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Serological evidence for high prevalence of Influenza D Viruses in Cattle, Nebraska, United States, 2003–2004

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ABSTRACT

Influenza D virus (IDV), a new member of the influenza virus family, was first reported in 2011 in swine in Oklahoma, USA, and then soon found in cattle across North America and Eurasia. Earlier studies suggested cattle serve as natural reservoir for IDV. The goal of this study is to perform a retrospective study looking at sera collected from Nebraska beef herds in 2003–2004 and 2014 for evidence of IDV antibodies. Results showed that all 40 randomly selected farms (2003–2004) we tested contained IDV seropositive adult animals and that approximately 98% of newborn calves (2014) had high levels of maternal antibodies against IDV. This study suggested that IDV exposures were present in Nebraska beef cattle since at least 2003.

1. Introduction

Since its identification in 2011, influenza D virus (IDV) has been isolated from cattle and/or swine in the United States, China, France, Italy, and Japan, and serologic evidence suggests it may also be affecting small ruminants such as goats and sheep (Chiapponi et al., 2016; Collin et al., 2015; Ducatez et al., 2015; Ferguson et al., 2015; Hause et al., 2014, 2013; Jiang et al., 2014; Murakami et al., 2016; Quast et al., 2015). Laboratory studies demonstrated cattle, swine, ferrets, and guinea pigs are susceptible to IDV infection (Collin et al., 2015; Ferguson et al., 2016; Hause et al., 2014, 2013; Sreenivasan et al., 2015). Serologic assays in two independent studies showed that IDV could potentially infect humans, although seropositivity rates in the studies differed. One of the studies reported 91% seropositivity among 35 persons working with cattle (White et al., 2016), and the other reported only 1% seropositivity among 741 persons with suspected high exposure to IDV (Eckard, 2016). Nevertheless, epidemiologic, serologic, and pathologic studies have suggested cattle are the primary natural reservoir for IDV (Collin et al., 2015; Ducatez et al., 2015; Ferguson et al., 2015, 2016; Hause et al., 2014; Jiang et al., 2014).

A previous study in young calves reported that 94% of newborn calves had high levels of maternal antibodies against IDV, which decreased in the next six months, leading to the increasing susceptibility to IDV (Ferguson et al., 2015). Laboratory studies suggested that IDV can be efficiently transmitted in cattle, with viral replications in the upper and lower respiratory tracts (Ferguson et al., 2016). An earlier study suggested that IDV was detected at higher frequency in cattle with bovine respiratory disease (BRD) than healthy cattle (Ferguson et al., 2015), which was consistent with the findings in two metagenomic studies (Mitra et al., 2016; Ng et al., 2015).

Although cattle are proposed as the natural reservoir for IDV, the natural history of IDV and the extent of IDV prevalence in bovine population is not yet clear. Evolutionary analyses of five gene segments suggested that IDV could have diverged from those in influenza C virus, another member in the *Orthomyxoviridae* family, from approximately 300 to over 1,200 years ago (Sheng et al., 2014). A serological study reported that IDV was circulating in Mississippi beef cattle as early as 2004. In this study, we aim to investigate the seroprevalence of IDV among randomly selected beef cattle farms in Nebraska between 2003 and 2004.

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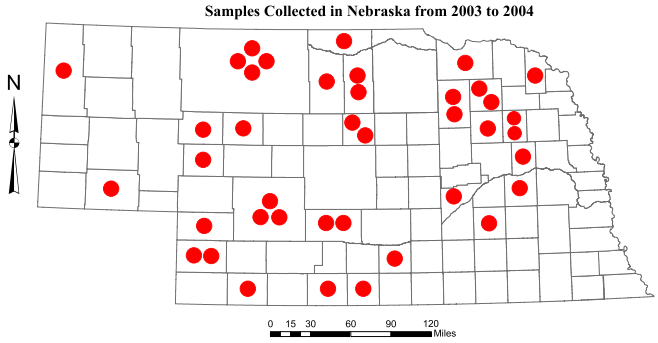

Fig. 1. Geographic distribution of the 40 Nebraska farms where the testing samples were collected (2003–2004).

2. Materials and methods

2.1. Viruses

D/bovine/Mississippi/C00013N/2014 (D/13N) and D/bovine/Mississippi/C00046N/2014 (D/46N) used in serological assays were genetically separated into two reported clusters of IDVs, which were also antigenically different (Collin et al., 2015; Ferguson et al., 2015).

2.2. Bovine serum samples

From September 2003 to May 2004, a total of 15,402 bovine serum samples were collected from 73 beef cattle farms, in which the total number of cattle were 20,865, across 42 counties in Nebraska [(Smith et al., 2005), Fig. 1]. All cattle were 2 years or older. Using these convenient samples, to evaluate the prevalence of IDV, we randomly selected 40 farms representing the 73 farms sampled (Fig. 1). From each farm, we selected 4–10 samples for serological testing. A total of 293 serum samples were analyzed for the presence of IDV antibody. If at least one serum sample is positive for each farm, by assuming these herds to be representative of beef cattle farms in Nebraska at the time, we would have 95% confidence that the prevalence of seropositive herds was 91–100%.

To evaluate the contemporary situation of IDV in cattle of Nebraska, we collected sera from 242 calves from one farm in the spring of 2014. These sera were collected from the same animals at 1 week post-birth, and again at approximately 3 months later.

Table 1
Cross-reactive antibody responses against D/13N and D/46N in the bovine sera samples from Nebraska (2003–2004).

Farm ID (n)[a]	Sampling date (mm/dd/year)	D/13N		D/46N		Overall seropositive (%)[d]
		GMT (lowest titer-highest titer)[b]	Seropositive (%)[c]	GMT (lowest titer-highest titer)[b]	Seropositive (%)[c]	
J5(10)	10/17/03	160 (40–640)	90.0	246 (160–640)	80.0	90.0
J6(10)	10/17/03	160 (80–320)	80.0	103 (40–160)	80.0	80.0
J7(6)	10/17/03	226 (160–320)	66.7	160 (160–160)	66.7	66.7
J8(6)	10/21/03	160 (160–160)	16.7	113 (40–320)	33.3	33.3
J9(6)	10/21/03	80 (40–160)	66.7	80 (40–160)	50.0	66.7
J10(8)	10/22/03	160 (80–320)	50.0	121 (40–320)	62.5	62.5
J14(10)	10/28/03	160 (80–320)	80.0	146 (40–320)	80.0	80.0
J17(10)	10/31/03	177 (80–320)	70.0	190 (40–320)	80.0	80.0
J18(10)	10/31/03	243 (160–320)	100.0	211 (160–320)	100.0	100.0
J19(8)	10/31/03	215 (80–640)	87.5	215 (80–640)	87.5	87.5
J20(8)	10/31/03	269 (160–320)	100.0	226 (160–320)	100.0	100.0
J23(7)	11/4/03	177 (40–320)	100.0	160 (40–320)	100.0	100.0
J25(10)	11/6/03	173 (40–1280)	90.0	235 (80–640)	90.0	90.0
J26(10)	11/7/03	147 (80–640)	80.0	320 (160–640)	80.0	80.0
J28(7)	11/10/03	143 (80–320)	85.7	180 (80–320)	85.7	85.7
J31(10)	12/5/03	147 (40–320)	80.0	190 (40–320)	80.0	80.0
J33(5)	11/19/03	95 (80–160)	80.0	190.3 (160–320)	80.0	80.0
J34(10)	11/19/03	195 (80–320)	70.0	238 (160–320)	70.0	70.0
J35(10)	12/3/03	226 (40–640)	80.0	177 (80–320)	70.0	70.0
J36(10)	11/21/03	139 (80–320)	50.0	160 (80–320)	50.0	50.0
J37(8)	11/21/03	160 (80–320)	87.5	131 (80–320)	87.5	87.5
J38(10)	11/24/03	215 (80–320)	70.0	173 (40–320)	90.0	90.0
J39(5)	11/26/03	226 (160–320)	80.0	381 (320–640)	80.0	80.0
J45(4)	12/4/03	113 (40–160)	100.0	226 (80–320)	100.0	100.0
J48(9)	12/8/03	173 (40–320)	100.0	173 (40–320)	100.0	100.0
J54(7)	12/22/03	184 (40–640)	71.4	279 (40–640)	71.4	71.4
J55(6)	12/31/03	184 (40–640)	83.3	279 (80–640)	83.3	83.3
J56(5)	10/23/03	113 (80–160)	80.0	226 (160–320)	80.0	80.0
J57(7)	1/22/04	95 (40–320)	57.1	113 (80–320)	57.1	57.1
J60(6)	2/25/04	320 (320–320)	83.3	368 (320–640)	83.3	83.3
J62(8)	2/27/04	190 (40–640)	100.0	269 (80–640)	100.0	100.0
J63(5)	3/1/04	121 (40–640)	100.0	211 (40–640)	100.0	100.0
J64(6)	3/8/04	243 (160–640)	83.3	243 (160–640)	83.3	83.3
J66(5)	3/12/04	226 (160–320)	80.0	320 (320–320)	80.0	80.0
J67(6)	3/31/04	160 (80–320)	100.0	285 (160–320)	100.0	100.0
J68(5)	4/14/04	269 (160–640)	80.0	381 (320–640)	80.0	80.0
J69(5)	4/22/04	320 (160–640)	80.0	538 (320–640)	80.0	80.0
J70(5)	4/26/04	190 (40–320)	80.0	269 (80–640)	80.0	80.0
J71(5)	5/4/04	279 (80–640)	100.0	320 (160–640)	100.0	100.0
J72(5)	5/21/04	135 (40–320)	80.0	135 (40–320)	80.0	80.0

[a] The 40 farms listed were selected randomly from 73 farms we sampled in Nebraska;
[b] Only those sera with a HI titer of 1:40 or more are used to calculate the GMT and the lowest and highest titers are measured from those sera with a HI titer of 1:40 or more;
[c] Seropositive rate was calculated based on those samples whose HI titers ≥1:40 for either D/13N or D/46N;
[d] Overall seropositive rates was calculated based on those samples whose HI titers ≥1:40 for D/13N, D/46N, or both.