less than 200 as the protective factors against FMD in the industrial dairy farms of Qazvin Province. Therefore, actions leading to a weakening of this group of known risk factors and strengthening of identified protective factors can help lower the odds ratio and the economic losses caused by FMD. Also, it is recommended to organize the business situation of traders and drovers in the market for the livestock purchase and sale because of their extensive and unlimited work area in livestock transfer. It seems necessary to hold training sessions for farm owners, farm workers, traders and drovers about the epidemiology of FMD to raise their awareness, attitude and practice in preventing disease by veterinarians and other veterinary technicians to improve the implementation of disease prevention programs.

Acknowledgement

The authors hereby would like to thank and appreciate the Veterinary Organization and all farmers in Qazvin Province for their sincere cooperation with the current study.

Conflict of interest: The authors declare no conflict of interest.

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