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Bovine babesiosis in India: Estimation of prevalence by systematic review and meta analysis

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ABSTRACT

Bovine babesiosis is a serious threat to the livestock sector especially in tropical countries like India. Understanding the epidemiology of the disease in the country is essentially important in strategizing the available methods to effectively control the disease. Keeping this as the background, the present study was undertaken to estimate the pooled prevalence of bovine babesiosis in India. The relevant literature pertaining to bovine babesiosis was identified and a total of 49 studies published between 1983 and 2018 were included in the final systematic review and meta-analysis. Meta-analysis was conducted using meta-package of R software and prevalence estimates were calculated. Bovine babesiosis was reported from 21 states of India with pooled prevalence estimate of 6% (95% CI = 4%–9%) using random effect model. Zone wise analysis revealed highest pooled prevalence in the west zone and north zone (8%) followed by east zone (7%), central zone (6%), south zone (4%) and northeast zone (4%). The results of meta-analysis indicated high variability between studies. In addition, the pooled seroprevalence was high (29%) compared to prevalence of active infection (5%) of bovine babesiosis in India. Further, the pooled prevalence estimate of *B. bigemina* infection in India was more (7%) compared to *B. bovis* infection (1%). The estimation of prevalence of active infection and seroprevalence separately will helps to understand the actual disease prevalence in the country. The study indicated the wide prevalence of bovine babesiosis in India which urges for immediate mitigation strategies.

1. Introduction

Bovine babesiosis is a tick-borne haemoprotozoan disease, caused by the parasite of the genus *Babesia*, imposing a significant burden on the global livestock sector with underestimated economic losses (Henning, 1956; McCosker, 1981; Uilenberg, 1995). In India, bovine babesiosis was first reported by Walker and Edward in 1927. Annual economic losses due to bovine babesiosis in India were estimated to be about 57.2 million US dollars (McLeod and Kristjanson, 1999). The two important species of the parasite causing bovine babesiosis in India are *Babesia bigemina* and *B. bovis*. In India, *B. bigemina* predominates over *B. bovis* with scattered reports about the latter (Idnani, 1938). These parasites are primarily transmitted by ticks of the species *Rhipicephalus* (*Boophilus*) *microplus*, and the animals under stress due to other ailments are potentially susceptible to infection. Clinically, the disease is characterized by anemia, fever, hemoglobinuria with eventual fatality (Sharma et al., 2013). In India, babesiosis was reported in indigenous as well as crossbred cattle and in buffaloes. The crossbred cattle exhibited a higher rate of susceptibility than zebu and buffaloes, the latter mainly act as carriers of infection without exhibiting clinical signs. The phenomenon of inverse age resistance in bovine babesiosis is notable with calves up to 9–12 months of age are generally resistant to infection.

In the Indian scenario, diagnosis of bovine babesiosis rely upon conventional parasitological methods mainly the examination of Giemsa stained blood smears. However, the technique has low sensitivity especially in carrier animals (Terkawi et al., 2011). Serological tests are popular in epidemiological surveillance with known lacunae of failure in detecting early infection. Molecular techniques like polymerase chain reaction (PCR) are found to be promising for the detection of *Babesia* parasites owing to its high specificity and sensitivity (Vijayakumar et al., 2017).

Despite its economic and animal health impacts, bovine babesiosis

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was severely neglected in terms of awareness, control interventions, and research for the development of effective vaccines. Being a tick borne disease, the climate change accelerated the expansion of niche of ticks with possible spread of the disease to newer geographical areas. This situation prompted the livestock farmers to accelerate the usage of acaricides for tick control with resultant emergence of acaricide resistant ticks. The effective control of bovine babesiosis thus demands a thorough understanding of the disease prevalence in different geographical areas and thereby high-risk areas can be marked and targeted for the execution of available control measures. In the majority of the surveillance studies, seroprevalence was calculated which usually provides an overestimation of disease burden. Understanding the active status of infection is also important to get the real time status of the disease in different geographical regions. Keeping in view of this, in the present study efforts are being taken to estimate the status of the disease in India in terms of pooled prevalence (combined prevalence estimate of multiple studies), infection prevalence (presence of *Babesia* sp. organism/antigen in the blood), and seroprevalence (presence of *Babesia* sp. specific antibodies) by systematic review coupled with meta-analysis.

2. Materials &methods

2.1. Literature search strategy

The study was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA) for meta-analyses and systematic reviews of observational studies (PRISMA, http://www.prisma-statement.org) (Supporting file 1). A review of literature published from 1983 to 2018 was conducted to obtain data about the prevalence and geographical distribution of bovine babesiosis in India. The keywords used to construct the search phrase in the database were Babesiosis AND India AND cattle, Babesiosis AND India AND buffaloes, Babesiosis OR piroplamosis AND India. The literature search was performed using the electronic databases including PubMed, Science Direct, BioMed Central, Google Scholar, Web of Science, J-gate@Consortium of e-Resources in Agriculture (CeRA) under the Indian Council of Agricultural Research and Scopus. The prevalence of bovine babesiosis was analyzed zone wise in all the six zones of India *viz.*, Central, South, East, West, North, and Northeast as the states and union territories of India is grouped into six zones based upon climatic, geographical and cultural features. Further, the retrieval language was restricted to English.

2.2. Inclusion and exclusion criteria

The reference lists of the identified studies were initially screened by the titles and further scrutiny by screening the abstracts. The literature was restricted to cross-sectional and longitudinal studies in cattle and buffalo reporting the prevalence of bovine babesiosis in India. Further, duplicate records were removed and the relevance of the results was analyzed. The following inclusion criteria were used to select articles; a) studies conducted in India b) published in peer review journals from 1983 to 2018 c) studies with information on incidence, prevalence, and distribution of bovine babesiosis in India d) studies with information about the diagnostic test used e) studies with sample size more than 100. The literature mentioning outbreak investigations without laboratory-based confirmation, case reports, reviews, clinical/experimental trials, studies with less sample size and those published before 1983 and after 2018 were totally excluded from the study.

2.3. Data extraction

All relevant data from the eligible studies were entered into a Microsoft Excel spreadsheet. The data extracted were the year of study, study area, sample size, number of animals positive for *Babesia* species, diagnostic method used, species of *Babesia* detected, article title, authors' name and year of publication. The prevalence was assumed as infection prevalence when assays like blood smear examination and PCR were employed whereas it was assumed as seroprevalence when assays like indirect ELISA, Capillary tube agglutination test, Dot ELISA, Indirect Fluorescent antibody test were employed. Infection prevalence was estimated to determine the presence of organism/antigen (current status of disease) whereas seroprevalence was calculated to determine the presence of antibodies (past exposure) against *Babesia* sp. in bovines. When different diagnostic methods are employed for single study, the overall prevalence estimate was determined by selecting the highest prevalence.

2.4. Statistical analysis

Meta analysis on bovine babesiosis was conducted using R version 3.2.5 with the R packages Meta and Metafor as reported earlier (Jacob et al., 2020). For each study, the point estimates and their confidence intervals (CIs) for the prevalence of bovine babesiosis was calculated. Briefly, the effect model was chosen depending on the level of heterogeneity. The level of heterogeneity was assessed by Cohran Q test whereas the extent of heterogeneity was measured with heterogeneity I^2 (Higgins I^2) statistic as reported earlier (Paramanandham et al., 2019; Jacob et al., 2020). Heterogeneity was quantified with the assumption of I^2 values of 25%, 50%, and 75% were considered as low, medium, and high heterogeneity (Higgins and Thompson, 2002; Higgins et al., 2003). The impact of heterogeneity was measured by calculating the H value. Random-effects model was used to estimate the log-effect size and its 95% confidence interval (CI) and statistical significance level.

Restricted maximum-likelihood (REML) estimator was used to calculate the variance between studies (τ^2). Graphical analysis of the funnel plot was conducted to estimate the possibility of publication bias as well as reporting bias with the horizontal axis showing the effect size (Hedges' g) of each study and the vertical axis showing the Standard Error (SE). Funnel plot asymmetry was adjusted by the Trim-and-fill method. Since the visual examination of funnel plot asymmetry is subjective, we employed statistical tests like Begg's rank test (Begg and Mazumdar, 1994) and Egger's regression test (Egger et al., 1997) to identify the publication bias. A significant result in both tests is an indication that the results might be affected by publication bias. Subgroup analysis was conducted based on the groups created on affected species, diagnostic method employed, and zones of India for determining the heterogeneity in each group. In addition, infection prevalence {based on antigen/organism detection (routine blood smear examination and molecular techniques like PCR)} and seroprevalence (based on antibody detection) was estimated in each subgroup and each state of India. A minimum number of three studies was set was a criteria for conducting meta analysis in each subgroup.

3. Results

3.1. Details of studies

After initial scrutiny of the article titles for those reporting the prevalence of bovine babesiosis and exclusion of those irrelevant, 83 articles were retrieved for further appraisal. After applying exclusion criteria 49 potential studies that were reviewed and subjected to meta-analysis.

3.2. Meta-analysis of the prevalence of bovine babesiosis in India

The number of studies on the prevalence of bovine babesiosis incorporated for the meta-analysis was 49 with the total number of samples as 67820 for the period 1983–2018. Further, details of selected studies along with state and zone-wise pooled infection prevalence and seroprevalence are depicted in Table 1.

As variation was expected between studies, random-effect model was

Table 1
Details of bovine babesiosis prevalence studies in India along with pooled prevalence estimates.

Sl. No	Authors	Pooled Prevalence			
		State	State wise Prevalence (%)	Zone	Zone wise Prevalence (%)
1.	Ananda et al., 2009	Karnataka	5	South zone	4
2.	Ananda et al., 2014				
3.	Harish et al., 2006				
4.	Krishnamurthy et al., 2016				
5.	Muraleedharan et al., 2005				
6.	Seshadri et al., 1985				
7.	Setty et al., 1985				
8.	Vijayakumar et al., 2017				
9.	Nair et al., 2011	Kerala	5		
10.	Kariyappa et al., 2017				
11.	Priya et al., 2017				
12.	Pradeep et al., 2019				
13.	Ponnudurai et al., 2017	Tamil Nadu	1		
14.	Velusamy et al., 2014				
15.	Jyothisree et al., 2013	Andhra Pradesh	8		
16.	Burrio et al., 1994	Telengana	1		
17.	Kumar et al., 2016	Gujarat	18	West zone	8
18.	Maharana et al., 2016				
19.	Vahora et al., 2012				
20.	Kolte et al., 2017	Maharashtra	4		
21.	Bhatnagar et al., 2015	Rajasthan	1		
22.	Agrawal et al., 2017	Punjab	11	North zone	8
23.	Aulakh et al. (2005)				
24.	Filia et al. (2015)				
25.	Kaur et al., 2016				
26.	Singh et al. (2012)				
27.	Sharma et al. (2013)				
28.	Sharma et al. (2016)				
29.	Singh et al. (2013)				
30.	Bhat et al. (2015)				
31.	Jithendran (1997)	Himachal Pradesh	6		
32.	Sharma et al. (2000)				
33.	Kumar et al. (2015)	Haryana	3		
34.	Banerjee et al. (1983)				
35.	Chaudhri et al. (2013)				
36.	Yadav et al. (1985)				
37.	Shaw (1989)	Jammu & Kashmir	2		
38.	Mishra et al. (1998)	Uttar Pradesh	17		
39.	Singh et al. (2007)				
40.	Khorajiya et al. (2017)				
41.	Agrawal et al., 2003	Chhattisgarh	13	Central	6
42.	Agrawal et al., 2017	Madhya Pradesh	2		
43.	Kala and Deo (2018)	Bihar	7	East zone	7
44.	Kumar et al., 2015				
45.	Debbarma et al. (2018)	West bengal	6		
46.	Barman et al., 2018	Assam	33	Northeast zone	4
47.	Ghosh et al. (2018)	Mizoram	0		
48.	Laha et al., 2015	NE three states	4		
49.	Saud et al. (2005)	Arunachal Pradesh	7		

selected for carrying out the meta analysis. The meta-analysis indicated high variability between studies ($\tau^2 = 1.94$; heterogeneity $I^2 = 99\%$ with heterogeneity chi square = 5102.01, degree of freedom = 48, H = 10.31 with a p-value of <0.001). The overall random pooled prevalence of bovine babesiosis in India was 6% (95% CI: 4–9%, PI: 0–52%). The infection prevalence (the presence of active infection) based on 44 studies was 5% (95% CI: 3–7%, PI: 0–42%) and the seroprevalence based on 5 studies was 29% (95% CI: 20–41%, PI: 5–75%).

Studies weighted approximately equal with weights on individual studies ranging from 1.7% to 2.2% due to high heterogeneity between studies. Fig. 1 represents the forest plot derived from the meta-analysis. Publication bias was checked by graphical analysis of the funnel plot (Fig. 2). The vertical and diagonal dashed lines in the funnel plot represent the overall estimated effect size and its 95% confidence limits, respectively, based on the random effect model. For determining the funnel plot asymmetry, rank correlation test (z value: 1.87, p = 0.062), Linear regression test (t value: 0.29, p = 0.7762) and Eggers test [Intercept = −0.808 (95% CI: 6.35 to −4.73, p = 0.77) were calculated. Egger's test of the intercept indicated bias in the funnel plots was not statistically significant (p = 0.77).

3.3. Subgroup meta-analysis for India

Subgroup analyses were conducted for the period (1983–2000 and 2001–2018), six zones of India (North, East, west, south, northeast and central zones), species of animal (cattle and buffalo), species of the parasite (*B. bigemina* and *B. bovis*), diagnostic method used (blood smear examination, molecular and serological methods) and states of India. The detailed summary of studies along with state and zone wise pooled prevalence estimate is mentioned in Table 1 and the details of the results of the meta-analysis are depicted in Table 2. Zone wise analysis revealed highest pooled prevalence in the west zone 8% (CI 95% = 2%–31%) and north zone 8% (CI 95% = 4%–15%) followed by east zone 7% (CI 95% = 1%–41%), Central zone 6% (CI 95% = 1%–28%) with the least prevalence of bovine babesiosis being reported from south zone 4% (CI 95% = 3%–7%) and Northeast zone 4% (CI 95% = 1%–27%) (Fig. 3). However, the number of studies was limited in the Central (n = 2), east (n = 3), Northeast (n = 4) and west (n = 5) zones. Highest number of

Study	Events	Total	Weight (fixed)	Weight (random)	IV, Fixed + Random, 95% CI
Agarwal et al., 2003, Chhattisgarh	294	2283	10.4%	2.1%	0.13 [0.12; 0.14]
Agarwal et al., 2017,Madhya Pradesh	3	138	0.1%	1.8%	0.02 [0.00; 0.06]
Agarwal et al., 2017,Punjab	27	104	0.8%	2.1%	0.26 [0.18; 0.35]
Ananda et al., 2009, Karnataka	16	132	0.6%	2.1%	0.12 [0.07; 0.19]
Ananda et al., 2014, Karnataka	58	566	2.1%	2.1%	0.10 [0.08; 0.13]
Aulakh et al., 2005, Punjab	6	101	0.2%	2.0%	0.06 [0.02; 0.12]
Banerjee et al., 1983, Haryana	168	687	5.2%	2.1%	0.24 [0.21; 0.28]
Bhat et al., 2015, Punjab	62	204	1.8%	2.1%	0.30 [0.24; 0.37]
Bhatnagar et al., 2015, Rajasthan	74	5257	3.0%	2.1%	0.01 [0.01; 0.02]
Burman et al., 2018, Assam	80	239	2.2%	2.1%	0.33 [0.28; 0.40]
Burrio et al., 1994, Hyderabad	2	200	0.1%	1.7%	0.01 [0.00; 0.04]
Chaudhri et al., 2013, Haryana	108	6163	4.3%	2.1%	0.02 [0.01; 0.02]
Debbarma et al., 2018, West bengal	18	310	0.7%	2.1%	0.06 [0.03; 0.09]
Filia et al., 2015, Punjab	57	184	1.6%	2.1%	0.31 [0.24; 0.38]
Ghosh et al., 2018, Mizoram	3	1153	0.1%	1.8%	0.00 [0.00; 0.01]
Harish et al., 2006, Karnataka	205	11755	8.2%	2.1%	0.02 [0.02; 0.02]
Jithendran., 1997, Himachal Pradesh	37	200	1.2%	2.1%	0.18 [0.13; 0.25]
Jyothisree et al., 2013, Andhra Pradesh	13	162	0.5%	2.1%	0.08 [0.04; 0.13]
Kala and Deo, 2018, Bihar	8	803	0.3%	2.0%	0.01 [0.00; 0.02]
Kariyappa et al., 2017, Kerala	20	246	0.7%	2.1%	0.08 [0.05; 0.12]
Kaur et al., 2016, Punjab	108	360	3.1%	2.1%	0.30 [0.25; 0.35]
Khorajiya et al., 2017, Uttar Pradesh	4	206	0.2%	1.9%	0.02 [0.01; 0.05]
Kolte et al., 2017, Maharashtra	36	899	1.4%	2.1%	0.04 [0.03; 0.06]
Krishnamurthy et al., 2016, Karnataka	31	300	1.1%	2.1%	0.10 [0.07; 0.14]
Kumar et al., 2015, Haryana	3	168	0.1%	1.8%	0.02 [0.00; 0.05]
Kumar et al., 2016, Gujarat	198	366	3.7%	2.1%	0.54 [0.49; 0.59]
Kumar et al., 2018, Bihar	180	500	4.7%	2.1%	0.36 [0.32; 0.40]
Laha et al., 2015, NE three states	12	333	0.5%	2.0%	0.04 [0.02; 0.06]
Maharana et al., 2016, Gujarat	104	480	3.3%	2.1%	0.22 [0.18; 0.26]
Mishra et al., 1998, UP	82	486	2.8%	2.1%	0.17 [0.14; 0.21]
Muraleedharan et al., 2005, Karnataka	99	4521	3.9%	2.1%	0.02 [0.02; 0.03]
Nair et al., 2011, Kerala	4	150	0.2%	1.9%	0.03 [0.01; 0.07]
Pradeep et al., 2019, Kerala	18	199	0.7%	2.1%	0.09 [0.05; 0.14]
Priya et al., 2017, Kerala	2	125	0.1%	1.7%	0.02 [0.00; 0.06]
Ponnudurai et al., 2017	4	228	0.2%	1.9%	0.02 [0.00; 0.04]
Saud et al., 2005, Arunachal Pradesh	7	100	0.3%	2.0%	0.07 [0.03; 0.14]
Seshadri et al., 1985, Karnataka	283	13762	11.3%	2.1%	0.02 [0.02; 0.02]
Setty et al., 1985, Karnataka	39	935	1.5%	2.1%	0.04 [0.03; 0.06]
Sharma et al., 2000, Himachal Pradesh	5	297	0.2%	1.9%	0.02 [0.01; 0.04]
Sharma et al., 2013, Punjab	10	411	0.4%	2.0%	0.02 [0.01; 0.04]
Sharma et al., 2016,Punjab	89	542	3.0%	2.1%	0.16 [0.13; 0.20]
Shaw, 1989, Jammu and Kashmir	26	1434	1.0%	2.1%	0.02 [0.01; 0.03]
Singh et al., 2007, Uttar Pradesh	184	371	3.8%	2.1%	0.50 [0.44; 0.55]
Singh et al., 2012, Punjab	11	703	0.4%	2.0%	0.02 [0.01; 0.03]
Singh et al., 2013, Punjab	4	104	0.2%	1.9%	0.04 [0.01; 0.10]
Vahora et al., 2012, Gujarat	129	4281	5.1%	2.1%	0.03 [0.03; 0.04]
Veluswamy et al., 2014, Tamil Nadu	32	2637	1.3%	2.1%	0.01 [0.01; 0.02]
Vijayakumar et al., 2017, Karnataka	16	148	0.6%	2.1%	0.11 [0.06; 0.17]
Yadav et al., 1985, Haryana	20	1887	0.8%	2.1%	0.01 [0.01; 0.02]
Total (fixed effect, 95% CI)		**67820**	**100.0%**	**--**	**0.08 [0.08; 0.08]**
Total (random effects, 95% CI)			**--**	**100.0%**	**0.06 [0.04; 0.09]**
Prediction interval					**[0.00; 0.52]**

Heterogeneity: $Tau^2 = 1.9358$; $Chi^2 = 5102.01$, df = 48 (P = 0); $I^2 = 99\%$

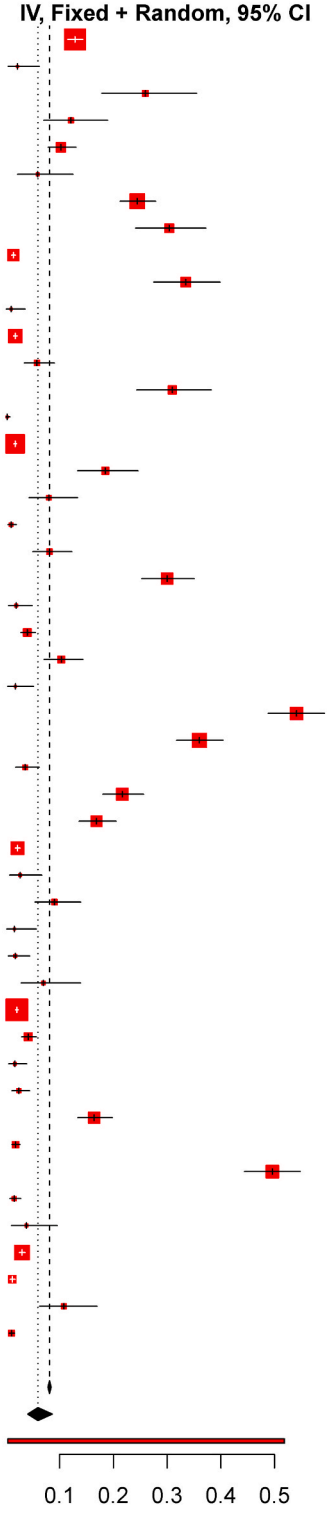

Fig. 1. Forest plot showing the details of the studies pertaining to bovine babesiosis from India along with their prevalence estimates and assigned weights. The CI in each study estimate is represented by lines in the plot. The precision of the estimate is considered as less whenever the lines of each study are wider. The square boxes represent point estimate of each study. The overall pooled estimate is represented by the diamond.

studies on bovine babesiosis was reported from North Zone (n = 20). The prevalence reports on bovine babesiosis was available from 21 states of India with highest number of studies being reported from Punjab (n = 9) with prevalence estimate of 11% (CI 95% = 5%–23%) and Karnataka (n = 8) with 5% (CI 95% = 3%–9%) and Kerala (n = 4) with 5% (CI 95% = 2%–11%). Highest prevalence of bovine babesiosis was recorded from Assam, 33% (CI 95% = 28%–40%) representing only one study (Barman et al., 2018) and least 0% (CI 95% = 0%–0.01%) from Mizoram again representing a single study (Ghosh et al., 2018). Prevalence of bovine babesiosis was high during 1983–2000 period (5%) with a total of eight studies compared to that of the 2001–2018 period (7%) with forty one studies showing an increase in the prevalence of bovine babesiosis. In

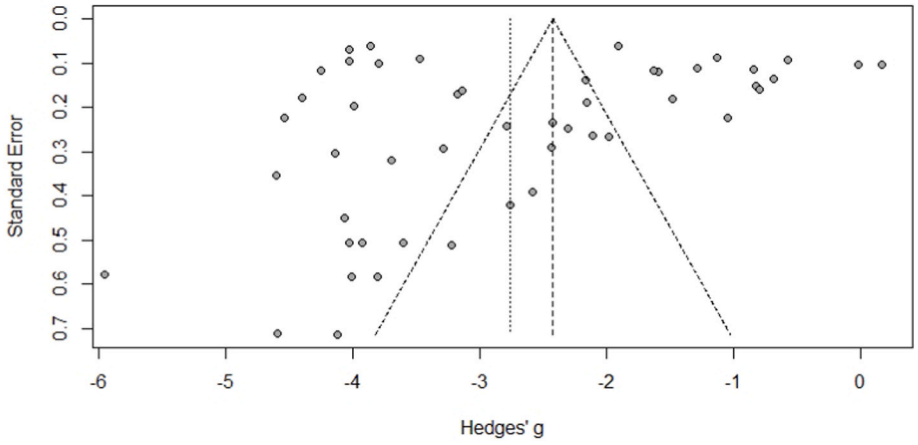

Fig. 2. Funnel plot of standard error (SE) by effect size (Hedges' g). The circles represent studies included in the meta-analysis.

order to understand the trend of bovine babesiois in India during 1983–2018, year-wise prevalence of bovine babesiosis in India was estimated by pooling multiple studied representing each year (Fig. 4). The highest prevalence was observed in 2007 from a study reported from Uttar Pradesh (Singh et al., 2007). In majority of the studies, bovine babesiosis was caused by *Babesia bigemina* (n = 37) with the prevalence estimate of 7% (CI 95% = 4%–10%) whereas *B. bovis* has been reported from only three studies with the prevalence of 1% (CI 95% = 0%–7%) representing Maharashtra (Kolte et al., 2017), Karnataka (Muraleedharan et al., 2005) and Tamil Nadu (Ponnudurai et al., 2017). Bovine babesiosis in India was more prevalent in cattle (9%) compared to buffaloes (5%). The meta-analysis based on the techniques employed revealed the highest prevalence with serology (29%) followed by nucleic acid-based techniques (9%) and standard blood smear examination (4%). In addition, for each subgroup antigen prevalence and seroprevalence were calculated.

4. Discussion

Tick-borne haemoprotozoan infections have been a persistent challenge to domestic cattle production in India owing to the prevailing conducive environment for the survival of ticks. Among these, bovine babesiosis requires a special mention as the impact of the disease is highly evident in India (McLeod and Kristjanson, 1999). In India, the data available on the disease prevalence is scattered and in the present study, attempts were made to generate pooled prevalence estimate of bovine babesiosis during 1983 and 2018 by systematic review and meta-analysis. The overall pooled prevalence estimate of bovine babesiosis in India was found to be 6% with an infection prevalence of 5% and a seroprevalence of 29%. In addition, the infection prevalence by blood smear examination was found to be 4% whereas by molecular methods the infection prevalence recorded was 9%. This clearly indicates the sensitivity of molecular methods in the detection of the subclinical and chronic forms of the disease in addition to the clinical presentation of bovine babesiosis (Mtshali and Mtshali, 2013). The significant aspect of the epidemiology of bovine babesiosis in India is the presence of carrier animals. Animals that recover from clinical disease become persistently infected with *B. bovis* and/or *B. bigemina* with low levels of parasitemia that serve as a source of infection to susceptible animals through competent tick vectors (Howell et al., 2007). The present study considered a minimum cut off for sample size of the selected studies as 100 to avoid small study effects thereby to minimize the heterogeneity between the studies and to ensure accurate estimation of effect size (Thornton and Lee, 2000). This was evident by Egger's and Begg tests that showed bias in the funnel plots was not statistically significant (van Enst et al., 2014).

Early detection and treatment are essentially important to effectively prevent the dissemination of the disease and the majority of the studies in India depend on the examination of Giemsa stained blood smear as the diagnostic method in spite of its limited sensitivity as well as specificity especially in the subclinical form of the disease. This often led to an underestimation of disease prevalence that may lead to negligence of the disease from national priorities of disease control. The impact may be felt as huge whenever the disease status will reach to such a juncture where the available control measures are insufficient to address the economic burden imposed by the disease. Even though more than a century crossed since the first report of disease in India, the control measures are impeded by the truth of unavailability of effective vaccines, limited chemotherapeutic choices (imidocarb or diminazene aceturate) and challenges in fast detection methods.

In India, during the period 2001–2018, the pooled prevalence was more (7%) compared to the period 1983–2000 (5%). It was also evident that the infection prevalence (an increase from 3% to 7%) and seroprevalence (increased from 21% to 37%) was also high during the recent years which impose an alarming threat to the available control programs. The increase in disease prevalence may also be attributed to the change in climate that might have led to the expansion of the niche of vectors (Bram et al., 2002). Further, the emergence of drug resistant parasites and acaricide resistance in the recent years might have equally contributed to the increased prevalence of bovine babesiosis in India (Sagar et al., 2020). In endemic areas like India, herd immunity to bovine babesiosis is existing due to the contious reinfection with *Babesia* spp. by natural vectors. The increased seroprevalence can thus be attributed to the establishment of herd immunity owing to the increase in the population of vector ticks and the emergence of acaricide resistance in the recent years (Foil et al., 2004). So it is highly recommended to undertake regular screening of representative bovine populations for babesiosis in high risk areas especially when animals with fever are not responding to antibiotics. This will help in detection of carrier animals and treatment of infected animals at the earliest thereby the possible livestock production loss can be reduced. Further, tick control measures including periodic application of acaricides need to be adopted. In the present study, the prevalence estimate for bovine babesiosis was higher in the North and west zones (8%) compared to other zones. The higher prevalence may be due to the abundance of tick vectors as well as susceptible animal population in those areas compared to other zones. Also, the infection prevalence in the Northeastern zone was 4% which is in accordance with the observation of Laha et al., 2015a who reported the prevalence of *B. bigemina* infection in cattle as 3.6% by polymerase chain reaction.

In India, the prevalence of disease was more with *B. bigemina* (7%) than *B. bovis* (1%) which is in agreement with Muraleedharan et al., 2005. It has been reported by Kolte et al., 2017 that in *B. bovis* enzootic stability with a low level of infection in animals may be present and the

Table 2
Summary of meta-analysis of prevalence of bovine babesiosis in India.

Parameters	Number of studies	Total samples	Pooled prevalence (%) (confidence interval at 95%level	Prediction interval (%) at 95% level	Heterogeneity analysis						
					Quantifying Heterogeneity				Test of Heterogeneity		
					I2 Value (%) with range	Tau square value with range	H value with range		Chi square heterogeneity statistics	DF	P -Value
Bovine babesiosis in India											
Total Prevalence	49	67820	6 (4–9)	0–52	99.1% [99.0%; 99.1%]	1.9358 [1.3165; 3.0635]	10.31 [9.81; 10.84]		5102.01	48	<0.001
Infection prevalence	44	65681	5 (3–7)	0–42	98.9% (98.7%; 99.0%)	1.6375 (1.0838; 2.6656)	9.42 (8.90; 9.96)		3811.86	43	<0.001
Sero-prevalence	5	2088	29 (20–41)	5–75	96.4% (93.9%; 97.9%)	0.3213 (0.1068; 2.7245)	5.29 (4.06; 6.90)		112.08	4	<0.001
Subgroup analysis by period											
Period I (1983–2000)											
Total Prevalence	8	19591	5 (2–12)	0–66	99.2% (99.0%; 99.4%)	1.9593 [0.8184; 8.4315]	11.48 (10.17–12.97)	923.19	7		<0.001
Infection Prevalence	7	18715	3 (1–6)	0–33	96.8% (95.1%; 97.9%]	1.1104 [0.4099; 5.5441]	5.56 [4.50; 6.86]	185.29	6		<0.0001
Seroprevalence	2	1173	21 (14–29)	–	89.6% [61.7%; 97.2%]	0.0977	3.11 [1.62; 5.98]	9.66	1		0.0019
Period II (2000–2018)											
Total Prevalence	41	48053	7 (4–10)	0–59	99.0% [98.9%; 99.1%]	2.1507 [1.4189; 3.5902]	10.08 [9.53; 10.65]	4060.66	40		<0.001
Infection Prevalence	38	47017	5 (4–8)	0–46	98.9% [98.7%; 99.0%]	1.7020 [1.0899; 2.9180]	9.44(8.88–10.04)	3207.02	37		<0.001
Seroprevalence	3	915	37 (25–50)	0–100	94.1% [86.3%; 97.5%]	0.2081 [0.0460; 8.6043]	4.13 [2.70; 6.33]	34.18	2		<0.0001
Subgroup analysis by zones											
North Zone											
Total Prevalence	20	16637	8 (4–15)	0–71	98.8% [98.5%; 99.0%]	2.3099 [1.2996; 4.9794]	9.05 [8.30; 9.87]	1557.27	19		<0.0001
Infection Prevalence	15	14643	5 (3–9)	0–47	98.2% [97.7%; 98.6%]	1.6001 [0.8076; 3.9730]	7.47 [6.66; 8.38]	782.17	14		<0.0001
Seroprevalence	5	2088	29 (20–41)	5–75	96.4% [93.9%; 97.9%]	0.3213 [0.1068; 2.7245]	5.29 [4.06; 6.90]	112.08	4		<0.0001
East Zone											
Total Prevalence	3	1613	7 (1–41)	0–100	98.9% [98.1%; 99.3%]	3.9985	9.40 (7.27–12.16)	176.77	2		<0.0001
Infection Prevalence	3	1613	7 (1–41)	0–100	98.9% [98.1%; 99.3%]	3.9985	9.40 (7.27–12.16)	176.77	2		<0.0001
Seroprevalence	–	–	–	–	–	–	–	–	–		–
West Zone											
Total Prevalence	5	11283	8 (2–31)	0–98	99.6% [99.5%; 99.7%]	3.2373 [1.1533; 26.8016]	16.67 (14.72–18.86)	111..89	4		<0.0001
Infection Prevalence	5	11283	8 (2–31)	0–98	99.6% [99.5%; 99.7%]	3.2373 [1.1533; 26.8016]	16.67 (14.72–18.86)	111..89	4		<0.0001
Seroprevalence	–	–	–	–	–	–	–	–	–		–
South Zone											
Total Prevalence	15	35838	4 (3–7)	1–24	96.4% [95.2%; 97.3%]	0.7680 [0.3751; 2.0982]	5.29 (4.59–6.11)	391.96	14		<0.0001
Infection Prevalence	15	35838	4 (3–7)	1–24	96.4% [95.2%; 97.3%]	0.7680 [0.3751; 2.0982]	5.29 (4.59–6.11)	391.96	14		<0.0001
Seroprevalence	–	–	–	–	–	–	–	–	–		–
Central Zone											
Total Prevalence	2	2421	6 (1–28)	–	90.4% [65.2%; 97.4%]	1.6229	3.23 (1.69–6.15)	10.42	1		0.0012
Infection Prevalence	2	2421	6 (1–28)	–	90.4% [65.2%; 97.4%]	1.6229	3.23 (1.69–6.15)	10.42	1		0.0012
Seroprevalence	–	–	–	–	–	–	–	–	–		–
Northeast zone											
Total Prevalence	4	1825	4 (1–27)	0–100	97.8% [96.4%; 98.7%]	4.5022 [1.3327; 65.7661]	6.81 [5.25; 8.83]	138.95	3		<0.0001
Infection Prevalence	4	1825	4 (1–27)	0–100	97.8% [96.4%; 98.7%]	4.5022 [1.3327; 65.7661]	6.81 [5.25; 8.83]	138.95	3		<0.0001
Seroprevalence	–	–	–	–	–	–	–	–	–		–
Subgroup analysis by species of animal											
Cattle											
Pooled prevalence	48	62951	6 (4–9)	0–56	98.9% [98.8%; 99.0%]	2.0416 [1.3900; 3.2674]	9.49 [9.00; 10.01]	4235.26	47		<0.001
Infection Prevalence	43	59472	5 (3–7)	0–43	98.7% [98.5%; 98.8%]	1.7149 [1.1315; 2.8155]	8.76 (8.25–9.30)	3221.11	42		<0.001
Seroprevalence	5	1424	33 (19–50)	3–88	96.1% [93.3%; 97.7%]	0.6078 [0.1999; 5.2308]	5.07 [3.86; 6.66]	102.81	4		<0.0001
Buffalo											
Pooled prevalence	10	6902	5 (1–18)	0–91	98.7% [98.3%; 99.0%]	4.5970 [2.1016; 15.9762]	8.81 [7.75; 10.01]	697.80	9		<0.0001
Infection Prevalence	7	6307	3 (1–13)	0–91	98.5% [97.9%; 98.9%]	4.5156 [1.7757; 22.5753]	8.10 [6.86; 9.56]	393.84	6		<0.0001
Seroprevalence	3	595	21 (4–61)	0–100	98.5% [97.4%; 99.1%]	2.3924 [0.6117; 95.7488]	8.18 [6.17; 10.84]	133.82	2		<0.0001

(*continued on next page*)

Table 2 (*continued*)

Parameters	Number of studies	Total samples	Pooled prevalence (%) (confidence interval at 95%level	Prediction interval (%) at 95% level	Heterogeneity analysis					
					Quantifying Heterogeneity			Test of Heterogeneity		
					I2 Value (%) with range	Tau square value with range	H value with range	Chi square heterogeneity statistics	DF	P -Value
Subgroup analysis by diagnostic method										
Blood smear examination	40	63697	4 (3–5)	0–26	98.5(98.3–98.7)	1.2102 (0.7645–2.0281)	8.11 (7.59; 8.65)	2562.31	39	<0.001
Molecular methods	13	3809	9 (5–17)	1–65	96.7% (95.6%; 97.6%)	1.6349 (0.7898; 5.2867)	5.54 (4.77; 6.44)	368.15	12	<0.0001
Serology	5	2088	29 (20–41)	5–75	96.4% (93.9%; 97.9%)	0.3213 (0.1068; 2.7245)	5.29 (4.06; 6.90)	112.08	4	<0.0001
Subgroup analysis by state										
Karnataka										
Total Prevalence	8	32119	5 (3–9)	1–35	97.7% [96.7%; 98.4%]	0.7784 [0.3243; 3.2978]	6.56 [5.50; 7.82]	301.21	7	<0.0001
Gujarat										
Total Prevalence	3	5127	18 (3–63)	1–100	99.7% [99.6%; 99.8%]	3.3418 [0.8988; >100.0000]	18.99 [16.20; 22.27]	721.41	2	<0.0001
Kerala										
Total Prevalence	4	720	5 (2–11)	0–63	71.0% [17.2%; 89.8%]	0.4814 [0.0216; 10.7046]	1.86 [1.10; 3.14]	10.34	3	0.0159
Punjab										
Total Prevalence	9	2713	11 (5–23)	0–77	96.2% [94.5%; 97.4%]	1.7436 [0.7518; 6.6133]	5.16 (4.26–6.25)	212.79	8	<0.0001
Haryana										
Total Prevalence	4	8905	7 (6–8)	0–98	99.5% [99.3%; 99.6%]	2.4408 [0.7437; 33.3922]	13.79 [11.72; 16.24]	570.78	3	<0.0001
Uttar Pradesh										
Total Prevalence	3	963	17 (2–74)	0–100	99.1% [98.5%; 99.4%]	5.2800 [1.3464; >100.0000]	10.45 [8.22; 13.28]	218.22	2	<0.0001
Subgroup analysis by species of parasite										
B.bigemina										
Total Prevalence	37	55231	7 (4–10)	0–55	99.2% [99.1%; 99.3%]	1.9547 [1.2640; 3.3790]	11.04 [10.44; 11.66]	4384.58	36	<0.001
Infection Prevalence	32	53143	5 (3–8)	0–43	98.9% [98.8%; 99.1%]	1.6332 [1.0116; 2.9496]	9.76 [9.14; 10.41]	2950.08	31	<0.001
Seroprevalence	5	2088	29 (20–41)	5–75	96.4% [93.9%; 97.9%]	0.3213 [0.1068; 2.7245]	5.29 [4.06; 6.90]	112.08	4	<0.0001
B.bovis										
Total prevalence	3	5648	1 (0–7)	0–100	96.4% [92.5%; 98.3%]	2.9432 [0.7000; >100.0000]	5.27 [3.64; 7.63]	55.57	2	<0.0001

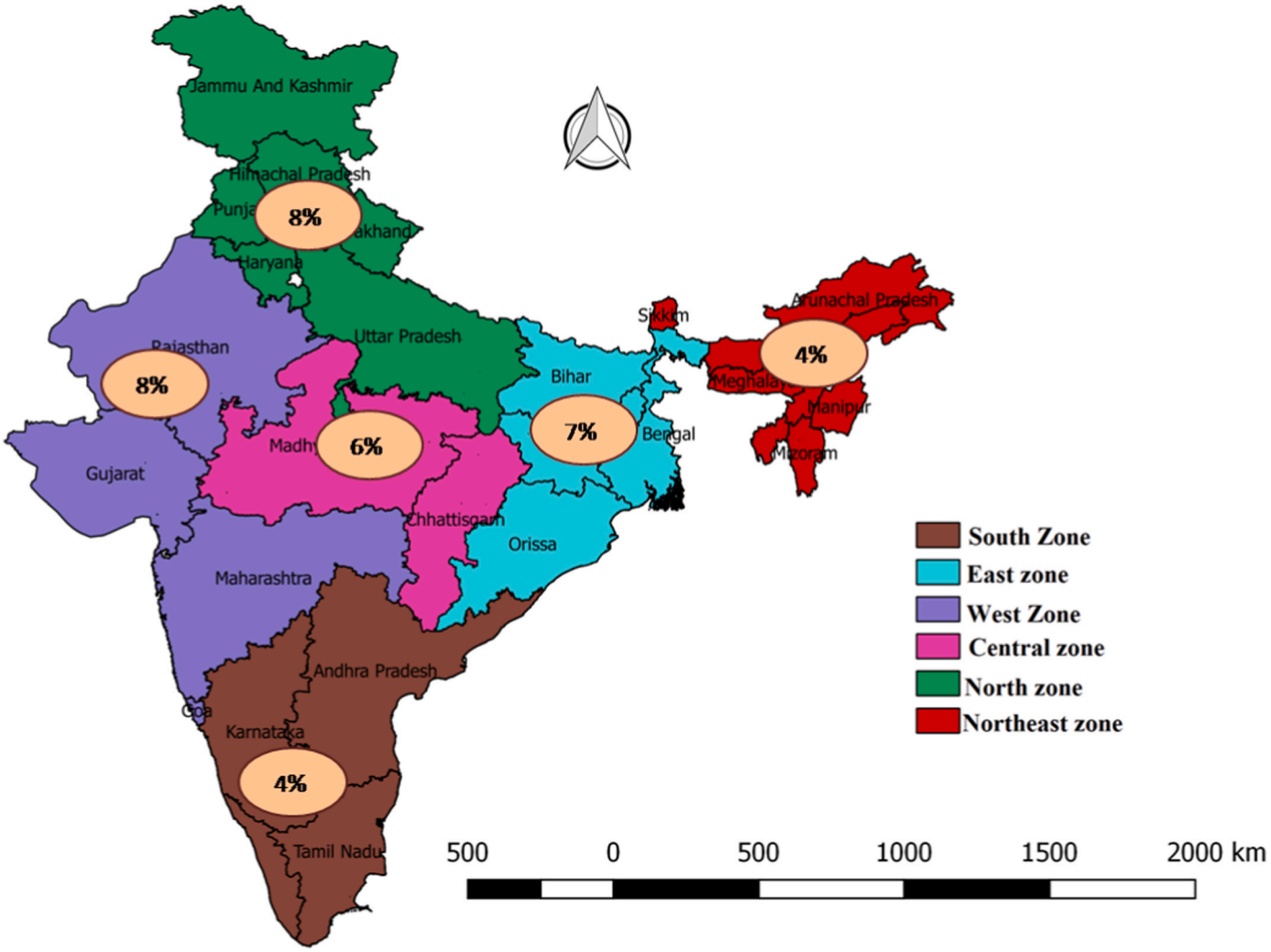

Fig. 3. India map showing the zone -wise prevalence estimates of bovine babesiosis. The figures inside the circles represent the prevalence in each zone.

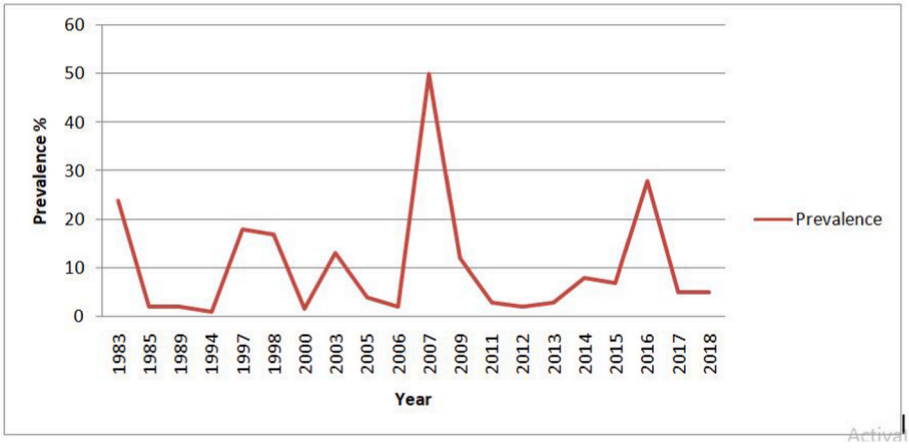

Fig. 4. Year-wise trend of prevalence of bovine babesiosis in India during 1983–2018.

detection of carrier status with very low parasitiemia is often difficult that may be the possible reason of underrepresentation of infection. Bovine babesiosis in India was more prevalent in cattle (6%) compared to buffaloes (5%). The result is in accordance with the finding of Mahmmod 2014 that buffaloes have more tolerance to clinical infection than cattle. In addition, inverse age resistance is evident in bovine babesiosis with young animals are less susceptible than older animals and *Bos indicus* are more resistant than *Bos taurus* (Laha et al., 2015b).

5. Conclusions

The study described the distribution of bovine babesiosis in India and

to the best of our knowledge, this study represents the first systematic review and meta-analysis on prevalence estimates of bovine babesiosis in India. The increase in disease prevalence in India is not only imposing a challenge to the ongoing control strategies of bovine babesiosis but also to the tick control programs. In the era of climate change, it is high time to revisit the ongoing tick control measures as there is a great threat of the expansion of niche of ticks in the near future.

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Statement of animal rights

Not Applicable.

Author statement

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Declaration of competing interest

The authors declare no conflict of interests.

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Appendix A. Supplementary data

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