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Review Article

Prevalence of Bovine Herpes Virus 1 in Yaks (*Bos grunniens*) from the Qinghai-Tibetan Plateau in China: A Meta-analysis

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Authors' Contribution
XC and YQ contributed to conception and design of analysis. HW and WL reviewed records. XC and HW analyzed the data. YQ and WG re-analyzed the disagreements. XC and YQ conducted statistical analysis. HW and WL prepared the manuscript.

Key words
BHV-1, China, Epidemiology, Systematic review, Yaks

ABSTRACT

Bovine herpesvirus 1 (BHV-1) is a virus capable of causing serious respiratory distress in yaks, and it can further result in reproductive diseases and late-term abortions. In this article, we conducted a systematic meta-analysis aimed at exploring BHV-1 prevalence in yaks of the Chinese Qinghai-Tibetan Plateau (QTP). To complete this analysis, we identified all relevant articles on this topic in both English and Chinese literature databases published through March 20, 2020. Studies were not included in this analysis if they were reviews, repeats of previous studies, included inconsistent or incomplete data, non-yaks study, or provided solely prevalence data. Using the identified studies, we were able to determine the number of BHV-1-infected yaks in the QTP, and to calculate the pooled prevalence. We ultimately identified 16 relevant studies (5737 total yaks), with a pooled BHV-1 infection prevalence rate of 38%, with the highest prevalence in Sichuan province and the lowest in Gansu province (58% and 18%, respectively). We found BHV-1 prevalence to be associated with both test time and method. Together, our results suggest that BHV-1 infections in yaks are becoming an increasingly widespread and serious concern. As such, it is essential that this prevalence continue to be monitored, and that effective regulatory efforts be implemented in order to prevent the continued spread of this disease.

INTRODUCTION

The yak, is a livestock of significant economic importance to native peoples of China, India, Bhutan, Nepal, and other nations, wherein it serves as a source of meat, leather, milk, transportation, and draught force (Qiu *et al*., 2015). Yaks live in high altitude (2,000 - 5,000 m) regions of the QTP and are emblematic of these high-altitude areas. There are an estimated 14.2 million yaks worldwide, with nearly 94% of these being found in China across a range of Provinces including Sichuan, Qinghai, Tibet, Xinjiang, and Gansu (Gong *et al*., 2014).

BHV-1 is a virus that was first discovered in cows in the US state of California in 1953, and which has since been shown to cause serious bovine diseases including infectious bovine rhinotracheitis (IBR), infectious balanoposthitis (IBP), and infectious pustular vulvovaginitis (IPV) (Durham, 1974). In yaks, infection with BHV-1 can lead to serious systemic, respiratory, neurological, or genital diseases, and can also cause late-term abortion (Newcomer *et al*., 2017).

The first evidence of BHV-1 infections of yaks was produced in 1986 (Wang *et al*., 1986), with the increasing prevalence of BHV-1 infection in the QTP is increasing (Mo and Liu, 2017), making the study of the infection a key issue affecting health and socioeconomic interest. Previous studies have estimated a wide range with respect to BHV-1 infection rates in yaks, with prevalence between 7.3% and 81.9%, with the wide variation likely resulting from limited study size and sampling areas (Yang, 2003; Shen *et al*., 2011; Han *et al*., 2016). By developing a more comprehensive understanding of yak BHV-1 epidemiology, it may be possible to better characterize current disease prevalence. At present there is a lack of systematic assessment of BHV-1 infection prevalence in China, and as such herein we conducted a meta-analysis aimed at estimating this prevalence in yaks of the QTP region of China, and we further assessed factors potentially

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associated with prevalence findings from previous studies, such as testing time or methodology, which also provided reference for relevant studies.

MATERIALS AND METHODS

We reviewed both English (PubMed and Science Direct) and Chinese (VIP, CNKI, and WANFANG Data) databases from their inception through March 20, 2020 to identify epidemiological studies of yak BHV-1 epidemiology. The MeSH terms used were: "BHV or BoHV or IBRV", "Yak", "QTP or China", and combinations or variations thereof.

Identified studies obtained through these search criteria were first screened based upon their titles and abstracts, excluding studies meeting the following criteria: 1) Non-yak studies, sampling site is out of QTP, and sample size < 15 yaks; 2) Non-research based publications such as press releases, newsletters, forum discussions, etc.; 3) Non-epidemiological studies such as basic science research for BHV-1; 4) Studies that did not disclose when the data was collected, sample size, or denominator for each reported prevalence or rate.

Studies that were not based on research, including newsletters or commentary; 3) Studies not providing information regarding the dates of data collection, sample sizes, or prevalence rate denominators.

All identified studies from the searches were independently assessed for eligibility and inclusion by 2 different authors, the manual revision was conducted on all displayed publications and first selections were based on information in the titles and/or abstracts. Selected publications had to be available for downloading and had to contain extractable data in English or Chinese about the presence of BHV-1 in yaks in QTP. The study was a controlled, primary study, so we did not contact authors of original studies for additional information. No attempt was made to identify unpublished reports. All discrepancies were reviewed by the third author PS (Chen *et al.*, 2018).

Identified studies were scored according to their content, with one point awarded for each of the following: clear research objective description, clearly described testing methodology, subject subgroup categorizations, and detailed descriptions of sampling methodology.

A meta-analysis approach was then employed to estimate pooled BHV-1 prevalence in yaks, using a random-effects model and with forest plots prepared using Stata 12 (Stata Corp. College Station, Texas). PRISMA guidelines were observed for this study, with the PRISMA checklist for information items being reported (Shamseer *et al.*, 2015).

RESULTS

We initially identified 879 total articles through our search efforts, of which 16 ultimately met the criteria for inclusion in this study (Fig. 1). Of these studies, 15 were in Chinese while 1 was in English, with the oldest having been conducted in 1988 (Table I).

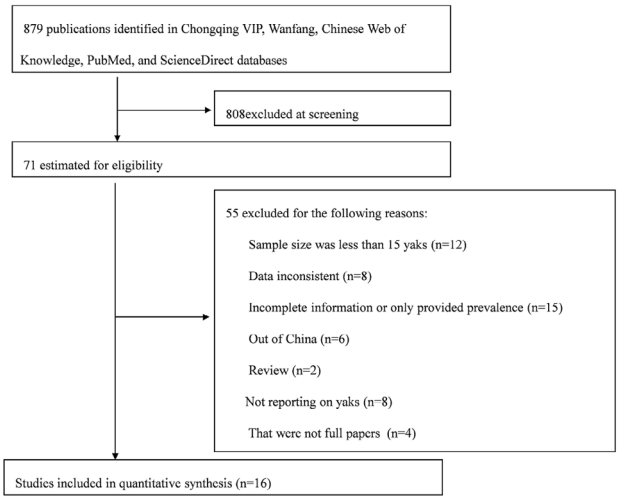

Fig. 1. Flow diagram of the selection of eligible studies.

A funnel plot was used to assess the degree of publication bias for these included studies, with the resulting plot being asymmetrical with respect to overall prevalence, suggesting a high likelihood of publication bias among these studies (Fig. 2).

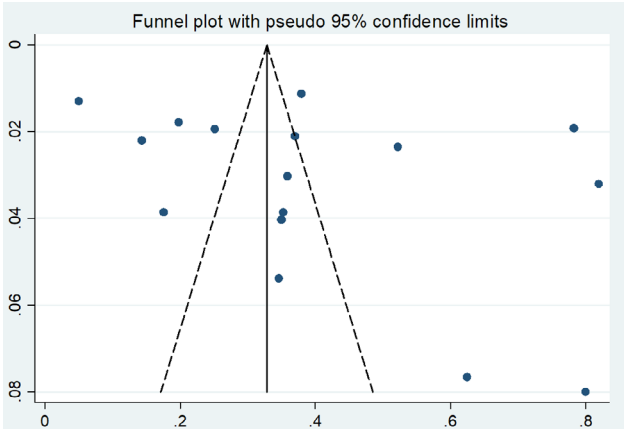

Fig. 2. Funnel plot with pseudo 95% confidence limits for examination of publication bias.

The included studies were focused on 5,737 total yaks in the QTP, across 5 Chinese provinces (Fig. 3).

Table I. Included studies of BHV-1 infection in yaks from QTP in China.

Study ID	Province	No. examined	No. positive	Prevalence	Test method	Study design	Quality score
Han *et al*., 2016	Tibet	1840	698	38%	ELISA	Cross sectional	3
He *et al*., 2014	Sichuan	460	360	78%	ELISA	Cross sectional	2
Shi *et al*., 2014	Xinjiang	25	20	80%	ELISA	Cross sectional	1
Yang, 2003	Qinghai	78	27	35%	IHA	Cross sectional	2
Dong *et al*., 1995	Qinghai	97	17	18%	IHA	Cross sectional	2
Han *et al*., 2010	Qinghai	251	90	36%	ELISA	Cross sectional	2
Hu *et al*., 2010	Xinjiang	525	194	37%	ELISA	Cross sectional	3
He and Han, 2011	Gansu	280	14	5%	ELISA	Cross sectional	1
Lv and Zhang, 2014	Qinghai	252	36	14%	ELISA	Cross sectional	2
He *et al*., 2016	Qinghai	450	235	52%	ELISA	Cross sectional	2
Shen *et al*., 2011	Qinghai	501	99	20%	ELISA	Cross sectional	1
Deng *et al*., 2015	Sichuan	153	54	35%	ELISA	Cross sectional	1
Tian *et al*., 1988	Qinghai	140	49	35%	ELISA	Cross sectional	1
Wang *et al*., 1991	Gansu	501	126	25%	IHA	Cross sectional	3
Yuan *et al*., 2016	Xinjiang	144	118	82%	ELISA	Cross sectional	2
Yuan *et al*., 2015	Xinjiang	40	25	63%	ELISA	Cross sectional	1

ELISA, enzyme-linked immunosorbent assay; IHA, indirect hemagglutination assay.

Table II. Pooled prevalence of BHV-1 infection in yaks from QTP in China.

Category	Group	No. studies	No. tested	No. positive	Prevalence (95% CI)	Heterogeneity		
						χ^2	P-value	I^2 (%)
Region	Tibet	1	988	381	39%(12-49)	284.18	0	98.20%
	Qinghai	8	2,244	765	34%(30-47)	384.6	0	95.10%
	Sichuan	3	990	519	52%(12-72)	327.5	0	99.10%
	Xinjiang	4	734	357	49%(37-94)	152.37	0	98.00%
	Gansu	2	781	140	18%(5-35)	74.44	0	98.70%
Test time	before 2010	8	2,543	837	33% (24-41)	154.43	0	95.50%
	2011 or later	8	3,194	1,325	41% (28-70)	1388.26	0	99.50%
Test method	ELISA	13	5,061	1,992	39% (30-57)	1542.56	0	99.20%
	IHA	3	676	170	25% (17-33)	6.89	0.032	71.00%
Total		16	5,737	2,162	38%(29-52)	1549.15	0	99.00%

Estimations of yak BHV-1 prevalence in these studies ranged between 5% and 82%, with an overall pooled prevalence of 38% (2,162/5,737), and with substantial heterogeneity (I^2=99.0%, P<0·001) (Tables I and II). BHV-1 prevalence in Gansu (18%, 140/781) were significantly lower than in other provinces, whereas the Sichuan province had the highest prevalence at 52% (519/990) (Table II).

For yaks tested through 2010, the pooled BHV-1 prevalence was 33% (837/2,543), whereas in yaks tested in or after 2011 this rate was 41% (1,325/3,194) in 2011 or later group (Table II). For yaks tested by ELISA, the pooled BHV-1 prevalence was 39% (1,992/5,061), whereas for yaks tested by IHA it was 25% (170/676) (Table II).

DISCUSSION

This is the first meta-analysis of which we are aware that has focused on yak BHV-1 prevalence in the QTP region, although many other studies have similarly investigated overall BHV-1 prevalence in yaks, we found BHV-1 prevalence in yaks of the QTP region to be markedly lower than rates in Indian yaks (Nandi and Kumar, 2010), which may be due to differences in herd sizes, breeding

management, or migratory behavior in these regions. Other possible reasons for this difference may be that there is more rainfall on average in India, which can predispose yaks to infection, and that yaks share grazing territory with other animal species during their migrations (Nandi *et al*., 2011; Han *et al*., 2016).

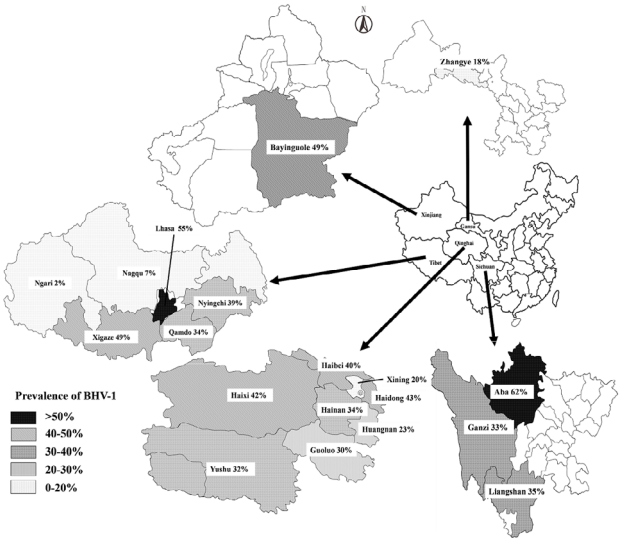

Fig. 3. Map of BHV-1 infection in yaks from QTP in China.

Our study found differences in prevalence of BHV-1 infection between before 2010 groups (33%) and 2011 or later groups (41%), which shows that the situation of BHV-1 infection in yaks has become more and more serious in recent years. Our findings also suggest an association between BHV-1 infection and the detection methods. The limited sensitivity in performing IHA, ELISA is accurate, sensitive, and become the mainstream method for BHV-1 detection (Kramps *et al*., 2004; Theurer *et al*., 2015), and as such ELISAs were used for detection in 88.2% of yaks (5,061/5,737) in 13 publications.

Meta-analyses offer the advantage of compiling many related but not identical studies into a somewhat cohesive dataset but owing to individual study variations it is not unusual to observe heterogeneity in the results of these analyses. We focused on only primary research studies in this article, and in so doing we detected substantial heterogeneity and risk of publication bias. Future primary controlled research studies are needed to validate these findings, as these studies are the most robust and reliable form of data available (Newcomer *et al*., 2017).

Our meta-analysis has several limitations. For one, while we identified many relevant articles via a systematic approach, not all of the data provided were useful, potentially biasing our findings based on data eligibility. In addition, for the Tibet region only a single study was included in this meta-analysis, and as such the estimated prevalence rate for this region may not be accurate. Lastly, we focused only on the publication year, geographical location, or test methodology of included studies, and other variables may also influence this prevalence rate, such as breeding modalities.

Our primary finding is that BHV-1 is widespread among yaks in the QTP region of China, potentially representing a significant socioeconomic concern for local governments. Future research into the management or treatment of BHV-1 in yaks is thus urgently needed in order to prevent further spread of this concerning disease.

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Statement of conflict of interest

The authors have declared no conflict of interest.

REFERENCES

Chen, X., Wang, X., Qi, Y., Wen, X., Li, C., Liu, X. and Ni, H., 2018. Meta-analysis of prevalence of bovine herpes virus 1 in cattle in Mainland China. *Acta Trop.*, **187**: 37-43. https://doi.org/10.1016/j.actatropica.2018.07.024

Deng, Y., He, X., Ren, Y., Ji, F., Bian, M., Aniu, S. and Huang, X., 2015. Serological investigation on infectious rhinotracheitis of cattle in panxi area of sichuan province. *Chin. J. Vet. Med.*, **51**: 42-43.

Dong, C., Cairang, L., Longfu, G., Shuzhen, L., Duojie, L., Sang, Y., Shengmei, K., Yinqing, C., Pai, Q. and Fahai, L., 1995. Serological investigation of 9 yak diseases in Maqin area. *Chin. Qinghai J. Anim. Vet. Sci.*, **25**: 34.

Durham, P.J., 1974. Infectious bovine rhinotracheitis virus and its role in bovine abortion. *N. Z. Vet. J.*, **22**: 175-180. https://doi.org/10.1080/00480169.1974.34161

Gong, X., Liu, L., Zheng, F., Chen, Q., Li, Z., Cao, X., Yin, H., Zhou, J. and Cai, X., 2014. Molecular investigation of bovine viral diarrhea virus infection in yaks (*Bos gruniens*) from Qinghai, China. *Virol. J.*, **11**: 29. https://doi.org/10.1186/1743-422X-11-29

Han, Z., Gao, J., Li, K., Shahzad, M., Nabi, F., Zhang, D., Li, J. and Liu, Z., 2016. Prevalence of circulating antibodies to bovine herpesvirus 1 in yaks (*Bos grunniens*) on the Qinghai-Tibetan Plateau, China. *J. Wildl. Dis.*, **52**: 164-167. https://doi.org/10.7589/2015-01-018

Han, Z., Hua, Q., Xiaolong, H., Kefeng, W. and Zhabu,

E., 2010. Serological survey of viral diarrhea/ mucosal disease and infectious rhinotracherris in yaks. *Chin. J. Anim. Infect. Dis.*, **18**: 56-59.

He, M., Bing, Z., Yuanwei, W., Cheng, T. and Huangrong, Z., 2014. Serological survey on infectious bovine rhinotracheitis in Northwest Sichuan Province. *Prog. Vet. Med.*, **35**: 130-132.

He, X. and Zhihui, H., 2011. Investigation on serology of bovine infectious rhinotracheitis and viral diarrhea mucosal disease in qinghai province. *J. Trad. Chin. Vet. Med.*, **30**: 29-32.

He, Y., Zhenbo, Q., Xurong, L. and Shan, L., 2016. 'Serological investigation of common yak diseases in the middle part of the northern foot of qilian mountain. *China Cattle Sci.*, **42**: 58-60.

Hu, W., Huaying, Y., Pingyuan, G., Pengwei, Z., Guiying, Y. and Zhiheng, S., 2010. Epidemiological investigation on infectious rhinotracheitis of yak. *Chin. J. Vet. Med.*, **46**: 75.

Kramps, J.A., Banks, M., Beer, M., Kerkhofs, P., Perrin, M., Wellenberg, G.J. and Oirschot, J.T., 2004. Evaluation of tests for antibodies against bovine herpesvirus 1 performed in national reference laboratories in Europe. *Vet. Microbiol.*, **102**: 169-181. https://doi.org/10.1016/j.vetmic.2004.07.003

Lv, J. and Lanqing, Z., 2014. Epidemiological investigation on viral diarrhea and infectious rhinotracheitis in yak cattle in qinghai province. *J. Domes. Anim. Ecol.*, **35**: 59-63.

Mo, J. and Qingyou, L., 2017. Comparative analysis on the large-scale development of dairy industry in China and Japan. *Jiangsu Agric. Sci.*, **45**: 303-307.

Nandi, S., Kumar, M., Yadav, V. and Chander, V., 2011. Serological evidences of bovine herpesvirus-1 infection in bovines of organized farms in India. *Transbound. Emerg. Dis.*, **58**: 105-109. https://doi.org/10.1111/j.1865-1682.2010.01185.x

Nandi, S. and Manoj, K., 2010. Serological evidence of bovine herpesvirus-1 (BoHV-1) infection in yaks (*Peophagus grunniens*) from the National Research Centre on Yak, India. *Trop. Anim. Hlth. Prod.*, **42**: 1041-1042. https://doi.org/10.1007/s11250-010-9526-1

Newcomer, B.W., Cofield, L.G., Walz, P.H. and Givens, M.D., 2017. Prevention of abortion in cattle following vaccination against bovine herpesvirus 1: A meta-analysis. *Prev. Vet. Med.*, **138**: 1-8. https://doi.org/10.1016/j.prevetmed.2017.01.005

Qiu, Q., Wang, L., Wang, K., Yang, Y., Ma, T., Wang, Z., Zhang, X., Ni, Z., Hou, F., Long, R., Abbott, R., Lenstra, J. and Liu, J., 2015. Yak whole-genome resequencing reveals domestication signatures and prehistoric population expansions. *Nat. Commun.*, **6**: 10283. https://doi.org/10.1038/ncomms10283

Shamseer, L., Moher, D., Clarke, M., Ghersi, D., Liberati, A., Petticrew, M., Shekelle, P., Stewart, L.A. and Prisma- P. Group. 2015. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: Elaboration and explanation. *Br. med. J.*, **350**: g7647. https://doi.org/10.1136/bmj.g7647

Shen, Y., Jinshan, C., Long, W., Jing, L., Guangwei, H. and Xiaorun, W., 2011. Serological investigation of infectious rhinotracheitis in cattle in Yushu, Qinghai province. *Anim. Husb. Vet. Med.*, **43**: 112.

Shi, Q., Ligang, Y., Jingwei, P., Jing, L, Jingjing, X., Li, S., Xiaodan, Y. and Haidong, Liu., 2014. Seroprevalence of infections bovine rhinotracheitis in yaks in Western Highland Regions, China. *China Dairy Cattle*, pp. 31-32.

Theurer, M.E., Larson, R.L. and White, B.J., 2015. Systematic review and meta-analysis of the effectiveness of commercially available vaccines against bovine herpesvirus, bovine viral diarrhea virus, bovine respiratory syncytial virus, and parainfluenza type 3 virus for mitigation of bovine respiratory disease complex in cattle. *J. Am. vet. med. Assoc.*, **246**: 126-142. https://doi.org/10.2460/javma.246.1.126

Tian, Y., Zhanyuan, W., Xueyuan, C., Jinge, S., Yulan, K. and Hailong, C., 1988. Diagnosis of bovine rhinotracheitis by ELISA. *Chin. J. Prev. Vet. Med.*, **10**: 34.

Wang, C., Yuming, W., Jun, Q., Shaolin, M. and Lanxiang, L., 1991. Investigation on infectious rhinotracheitis in cattle in zhangye district. *Chin. J. prev. Vet. Med.*, **13**: 36-37.

Wang, C., Chonghua, L., Ruiliang, D., Shumin, C., Quanfu, M., Dachang, Y., Kanglin, G., Guoteng, Z. and Xichi, H., 1986. Isolation and identification of infectious bovine rhinotracheitis virus from yak. *Chin. Vet. Sci.*, **16**: 5-6.

Yang, C., 2003. Serological investigation of infectious rhinotracheitis in cattle in Gangcha of Qinghai. *Chin. Qinghai J. Anim. Vet. Sci.*, **33**: 39.

Yuan, L., Jing, L., Jingwei, P., Yan, L. and Yayin, Q., 2016. Epidemiological investigation on main respiratory diseases of yak in tianshan mountains. *Chin. J. Vet. Med.*, **52**: 47-48.

Yuan, L., Yan, L., Jingwei, P., Jing, L., and Ergeng, T., 2015. Serological examination report on 5 respiratory diseases of yak in tianshan. *J. Anim. Sci. Vet. Med.*, **34**: 25-27.