



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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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.

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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

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).

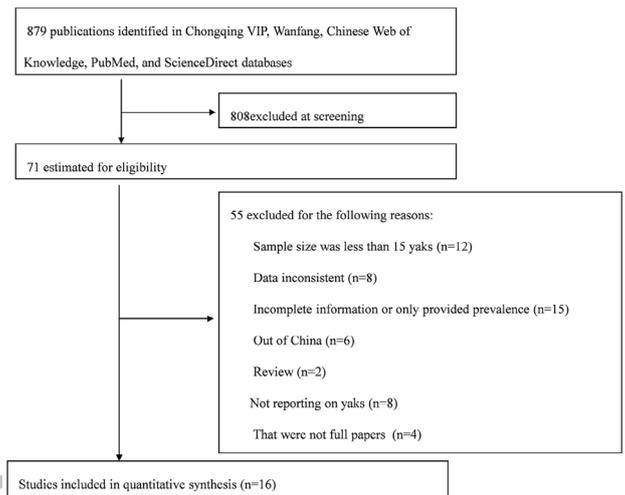


Fig. 1. Flow diagram of the selection of eligible studies.

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).

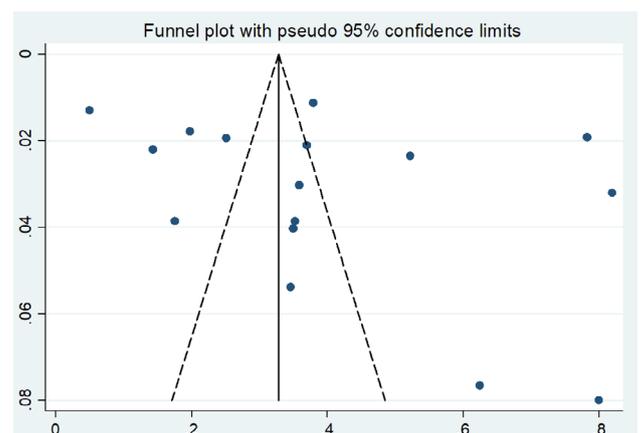


Fig. 2. Funnel plot with pseudo 95% confidence limits for examination of publication bias.

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.	No.	No.	Prevalence	Heterogeneity		
		studies	tested	positive	(95% CI)	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

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