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REGULAR ARTICLES

Cattle seroprevalence and risk factors associated with bovine viral diarrhea in the northeastern of Colombia

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Abstract

Bovine viral diarrhea (BVD) is one of the most common and economically significant viral infections in cattle. Different risk factors have been associated with viral exposure and transmission, generating endemic regions with different biotype circulations. To find the BVD status in the northeastern region of Colombia, this study aimed to determine the seroprevalence and risk factors associated with the disease in non-vaccinated farms. For this purpose, a two-time point sampling strategy was developed, obtaining serum from 1157 animals housed in 25 farms distributed in 46 townships, thus for antibody detection against non-structural protein 3 (NS3, p80) of bovine viral diarrhea virus (BVDV) using an indirect ELISA test. For the first time in Colombia, the presence of serological persistent cattle was evaluated in 1047 animals 3 weeks later of first sampling. The information on a standardized questionnaire with closed and dichotomic answers was used to calculate the putative risk factors. The association analysis by univariate and multivariate logistic regression reported odds ratios (OR) with a 95% of confidence interval (C.I). The overall seroprevalence was 65% (95% CI 62.5–72.9%), with variations according to age ranges. The prevalence of persistent serological positive corresponded to 37.7% (95% CI 34.2–41.5). The risk factors found by multivariate analyses were the lease of pastures (OR = 2.071 CI 1.485–3.690), the use of the same needle (OR = 2.249 CI 1.354–3.736), the molasses supplementation (OR = 2.742 CI 1.156–5.807), and the native Creole breed (OR = 1.895 CI 1.416–2.804). The results of this study confirmed the endemism and higher common exposure to BVDV, as well as the presence of serological persistent cattle in Valledupar, Colombia.

Keywords Bovine viral diarrhea · Abortion · Infectious diseases · Animal health

Introduction

Bovine viral diarrhea (BVD) is one of the most significant contagious diseases in the cattle industry, generating remarkable economic losses related with an increased calves' mortality and respiratory and digestive alterations (Ridpath 2010; Lanyon et al. 2014). Bovine viral diarrhea virus (BVDV) is a small, single-stranded enveloped positive-sense RNA pestivirus, recognized for the induction of reproductive failure in affected females represented by embryonic loss, abortions, slow fetal growth, and teratogenesis (Lanyon et al. 2014). This diverse clinical manifestations vary according to BVDV biotypes, divided into non-cytopathic (NCP), and cytopathic (CP) (Ridpath 2010). Several studies have been conducted to evaluate the seroprevalence of animals among different cattle populations present in contrasting regions around the world, thus recognizing different epidemiological patterns of viral transmission and circulation, figuring out a wide range of epidemiologically associated risk factors related to demographic characteristics, cultural production practices, scarce control of reproductive management, and misdiagnosis (Greiser-Wilke et al. 2003).

In this sense, BVD control programs should recognize the main risk factors across herds, and for this issue, implementing screening strategies will offer useful information on BVDV circulation and spreading at the herd level with evaluating serological persistent animals that could show the

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exposure to multiple strains even within the same biotype and possible sustained infections from continuous exposure to unvaccinated animals (Laureyns et al. 2010). Besides this, the presence of persistently infected (PI) animals within the herds and the indiscriminate movement of animals between different farms and regions increase the viral shedding and distribution (Ridpath 2010; Lanyon et al. 2014).

In Colombia, BVD's first outbreak occurred in Friesian calves imported from Nederland in 1975 (Parra et al. 1994), and the first isolation of BVDV's NCP biotype was confirmed in 1981 (Gallego et al. 1986; Rweyemamu et al. 1990). The first serological screening using samples from nine regions of the country revealed 47.2% of BVDV seropositivity confirming the ease of virus spreading (Griffiths et al. 1983). Currently, a reduced number of earlier reports have estimated an increasing seroprevalence in non-vaccinated farms over time, but little is known about the prevalence of serologically persistently animals, and the information about risk factors is lacking, particularly for the northeastern region of the country (Cedeño et al. 2011; Cruz et al. 2014; Ramirez et al. 2016; Moreno et al. 2017). Therefore, the present study aimed to investigate the seroprevalence and potential risk factors associated with BVD infection in non-vaccinated cattle farms from Valledupar, northeastern Colombia.

Materials and methods

Study area

The study was carried out in 46 farms from 25 townships of 102 villages placed in the rural area of Valledupar's municipality, geographically situated at N 10°27′37″ E 73°15′35″ in Cesar's department in the northeastern region of Colombia, covering 4977 Km^2 of surface evaluated area. This region has been situated in an altitude of 180 m.a.s.l. and characterized by having 36 °C of average temperature throughout the year. The rain pattern is bimodal, with a marked dry season during the first months of the year and two rainy seasons in April to June and September to November month's interval, having an average annual rainfall of 1124 mm per year (IDEAM 2014).

Study population

The study was focused on bovine livestock maintained under traditional and cultural husbandry practices on extensive and semi-intensive systems, characterized mainly by dual-purpose cattle production. These animals did not receive any previous BVDV vaccine and reared together with other animals, sharing the same grazing areas without considering sex, age, or weight parameter differentiation. The population census in Valledupar's municipality corresponded to 157,872 animals according to the regional and national registry of cattle. The farms were composed by zebu, Creole, crossbreed, and native Creole (Criollo Caqueteño) cattle (ICA 2016).

Study design and sampling

An epidemiological cross-sectional study was carried out using a sample estimated from an overall census of 157,872 bovines, considering 50% of expected prevalence (Motta et al. 2013), 95% as confidence interval, and 3% of estimated error according to Thrusfield et al. (2018) postulates. Using these parameters, the sample size was calculated in Epinfo™ software version 7 (CDC) estimating 1068 animals. Finally, considering the field's losses, 1157 animals were randomly sampled from 46 farms in 25 different villages in later 2016 October and earlier 2017. To find serological persistent animals within the evaluated cattle population, a second sampling based on 1098 bovines was conducted 3 weeks later. The statistical differences between both samplings were evaluated by the Z test.

Sample collection and serological evaluation

All procedures involving the blood collection of animals followed the national and international protocols for research in veterinary medicine. The blood samples were collected from the tail vein using vacuum tubes (Vacutainer) without anticoagulant. These samples were preserved in refrigeration at 4 °C until arriving at the laboratory, and the sera were obtained by centrifugation at 500 × *g* for 10 min and conserved at −20 °C until ELISA testing. To track the antibodies produced during natural exposition to BVDV, the competitive INGZIM BVD Compact ELISA based on recombinant p80 (NS3) antigen and their binding p80 MAbs was used following the manufacturer's instructions. To detect p80 (NS3) antibodies' presence, the sampled animals' sera were diluted at 1:5 and incubated for 1 h on NS3 antigen-coated plates. Specific antibodies were quantified blocking the binding percentage of second MAb specific for BVDV p80. Finally, the cut-off was estimated following the formulae [cut-off (positive) = 0.3 × (OD of negative control); cut-off (negative) = 0.3 × (OD of negative control]. The samples with OD over or below cut-off were interpreted as positive or negative, respectively (Frey et al. 1998)

Statistical and association analyses

The prevalence was calculated using the Epi Info™ software version 7 (CDC). The 95% confidence intervals (CI) for prevalence values were estimated using the SAS® software (SAS INSTITUTE 9.0). Prevalence results were introduced into ArcGIS 10. 1 (ESRI) software using https://sites.google.com/site/seriescol/shapes for designing the isopleth map with Kriging interpolation by estimated prevalence. To assess risk factors associated with seropositivity of BVD in sampled farms, 108 variables including sex, age, breed, the presence of other animal species, land extension, water source, food, type of reproduction, pasture leasing, purchase and sale of animals, management practices, and biosecurity were tested by univariate analysis and Pearson's Chi-square test. Subsequently, a multivariate model was conducted including variables with $p \leq 0.5$ from univariate analysis. The multivariate analysis was performed using a logistic regression model analyzed by SPSS version 20 software (SPSS Inc., Chicago, II, EE. UU).

Results

Seroprevalence

The ELISA results of the first sampling (n = 1157) showed 755 positive animals, estimating a 65.2% (95% CI 60.7–70.0%) overall seroprevalence, remarking at 100% of positivity at farm level (95% CI 74.0–13.2 %). The seroprevalence considering sex was 67.5% (95% CI 62.5–72.9%) and 54.1% (95% CI 44.4–65.3%) for females and males, respectively. Considering age's interval, the animals younger than 1-year-old showed 54.0% of positivity, whilst those among 1 to 2 years old presented 60.5% of positivity. The animals from 2 to 3 years old showed 65.3% of positivity, and animals more than 3 years old showed 69.9% of positivity (Table 1). The level of involvement map represented a heterogeneous distribution of BVD positive farms within localities, including 6 localities with low (2.8–5) and 8 with high affectations (8.5–9.9), respectively (Fig. 1).

The second sampling used (n =1098) showed 415 persistent seropositive animals with a seroprevalence of 37.7% (95% CI 34.2–41.5). Considering different age ranges, cattle within 3 to 24 months (about 2 years) presented 37.2% of seropositivity, whilst bovines older than 24 months showed 37.8%. The comparison between both samplings by the Z test

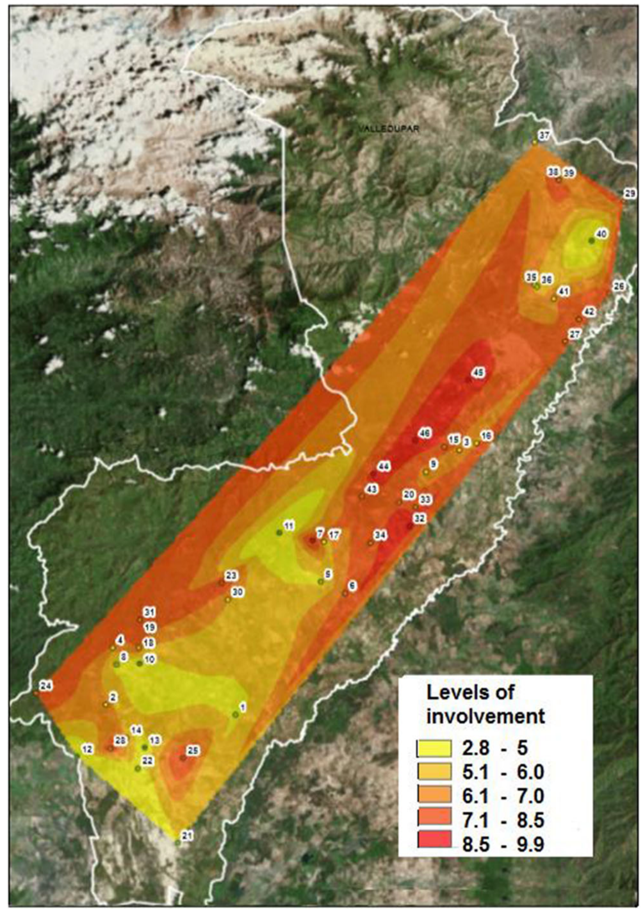

Fig. 1 Level of involvement of the BVDV in northeastern area of Colombia

resulted in $p \leq 0.005$, finding statistically significant differences (Table 1).

Risk analysis

The univariate analysis significance results ($p \leq 0.1$) are displayed in Table 2. For this study, the risk factors were

Table 1 Percentage of positive animals (*first sampling*) and serological persistent positive (*second sampling*) for BVD according to age in the northeastern area of Colombia

Sampling	Sampled animals(n)	Positive herd (%)	Positiveanimals (n)	Positive (%)	CI
Total first sampling	1157	100	755	65.2	60.7–70.0
Under 1 year	237	76.0	128	54.0	45.2–63.9
1–2 years	137	67.5	83	60.5	48.5–74.7
2–3 years	107	56.5	71	66.3	52.2–83.2
More than 3 years	676	95.6	473	69.9	63.8–76.4
Total second sampling	1098	80.4	415	37.7	34.2–41.5
3–24 months	51	56.5	19	37.2*	23.1–57.1
More than 24 months	1047	78.2	396	37.8*	34.2–41.6

CI, confidence interval (95%). *Percentage of persistent serological positive animals among previously sampled populations

Table 2 Univariate analysis of the risk factors associated with BVD seroprevalence in the cattle of the northeastern area of Colombia

General variables	OR	X^2	p	CI
Male sex	0.673	6.058	0.006*	0.491–0.925
Age under 1 year	0.549	16.63	0.000*	0.410–0.734
Creole breed	0.581	17.13	0.000*	0.448–0.751
Crossbreed breed	0.166	29.61	0.000*	0.076–0.338
Brahman breed	0.492	16.12	0.000*	0.344–0.696
Gylorando breed	0.634	9.133	0.001*	0.469–0.851
Native undetermined breed	0.702	5.191	0.011*	0.515–0.950
Native creole breed	1.529	11.45	0.000*	1.194–1.958
Management and biosafety measures				
Same needle usage	2.281	22.36	0.000*	1.609–3.237
Entry of vaccinated cattle	0.686	9.267	0.001*	0.537–0.874
Pasture's leasing	1.698	10.16	0.000*	1.227–2.374
Other species presence	0.381	6.177	0.006*	0.168–0.843
Breeding animals buying	1.267	2.864	0.045*	0.961–1.667
Proper food storage	0.551	3.259	0.035*	0.283–1.074
Feeding with pellet	2.706	3.533	0.030*	0.976–9.301
Molasses supplementation	2.304	7.383	0.003*	1.267–4.437
Mineral's supplementation	0.688	7.645	0.002*	0.527–0.896

OR, odds ratio; *CI*, confidence interval (95%), *Statistically significant

considered for variables with OR higher than 2, as previously recommended (Dohoo et al. 2003). The study found the usage of the same needle (OR = 2.281 CI 1.609–3.237), pellet feeding (OR = 2.706 CI 0.976–9.301), and molasses supplementation (OR = 2.304 CI 1.267–4.437) as risk factors. As protective factors (OR below 1), male sex (OR = 0.6737 CI 0.491–0.925) and animals younger than 1 year (OR = 0.549 CI 0.410–0.734) were recognized. Besides this, some breeds presented protective association such as Creole breed (OR = 0.581 CI 0.448–0.751), crossbreed (OR = 0.166 CI 0.076–0.338), Brahman (OR = 0.492 CI 0.344–0.696), Gylorando (OR = 0.634 CI 0.469–0.851), and native Creole breed (OR = 0.702 CI 0.515–0.950). Additionally, the presence of other animal species (OR = 0.381 CI 0.168–0.843) and proper food storage (OR = 0.551 CI 0.283–1.074) were also estimated as protective factors (Table 2).

The statistically significant variables obtained by the univariate model were analyzed on multivariate analysis considering the same categorical thresholds, identifying as risk factors the pasture's leasing (OR = 2.071 CI 1.485–3690), the same needle usage (OR = 2.249 CI 1.354–3.736), molasses supplementation (OR = 2.742 CI 1.156–5.807), and presence of native Creole breed (OR = 1.895 CI 1.416–2.804). The estimated protective factors corresponded to the presence of cattle below 1-year-old (OR = 0.543 CI 0.376–0.745), crossbreed (OR = 0.710 CI 0.501–1.038), and Brahman breed (OR = 0.463 CI 0.271–0.755) (Table 3).

Table 3 Multivariate logistic regression analysis of variables associated with BVD seroprevalence in bovine of the northeastern areas of Colombia

General variable	β	p	Exp (B)	CI (95%)
Age under 1 year	−0.636	0.000*	0.543	0.376–0.745
Creole breed	−0.342	0.078*	0.710	0.501–1.038
Brahman breed	−0.770	0.002*	0.463	0.271–0.755
Native creole breed	0.689	0.000*	1.895	1.416–2.804
Same needle usage	0.810	0.002*	2.249	1.354–3.736
Pasture's leasing	0.728	0.001*	2.071	1.485–3.690
Molasses supplementation	0.952	0.021*	2.742	1.156–5.807

Potential risk factors ($p \leq 0.05$) were selected for inclusion in the multivariate model.

CI, confidence interval (95%), *statistically significant

Discussion

This is the first report of seroprevalence and risk factors associated with BVDV exposure in cattle located in Valledupar, northeastern Colombia. An overall seroprevalence of 65% in the studied herds at the first sampling evidenced higher rates of viral exposure and transmission (Lindberg and Houe 2005). Similar and higher seroprevalence proportions have been described in farms without effective control measures and under extensive or semi-intensive production systems such as the 65.5%, 52.3%, 49.7%, and 47.8% reported in studies conducted in the northeastern areas of Brazil, Kenia, China, and Mexico, respectively (Segura-Correa et al. 2016; Fernandes et al. 2018; Hou et al. 2019; Olum et al. 2020).

In Colombia, previous studies confirmed higher seroprevalence of BVDV in dairy, beef, and dual-purpose cattle. Studies conducted on dairy herds showed 32.77%, 55.1%, 76.4%, and 75.7% of seroprevalence in cattle localized in Pasto, Boyacá, and Antioquia departments (Cedeño et al. 2011; Cruz et al. 2014; Ramirez et al. 2016; Moreno et al. 2017). Moreover, in a study conducted on beef and dual-purpose cattle located in the mid-Magdalena, region with similar agroecological conditions with Valledupar identified 62.6% of BVD seroprevalence, reflecting the possible impact of environmental factors with viral exposure and transmission (Camacho et al. 2015). A study focused on cattle and mixed herds (cattle and bubaline) identified 58.0% and 51.9% of seroprevalence, respectively (Motta et al. 2013). These studies reflected the BVDV circulation in several regions of Colombia and suggested that control measures and husbandry practices could influence, as well as environmental conditions, on viral spreading and exposure reflected by high serological positiveness even in presence of other related species.

The overall estimated seroprevalence in this study was higher than the previously identified in cattle present in other the northern areas of Colombia over time. The first BVD report showed 5.7% of seropositivity in 2234 samples from 82 herds of Cordoba department with 46.3% farms affection (Otte et al. 1989). Posteriorly, other study in this department showed a seroprevalence of 29.4% in 170 cows from 32 herds (Betancur et al. 2007). Similarly, in 2011, the seroprevalence in Cesar's department corresponded to 46% evaluated in 300 cows from 6 farms (Peña-Cortes 2011). Posteriorly, in the neighboring municipalities of Valledupar (Aguachica and Rio de Oro), a seroprevalence of 48% was found in 905 cattle sampled from 27 farms (Gálvis et al. 2016). This situation confirms the increase of BVDV spreading in the cattle population localized in the northern areas of Colombia. Besides this, the husbandry practices in Valledupar allow increased mobility of animals, particularly those in calf stages, a situation evidenced by a reduced number of animals subjected to the second sampling for serological persistence confirmation. This high mobility flow and the abovementioned conditions could affect the cattle's viral exposure and, finally, the possible establishment of BVDV of endemic infections.

Additionally, the level of involvement map reflects the reduced distance between different herds, supporting the possible higher uncontrolled flux of animals among herds with a probable indiscriminate pasture's leasing, influenced by dry seasons generating a reduced grass availability and an increased contact between animals during grazing. In this study, the first sampling was developed during the dry epoch, a situation that could impact on the results. It is important to consider that the high seroprevalence at the herd level could be a hint of PI animal presence. However, further studies ought to be conducted for PI identification, considering their major impact on viral dispersion, proposing test and cull strategy for the control and eradication of BVDV based on different country experiences (Greiser-Wilke et al. 2003).

The presence of persistent serological positive animals in the second sampling could reflect possible new exposure to different circulating BVDV CP strains present in field, thus considering the high viral variability and the non-previous vaccination against the disease on the evaluated farms (Quintero et al. 2019). The serological persistence in younger cattle could be influenced by maternal immunity persistence as well as the transplacental infection with CP strain after 120 pregnancy days (Sagar and Ridpath 2005). Similarly, the high seroprevalences founded on the evaluated groups allows to infer a little benefit of vaccination against BVDV as an effective control measure (Lanyon et al. 2014). In this condition, a high viral transmission within herds may circumvent the prevention for fetal infection and the occurrence of PI animals (Lindberg and Houe 2005). Besides this, recognized persistent serological positive animals in the evaluated populations could reflect exposure to different BVDV genotypes, thus affecting the vaccination overall effectiveness (Fulton et al. 2020).

Interestingly, the multivariate risk analysis recognized for the first time as BVD risk factors the pellet feeding and molasses supplementation. These conditions are often present in the Colombian traditional husbandry systems, particularly during dry seasons characterized by a continuously reduced grass offer, deriving on drinking and feeding bowl sharing, increasing the direct contact between animals which could increment viral transmission (Han et al. 2018). Similarly, pasture leasing is a widespread practice in Valledupar's region, generating as previously discussed an increased flux of animals from different age ranges that share the same grazing areas, extending direct contact probability between bovines within the herds. Related to this, a study using Bayesian network analysis showed high BVD seropositivity in herds with frequent closed animal contacts between farms and herds with animals sharing the same grazing areas (Han et al. 2018).

Furthermore, the same needle's usage for drug and vaccine administration is a very frequent practice in extensive and semi-intensive production systems in Colombia. In this study, this condition was clearly identified as an important risk factor for BVDV exposure, inviting to improve the animal management and biosecurity practices adopted by farmers for reducing the viral infection-associated impacts.

Multivariate risk analysis identified as a protective factor the presence of calves aged less than 1 year inside herds, a condition previously reported in China, considering a reduced prevalence of BVDV in calves (Hou et al. 2019). Furthermore, cattle older than 18 months showed higher prevalence levels than youngster cattle in Ethiopia (Aragaw et al. 2018). In our study, this protective condition could be related to a reduced exposure based on calves' husbandry practices, maternal passive immunity persistence within the evaluated animals, and a clear absence of exposition by reproductive pressure (Brownlie 1990).

About breeds, the multivariate risk analysis evidenced native Creole breed at more risk for BVDV exposure in comparison to the Brahman breed, which resulted in a protective factor. Native Creole cattle and crossbreeds were more likely to be seropositive compared to other breeds in Ethiopia (Aragaw et al. 2018). This condition could be associated with cultural husbandry practices, considering that Brahman purebred animals are kept in improved management condition systems based on their genetic merit and value. Otherwise, native Creole breed is often used by farmers in traditional extensive systems, with a reduced application of biosecure practices, increasing the BVDV exposure probability.

This study confirmed the endemism of BVD in cattle localized in the Valledupar, northeastern Colombia. The high overall seroprevalence shows increased viral exposure of cattle in non-vaccinated farms. Based on a second sampling, finding persistent serological positive animals within different age ranges may reveal a continuous exposure to different viral genotypes or even evidence maternal immunity persistence.

The main risk factors found in this study could be associated with an increased flux of animals within farms, sharing of the same grazing areas, conditions that increase direct contact and viral exposure. The same needle usage and the increased seropositivity in native Creole breed evidence the impact of cultural husbandry practices on BVDV transmission in a particular region and invite to improve management strategies to minimize the consequences of the disease within cattle populations. Even this study recognized persistent serological positive animals for the first time in Colombia; further studies should be conducted to find PI animals in the Valledupar's region, following up to implement test and cull protocols in addition to the improvement of biosecurity measures.

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Author contributions Lorena Catalina Martínez–Rodríguez conceptualized the study, performed research and data analysis, and contributed with new methods or study models. Blanca Lisseth Guzmán-Barragán validated the study designed, developed data curation and analysis, and wrote and drafted the present manuscript. Diego Ordoñez analyzed data and wrote and edited the manuscript. Gabriel Andres Tafur-Gómez validated the study designed, developed data curation and analysis, contributed with new methods or models, and wrote and edit the draft paper. All authors have read and agreed to the published version of the manuscript.

Declarations

Ethics approval The animals used in this study received handling and treatment under qualified veterinary supervision following the animal experimentation rules described in the International Guiding Principles for Veterinary Research Involving Animals. The owners of the animal's assigned informed consent before their inclusion, and the personal or farm information were treated according to the habeas data Colombian laws.

Conflict of interest The authors declare no competing interests.

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