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Theileriosis prevalence status in cattle and buffaloes in India established by systematic review and meta-analysis

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ABSTRACT

The present study on theileriosis prevalence in cattle and buffaloes of India was reckoned by systematic review and meta-analysis. The studies on theileriosis prevalence reported during the period 1984–2019, were collected by using online databases, and offline literature and meta-analyses was done in R-Software. The theileriosis prevalence was 20% [95% level, CI 16–25%, PI 2–74%], obtained by using 70,688 samples. The increasing trend of theileriosis prevalence was observed in the recent period [2011–19] when compared to past years. A higher theileriosis prevalence in the Central zone [24%] than in other zones was observed. The state-wise analysis revealed a higher prevalence in Puducherry and Assam. The method-wise breakdown revealed a higher prevalence by serology for India [39%] in comparison to other methods. Host species-wise scrutiny indicated a higher prevalence in cattle [22%] than buffaloes [14%]. Theileriosis was caused by *Theileria* (*T.*) *annulata* [21%], *T. orientalis* [16%], and *T.* species [17%] in India. The theileriosis prevalence established by systematic review and meta-analysis in the present study forms the first report from India to the best of our knowledge. It also documents a valuable literature resource on theileriosis prevalence studies in India. This study helps in identifying the theileriosis high-risk zones and states in India. It will help the policymakers and various stakeholders in decision making and wisely using the scarce resources available in implementing preventive strategies effectively. Further, theileriosis prevention can be employed by adopting effective therapeutic measures and vector control strategies, which will augment the profits to dairy farmers in India.

Keywords: India, Meta-analysis, Prevalence, Systematic review, Theileriosis

Theileriosis is a common protozoan parasitic disease of dairy cattle and buffaloes in India and the World. Bovine tropical theileriosis, a tick-borne haemoprotozoan disease of cattle and buffaloes caused by *Theileria* (*T.*) *annulata,* a major constraint to the dairy industry and livestock production in India. As a whole, various Theileria species affect cattle and buffaloes, the most pathogenic and economically important species are *T. annulata* (Bovine tropical theileriosis), *T. parva* (East Coast fever), *T. orientalis* (Oriental theileriosis) and are transmitted by Ixodid ticks of the genera *Hyalomma* and *Rhipicephalus* species. In India, bovine theileriosis was first reported in 1905 by Lingard as reported earlier (Mohan 1972). In addition to *T. annulata* infection in cattle and buffaloes in India, *T. orientalis* has also been reported in the past. In India, the cattle and buffalo population is 192.5 and 109.8 million and ranks first in milk production and buffalo population in the World (BAHS 2019). Theileriosis causes severe economic loss due to decreased weight gain, drop in milk yield, abortions, and in some cases leads to death in animals. Globally, the annual economic loss of US$ 13.9 to US$ 18.7 billion is due to tick-borne diseases as reported earlier (Atif *et al*. 2012). The annual economic loss due to bovine tropical theileriosis in India has been estimated to the tune of US$ 384.3 million per annum (Minjauw and McLeod 2003). The estimated economic loss due to tropical theileriosis in India is US$ 1,295 million (₹ 8,426.7 crore) annually (Narladkar 2018). Hence, it is necessary to focus on the theileriosis prevalence in cattle and buffaloes in India and to know the status of this disease.

Various studies are being reported on the prevalence estimates calculated by using a meta-analysis for different livestock diseases and consider it as an innovative tool as reported (Krishnamoorthy *et al*. 2020). The main purpose of doing a meta-analysis is to summarize and integrate results from numerous individual reports, analyze result variations between the studies, use individual reports with small sample sizes to estimate the prevalence and analyze endpoints that require larger sample sizes, increase precision in estimating prevalence, determine if new studies are needed to further investigate an issue and generate new hypotheses for future studies (Krishnamoorthy *et al*.

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2019a,b). The essential steps addressed in a meta-analysis study are the recognition and assortment of studies, heterogeneity between studies, information availability, and data analysis (Walker *et al*. 2008). There are scarce studies centered on the meta-analysis method, few of them reported on subclinical and clinical mastitis, major mastitis pathogens prevalence in India (Krishnamoorthy *et al*. 2017), anaplasmosis in dairy animals in India and the World (Krishnamoorthy *et al*. 2019a), livestock-associated methicillin-resistant *Staphylococcus aureus* in animals in India (Krishnamoorthy *et al*. 2019b), and babesiosis prevalence in the World (Jacob *et al*. 2020). However, no prevalence estimates were available for theileriosis in cattle and buffaloes by using systematic review and meta-analysis for India. Hence, the present study was conducted to know the prevalence estimates for theileriosis in India along with various subgroup analyses based on year-wise, zone-wise, state-wise, host species-wise, method-wise, *Theileria* species-wise.

MATERIALS AND METHODS

Literature search: The literature search was performed systematically on the prevalence of theileriosis in cattle and buffaloes in India by using appropriate keyword searches. The databases included for the search were PubMed, Science Direct, Springer's, Scopus, Google Scholar, Indianjournals.com, J-Gate @ Consortium of e-Resources in Agriculture (CeRA) under Indian Council of Agricultural Research (ICAR), research abstracts in proceedings/ compendium of conferences, seminars, symposia, and other published works of literature. More than 500 articles were searched, reviewed, selected, and the data obtained were subjected to meta-analysis to determine the prevalence estimates. The prevalence studies were divided into five zones, viz. North, East, West, South, and Central zones based on the states in India. The details collected include the author's name, year, state or country, diagnostic methods used, *Theileria* species detected, number of positive samples, and number of samples tested in dairy animals such as cattle and buffaloes. The retrieval period for the studies was from 1984–2019 based on the availability, and the language was limited to English only. Further, the peer-reviewed articles, original research articles, and references cited from the retrieved studies were searched again to backtrace the past years' published articles on theileriosis prevalence.

Selection of studies: The cross-sectional and longitudinal studies on theileriosis prevalence conducted on cattle and buffaloes in India was selected for analysis. The studies should have the following inclusion criteria: (1) *Theileria* species frequency or antibodies detected, (2) total number of animals tested or screened, (3) year of the study conducted, (4) studies with prevalence values reported, (5) place or location of study, (6) study type and (7) studies which have used the standard methodology of confirmatory tests including blood smear examination with different staining methods, molecular methods by different PCRs and serological diagnosis by different ELISA's. Exclusion criteria for the studies were: (1) *Theileria* species frequencies was not reported, (2) studies such as case reports, review articles and outbreaks investigations were not included for analysis purpose. Further, the quality assessment of the studies was done by using a fixed rating scale devised. The scale included the following: representativeness of the sample, sample size, the methodology used, prevalence values, and outcome assessment with each having the maximum score of 2, 1, 3, 2, and 2, respectively. The maximum score for quality assessment of studies was 10 and the minimum score was assigned as per the study criteria.

Data entry: The theileriosis prevalence studies were analysed thoroughly and reviewed systematically before initiating the data entry process onto predesigned Microsoft Excel sheets. These include the name of authors, year of publication, period of study, numbers of animals positive for theileriosis, total number of cattle and buffaloes tested, and the confirmation method used for theileriosis diagnosis. The confirmation method used for the diagnosis of theileriosis prevalence was blood smear examination with different staining methods, molecular methods using different PCRs, and serological diagnosis by using different types of ELISA's. The theileriosis prevalence considered for overall prevalence estimation was the value of the highest prevalence obtained by different diagnostic methods obtained in a study.

Meta-analysis: The meta-analysis on theileriosis prevalence in cattle and buffaloes in India was conducted by using the R Open source scripting software (Comprehensive R Archive Network) version 3.2.5 and the R package used was "meta" as reported earlier (Schwarzer 2007). The graphical representation of meta-analysis was done by using a forest plot or confidence interval plot. The generalized linear mixed model and Logit transformation for proportion, i.e. 'sm=PLOGIT' was used in the analysis. The studies were represented by a square at a point estimate of prevalence and a horizontal line extending either side of the square block depicts a 95% confidence interval (CI). The shaded dark line below the forest plot represents the prediction interval (PI) at 95% level. The heterogeneity between the studies was determined by using the I-square, Tau square, H value, and P values obtained and given in the last line of the forest plot. To minimize the heterogeneity between the studies on theileriosis prevalence, the subgroup analysis was carried out based on the various parameters as described earlier (Krishnamoorthy *et al*. 2019a). The Cochran Q statistics were calculated as reported in the previous studies (Krishnamoorthy *et al*. 2017, Krishnamoorthy *et al*. 2019a,b). The forest plots were prepared for the theileriosis prevalence for overall prevalence estimate, year-wise, zone-wise, state-wise, host species-wise, method-wise, and *Theileria* species-wise. The prevalence estimates for theileriosis in cattle and buffaloes in India was expressed as a percentage and along with CI and PI at 95% level.

RESULTS AND DISCUSSION

Theileriosis prevalence studies: Theileriosis is caused by several *Theileria* (*T.*) species. *T. parva* causes East Coast fever, *T. annulata* causes Tropical theileriosis or Mediterranean theileriosis, and *T. orientalis* (*T. orientalis/buffeli* group) causes Oriental theileriosis in cattle and buffaloes (OIE 2014). The details of theileriosis prevalence studies from India included in the meta-analysis are given in Fig. 1. The number of prevalence studies included for meta-analysis was 80 from India after the systematic review. The year-wise and state-wise number of studies from India included for meta-analysis are given in Fig. 2. More studies were reported during the year 2017 [17]. The prevalence studies included were 13, 8, and 59 during the period 1984–2000, 2001–10, and 2011–19, respectively and with the total number of samples 70,688 obtained from cattle and buffaloes in India. The prevalence studies from India covered 21 states and one union territory, with more number of studies from Tamil Nadu [12], followed by Gujarat [7], Karnataka [6], Rajasthan [6], Haryana [5], Kerala [5], Maharashtra [5], Jammu and Kashmir [4], Madhya Pradesh [4], Punjab [4], Uttar Pradesh [3], Bihar [2], Himachal Pradesh [2], Mizoram [2], Odisha [2], Telangana [2], Uttarakhand [3], West Bengal [2] and one study each from Andhra Pradesh, Assam, Chhattisgarh, and Puducherry. The

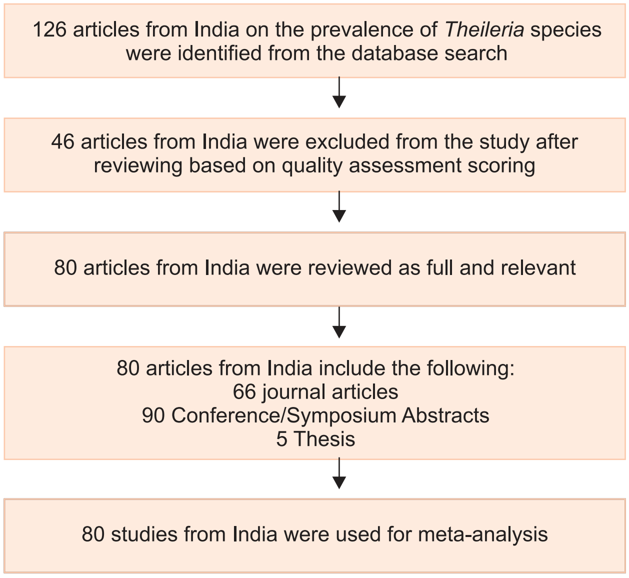

Fig. 1. Flow chart showing theileriosis prevalence studies from India included for meta-analysis.

details of the studies on theileriosis prevalence with author name, year, states, zones, along with quality assessment scores are presented in Table 1. The studies with a quality assessment score of 5 and above were included for a meta-

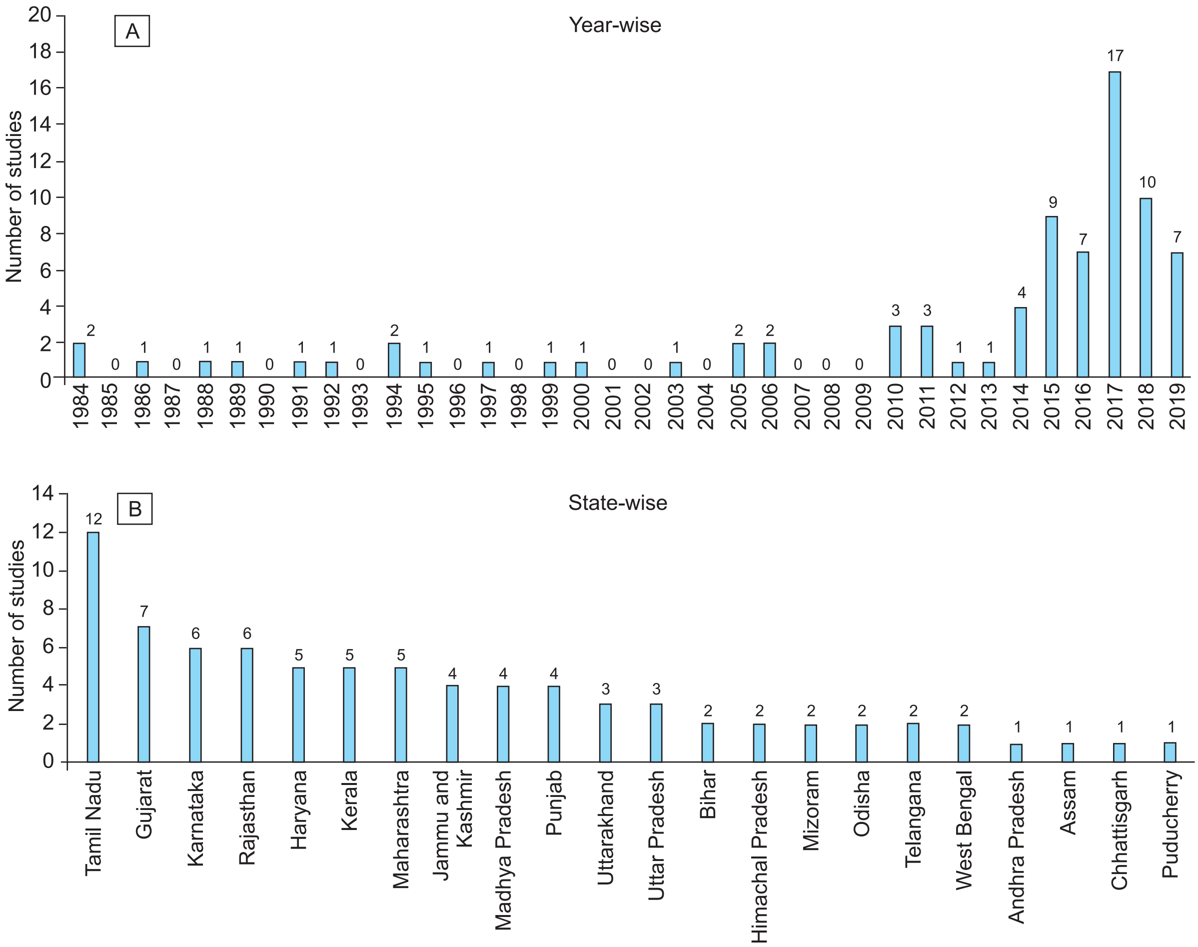

Fig. 2. Year-wise (A) and statewise (B) number of theileriosis prevalence studies from India

Table 1. Theileriosis prevalence studies from India included in the meta-analysis with their quality assessment scores

No.	Studies [Author and year]	Place of study	Zone	Quality assessment of studies#					
				Representativeness of the sample	Sample size (Maximum score=1)	Methodology used (Maximum score=2)	Prevalence values (Maximum score=2)	Outcome assessment (Maximum score=2)	Overall score
1.	Anandan and Lalitha, 1984	Tamil Nadu	South	**	*	*	**	*	7
2.	Venkataraman *et al*. 1984	Tamil Nadu	South	*	*	**	**	*	7
3.	Sisodia and Mandial, 1986	Madhya Pradesh	Central	*	*	*	*	*	5
4.	Datta *et al*. 1988	Bihar	East	*	*	*	**	*	6
5.	Shaw, 1989	Jammu and Kashmir	North	**	*	*	**	*	7
6.	Singh, 1991	Gujarat	West	**	*	*	*	*	6
7.	Bondopadhyay *et al*. 1992	West Bengal	East	*	*	*	*	*	5
8.	Das, 1994	Uttar Pradesh	North	*	*	**	*	*	6
9.	Muraleedharan *et al*. 1994	Karnataka	South	**	*	*	**	*	7
10.	Gomathinayagam *et al*. 1995	Tamil Nadu	South	*	*	**	**	*	7
11.	Jithendran, 1997	Himachal Pradesh	North	**	*	*	**	*	7
12.	Sharma *et al*. 1999	Himachal Pradesh	North	*	*	*	**	*	6
13.	Soundarajan *et al*. 2000	Tamil Nadu	South	*	*	**	**	*	7
14.	Ramesh *et al*. 2003	Karnataka	South	**	*	*	**	*	7
15.	Raina *et al*. 2005	Jammu and Kashmir	North	*	*	*	*	*	5
16.	Sandhu, 2005	Punjab	North	*	*	*	**	*	6
17.	Ram *et al*. 2006	Haryana	North	**	*	**	**	*	8
18.	Ram *et al*. 2006	Rajasthan	West	**	*	**	**	*	8
19.	Godara and Sharma, 2010	Rajasthan	West	*	*	*	**	*	6
20.	Godara *et al*. 2010	Rajasthan	West	*	*	*	**	*	6
21.	Parthiban *et al*. 2010	Tamil Nadu	South	*	*	***	*	*	7
22.	Aparna *et al*. 2011	Kerala	South	*	*	*	**	*	6
23.	Nair *et al*. 2011	Kerala	South	**	*	***	**	*	9
24.	Panda *et al*. 2011	Odisha	East	*	*	*	**	*	6
25.	Singh *et al*. 2012	Punjab	North	*	*	*	**	*	6
26.	Chaudhri *et al*. 2013	Haryana	North	*	*	*	**	*	6
27.	Kohli *et al*. 2014	Uttarakhand	North	**	*	***	**	*	9
28.	Kundave *et al*. 2014	Gujarat	West	*	*	***	*	*	7
29.	Sarma *et al*. 2014	Mizoram	East	*	*	*	**	*	6
30.	Velusamy *et al*. 2014	Tamil Nadu	South	**	*	*	**	*	7
31.	Anupama *et al*. 2015	Tamil Nadu	South	*	*	***	*	*	7
32.	Chauhan *et al*. 2015	Gujarat	West	*	*	***	**	*	8
33.	George *et al*. 2015	Andhra Pradesh	South	**	*	***	**	*	9
34.	George *et al*. 2015	Telangana	South	**	*	***	**	*	9
35.	Kumar *et al*. 2015	Gujarat	West	*	*	*	**	*	6
36.	Kumar *et al*. 2015	Punjab	North	*	*	*	**	*	6
37.	Mote *et al*. 2015	Maharashtra	West	**	*	*	**	*	7
38.	Tuli *et al*. 2015	Punjab	North	**	*	***	**	*	9
39.	Waskel and Gaur, 2015	Madhya Pradesh	Central	**	*	*	**	*	7
40.	Agrawal, 2016	Madhya Pradesh	Central	*	*	*	**	*	6
41.	Bhardwaj, 2016	Jammu and Kashmir	North	**	*	***	**	*	9

Table 1. Theileriosis prevalence studies from India included in the meta-analysis with their quality assessment scores

No.	Studies [Author and year]	Place of study	Zone	Quality assessment of studies#					
				Representativeness of the sample	Sample size (Maximum score=1)	Methodology used (Maximum score=2)	Prevalence values (Maximum score=2)	Outcome assessment (Maximum score=2)	Overall score
42.	Charaya *et al*. 2016	Haryana	North	**	*	***	**	*	9
43.	Krishnamurthy *et al*. 2016	Karnataka	South	**	*	*	**	*	7
44.	Maharana *et al*. 2016	Gujarat	West	*	*	*	**	*	6
45.	Naik *et al*. 2016	Chhattisgarh	Central	*	*	*	**	*	6
46.	Padhiyar *et al*. 2016	Gujarat	West	*	*	***	**	*	8
47.	Bhosale, 2017	Maharashtra	West	*	*	*	**	*	6
48.	Debbarma *et al*. 2017	West Bengal	East	**	*	*	**	*	7
49.	Dadhich *et al*. 2017	Madhya Pradesh	Central	**	*	*	**	*	7
50.	Dharanesha *et al*. 2017	Karnataka	South	*	*	*	**	*	6
51.	Ganguly *et al*. 2017	Haryana	North	**	*	*	**	*	7
52.	Goyal *et al*. 2017	Rajasthan	West	*	*	***	*	*	7
53.	Inglepatil, 2017	Maharashtra	West	*	*	***	**	*	8
54.	Jamadade, 2017	Maharashtra	West	*	*	***	**	*	8
55.	Kariyappa *et al*. 2017	Kerala	South	**	*	*	**	*	7
56.	Khorajiya *et al*. 2017	Uttar Pradesh	North	*	*	*	**	*	6
57.	Kolte *et al*. 2017	Maharashtra	West	**	*	***	**	*	9
58.	Kundave *et al*. 2017	Uttar Pradesh	North	*	*	***	**	*	8
59.	Nimisha *et al*. 2017	Kerala	South	*	*	*	**	*	6
60.	Parmar and Upadhyay, 2017	Uttarakhand	North	*	*	*	**	*	6
61.	Ponnudurai *et al*. 2017	Tamil Nadu	South	**	*	***	**	*	9
62.	Priya *et al*. 2017	Kerala	South	*	*	***	**	*	8
63.	Sahoo *et al*. 2017	Odisha	East	**	*	*	**	*	7
64.	Ananda *et al*. 2018	Karnataka	South	*	*	*	*	*	5
65.	Brahma *et al*. 2018	Assam	East	**	*	*	**	*	7
66.	Devadevi *et al*. 2018	Puducherry	South	*	*	***	*	*	7
67.	Edith *et al*. 2018	Tamil Nadu	South	**	*	***	**	*	9
68.	Ghosh *et al*. 2018	Mizoram	East	**	*	*	**	*	7
69.	Hemalata and Vaishnava, 2018	Rajasthan	West	*	*	*	**	*	6
70.	Kala *et al*. 2018	Bihar	East	*	*	*	**	*	6
71.	Kumar *et al*. 2018	Telangana	South	**	*	*	**	*	7
72.	Nagar *et al*. 2018	Uttarakhand	North	*	*	*	**	*	6
73.	Sharma *et al*. 2018	Rajasthan	West	*	*	***	**	*	8
74.	Brahmbhatt *et al*. 2019	Gujarat	West	*	*	*	**	*	6
75.	Edith *et al*. 2019	Tamil Nadu	South	*	*	***	**	*	8
76.	Farooq *et al*. 2019	Jammu and Kashmir	North	**	*	***	**	*	9
77.	Ganguly *et al*. 2019	Haryana	North	*	*	***	**	*	8
78.	Jayalakshmi *et al*. 2019	Tamil Nadu	South	*	*	*	**	*	6
79.	Jeyathilakan *et al*. 2019	Tamil Nadu	South	*	*	*	**	*	6
80.	Patil and Satbige, 2019	Karnataka	South	*	*	***	**	*	8

Note: CI, Confidence interval; PI, Prediction interval; NS, Not significant; *, Significant (P<0.05); **, Highly significant (P<0.01).

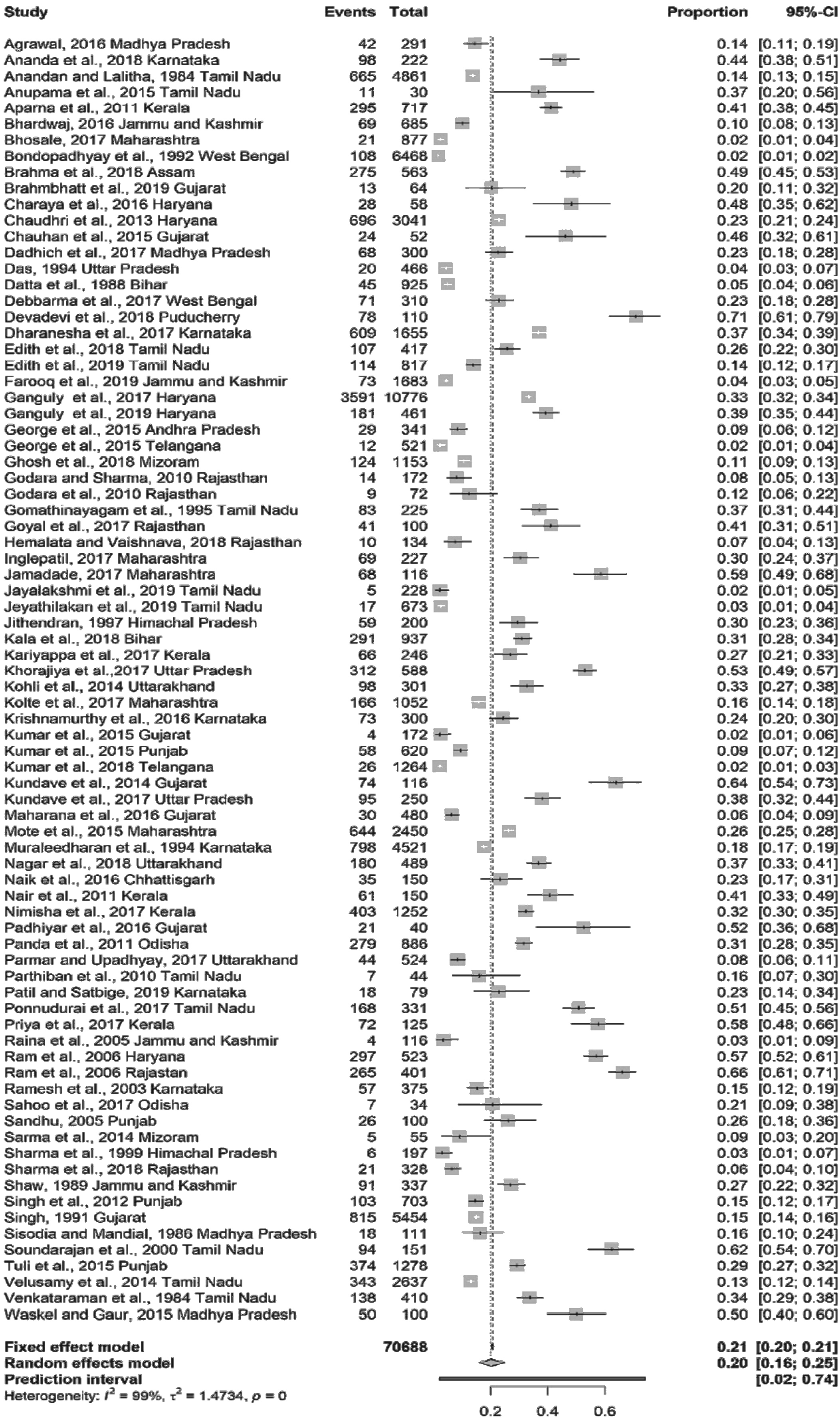

Fig. 3. Forest plot showing the theileriosis studies from India and their prevalence estimates.

analysis. More number of studies reported on the prevalence was from cattle than buffaloes and for *T. annulata* [43] in India indicating the importance of these host-species and *T.* species in India.

Theileriosis prevalence in India: The particulars of meta-analysis results on theileriosis prevalence in India are presented in Table 2. The forest plot for theileriosis prevalence studies from different states in India is depicted in Fig. 3. The pooled estimates for theileriosis prevalence was 20% [95% level, CI 16–25%, PI 2–74%] in India and no studies with meta-analysis are available for comparison. However, a lower theileriosis prevalence of 14% was reported in cattle from Iran based on a meta-analysis (Soosaraei *et al*. 2018). The prevalence of theileriosis was higher when compared to other tick-borne diseases namely, anaplasmosis [11%] prevalence by meta-analysis (Krishnamoorthy *et al*. 2019a) and lower in comparison to Babesiosis [29%] in the World by meta-analysis (Jacob *et al*. 2020). The theileriosis prevalence was high during 2011–19 [22%] and showed an increasing trend in recent years. This may perhaps due to the advancement in molecular diagnostic approaches being used for theileriosis diagnosis in India. The zone-wise and state-wise theileriosis prevalence in India are presented in Table 2 and Fig. 4. The zone-wise analysis revealed an increased prevalence of theileriosis in the Central zone [24%] from less number of studies, which concurred with previous studies (Waskel and Gaur 2015, Naik *et al*. 2016, Dadhich *et al*. 2017) and less in the East zone [15%]. This may be due to the differences in agroclimatic factors, dairy animal rearing systems, management practices, cattle, and buffalo breeds in that particular geographical area. The highest prevalence of theileriosis was observed in Puducherry [71%], followed by Assam [49%], Haryana [39%], Kerala [39%], and lowest in Telangana [2%], West Bengal [7%], and Andhra Pradesh [8%] was observed. The host species-wise analysis indicated a higher theileriosis prevalence of 22% in cattle when compared to buffaloes [14%]. This may probably be due to the more number of studies reported from cattle than buffaloes and also cattle are the main host for theileriosis as reported (Anwar 2018). Further, the buffaloes might act as a reservoir for the theileriosis, less presence of tick vectors, resistance to diseases, or healthier buffaloes in comparison to cattle (Anwar 2018). Based on the method of detection of theileriosis, it was observed that the prevalence was high in serology [39%], followed by molecular methods [27%] and blood smear examination method [14%]. It might be due to the presence of antibodies for more time duration in the host when compared to the parasite antigens. It also suggested that more cattle and buffaloes are being infected and having antibodies against theileriosis for a longer duration. Furthermore, theileriosis may be present in the carrier animals with low parasitemia and be unable to detect by molecular methods but with circulating antibodies, it can be detected by serology. This could also be expected to be subclinical theileriosis infection in cattle and buffaloes as narrated earlier (Soundarajan *et al*. 2000). The drugs used for therapeutic purposes against theileriosis may also result in the removal of parasites from the blood, but with the presence of circulating antibodies, it may be detected by serological methods. Further, the serological tests are suitable for large-scale epidemiological studies on theileriosis in endemic regions (Jamadade 2017) and also the seroconversion against theileriosis was independent of the breed of the cattle as mentioned (Ram *et al*. 2006). Based on antigen detection methods, the theileriosis prevalence was high in molecular methods compared to the blood smear examination method. The results from the present study concurred with previous studies (Edith *et al*. 2018, Farooq *et al*. 2019) since PCR is a more sensitive method. The piroplasms show multiple structural forms that culminate in false-negative theileriosis diagnosis by blood smear examination in most cases. To overcome this limitation of blood smear examination and to study the presence of the parasite in a large cattle population, PCR-based molecular diagnosis may be adopted (Devadevi *et al*. 2018). Furthermore, a report assessed three diagnostic methods such as blood smear examination, PCR, and indirect fluorescent antibody test and endorsed that PCR test was able to detect low-grade infections in carrier animals with high sensitivity (Durrani *et al*. 2010). The *Theileria* species-wise analysis indicated a high prevalence of *T. annulata* [21%] followed by *T.* species [17%], *T. orientalis* [16%]. In India, *Theileria annulata* causing bovine tropical theileriosis showed high prevalence compared to *Theileria orientalis*, which causes Oriental theileriosis. *T. annulata* is the important species causing theileriosis in India, which is a highly pathogenic and fatal disease in cattle and buffaloes, also mainly transmitted by tick vector (*Hyalomma anatolicum anatolicum*). The oriental theileriosis was first reported in India during 2003 in Karnataka (Ramesh *et al*. 2003) and afterward studies on *T. orientalis* were reported from Assam, Kerala, Maharashtra, Mizoram, Odisha, Tamil Nadu, and Telangana (Anupama *et al*. 2015, George *et al*. 2015, Vinodkumar *et al*. 2016, Kolte *et al*. 2017, Sahoo *et al*. 2017, Ghosh *et al*. 2018, Brahma *et al*. 2018). This might be due to the spread of the *T. orientalis* infection through the transportation of infected animals and tick vectors from other countries to India. The Cochran Q statistics showed a highly significant [$P<0.01$] difference between the studies based on year-wise, zone-wise, state-wise, host species-wise, method-wise, and *Theileria* species-wise except for the Mizoram, Odisha, and Telangana states which showed no significant difference and were having two studies each. Further, there was high heterogeneity between these studies that was observed for theileriosis prevalence estimates and could be due to innumerable factors comprising age, breed, sex, parity of cattle, genetic characteristics, weather conditions, and managemental practices in that particular geographical areas.

Theileriosis control and prevention is mainly by targeting tick control, using chemotherapeutic agents, vaccination, and introducing tick resistant cattle breeds. Even though

Table 2. Theileriosis prevalence estimates in India for various parameters based on meta-analysis

No.	Parameter	Period	Number of studies	Total	Prevalence (%) [CI at 95% level]	PI (%) at 95% level	Tests for heterogeneity				
							I^2 value (%)	Tau square value	H value	Degrees of freedom	Cochran Q statistics
1	India	1984–2019	80	70,688	20 [16–25]	Feb-74	99.4	1.473	13.26	79	9095.60**
2a.	India period-I	1984–2000	13	24,326	15 [8–25]	Jan-75	99.6	1.571	15.68	12	1809.00**
2b.	India period-II	2000–2010	8	1,803	20 [9–38]	Jan-86	98.0	1.535	7.16	7	500.60**
2c.	India period-III	2011–2019	59	44,559	22 [17–27]	Feb-75	99.4	1.401	12.61	58	4872.90**
3	North Zone	1989–2019	21	23,396	20 [14–29]	Feb-73	99.4	1.236	13.34	20	2024.70**
3a.	Haryana	2006–2019	5	14,859	39 [29–50]	Oct-79	98.8	0.259	9.17	4	284.60**
3b.	Himachal Pradesh	1997 and 1999	2	397	10 [2–42]	–	94.4	1.661	4.24	1	57.60**
3c.	Jammu and Kashmir	1989–2019	4	2,821	9 [4–19]	0–88	97.4	0.807	6.15	3	151.10**
3d.	Punjab	2005–2015	4	2,701	18 [11–28]	Feb-76	95.9	0.298	4.92	3	129.10**
3e.	Uttarakhand	2014–2018	3	1,314	23 [10–43]	0–100	97.8	0.673	6.79	2	137.80**
3f.	Uttar Pradesh	1994 and 2017	3	1,304	24 [6–61]	0–100	99.1	1.939	10.46	2	339.20**
4	East Zone	1988–2018	9	11,331	15 [7–28]	Jan-77	99.2	1.420	11.28	8	1986.00**
4a.	Assam	2018	1	563	49	–	–	–	–	–	–
4b.	Bihar	1988 and 2018	2	1,862	13 [3–41]	–	98.8	1.179	9.18	1	237.10**
4c.	Mizoram	2014 and 2018	2	1,208	11 [9–13]	–	0	0	1.00	1	0.16^{NS}
4d.	Odisha	2011 and 2017	2	920	31 [28–34]	–	0	0	1.00	1	1.96^{NS}
4e.	West Bengal	1992 and 2017	2	6,778	7 [1–34]	–	99.3	2.033	12.16	1	222.40**
5	West Zone	1991–2019	18	12,307	20 [12–32]	Jan-82	99.2	1.815	11.43	17	1274.40**
5a.	Gujarat	1991–2019	7	6,378	22 [9–45]	Jan-93	98.3	2.032	7.67	6	269.50**
5b.	Maharashtra	2015–2017	5	4,722	20 [7–45]	0–96	99.4	1.744	12.60	4	416.20**
5c.	Rajasthan	2006–2018	6	1,207	18 [7–38]	0–91	97.2	1.606	5.93	5	443.50**
6	South Zone	1984–2019	27	22,702	22 [15–31]	Feb-80	99.4	1.598	13.27	26	2304.90**
6a.	Andhra Pradesh	2015	1	341	8	–	–	–	–	–	–
6b.	Karnataka	1994–2019	6	7,152	26 [18–35]	Jul-62	97.5	0.268	6.33	5	299.50**
6c.	Kerala	2011 and 2017	5	2,490	39 [30–48]	13–73	93.8	0.164	4.00	4	50.90**
6d.	Puducherry	2018	1	110	71	–	–	–	–	–	–
6e.	Tamil Nadu	1984–2019	12	10,824	20 [11–33]	Jan–81	99.3	1.536	11.91	11	766.80**
6f.	Telangana	2015 and 2018	2	1,785	2 [2–3]	–	0	0	1	1	0.11^{NS}
7.	Central Zone	1986–2017	5	952	24 [15–35]	Apr-72	91.4	0.355	3.41	4	50.80**
7a.	Chhattisgarh	2016	1	150	23	–	–	–	–	–	–
7b.	Madhya Pradesh	1986–2017	4	802	24 [14–38]	Jan-89	93.2	0.455	3.84	3	50.70**
8a.	Cattle	1984–2019	76	66,578	22 [17–27]	Feb-76	99.4	1.443	13.15	75	8212.70**
8b.	Buffaloes	1994–2019	20	4,059	14 [8–23]	Jan-77	97.1	1.943	5.89	19	961.40**
9a.	Blood smear examination	1984–2019	64	64,406	14 [11–18]	Feb-64	99.4	1.355	13.08	63	7550.70**
9b.	Molecular methods	2010–2019	27	9,695	27 [19–36]	Mar-80	98.4	1.267	7.84	26	1518.80**
9c.	Serology	1984–2017	8	2,629	39 [23–59]	Mar-93	98.8	1.299	8.97	7	577.70**
10a.	*Theileria annulata*	1984–2019	43	42,499	21 [16–27]	Mar-73	99.4	1.254	13.21	42	3397.90**
10b.	*Theileria orientalis*	2003–2018	10	3,499	16 [8–31]	Jan-81	98.3	1.625	7.70	9	694.90**
10c.	*Theileria* species	1989–2018	38	26,852	17 [12–24]	Feb-72	99.2	1.522	10.86	37	4841.40**

Note: CI, Confidence interval; PI, Prediction interval; NS, Not significant; *, Significant (P<0.05); **, Highly significant (P<0.01).

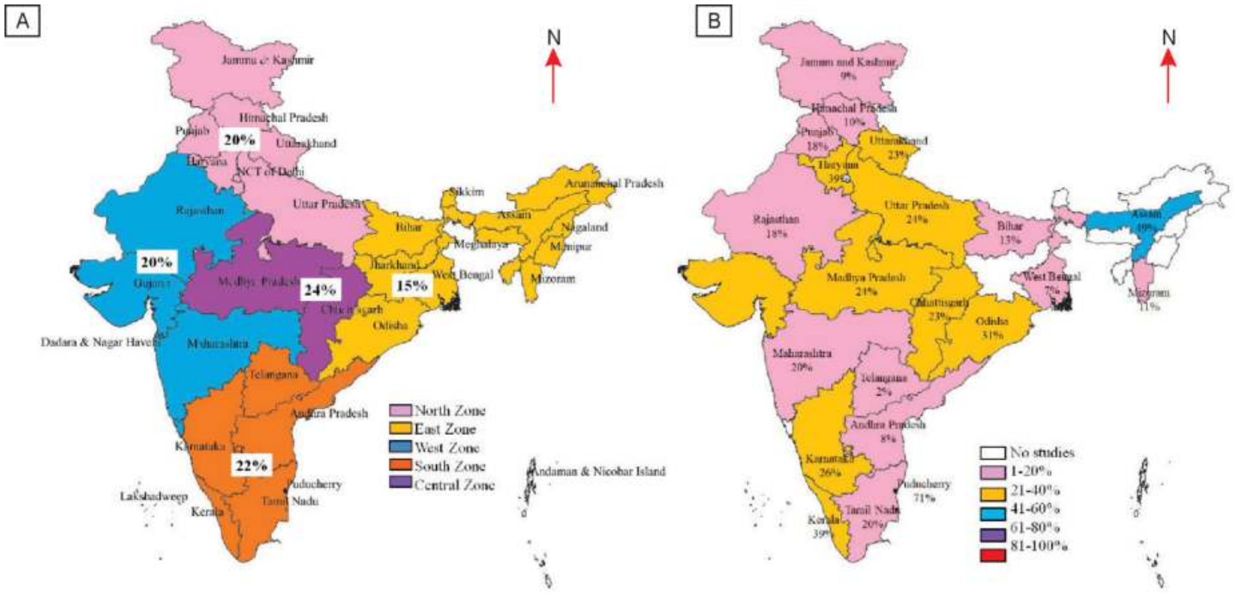

Fig. 4. India map showing the zone-wise (A) and statewise (B) prevalence estimates of theileriosis based on meta-analysis.

chemotherapeutic agents such as buparvaquone was available as a treatment option, drug resistance was a major problem faced in the field conditions. As an alternate method, a state of premunity can be created by chemo immunization, by using pre-fed ticks and sporozoites vaccine and simultaneous tetracycline or buparvaquone treatments. An inapparent or mild reaction usually occurs in theileriosis and the host immune response controls the infection in due course of time. The cattle that recover from theileriosis infection become carriers usually as reported (OIE 2014). Farm management as a means to control the theileriosis involves a restriction of livestock movement and implementation of quarantine measures to keep the area tick-free, susceptible cattle away from the tick-infested or infected animals. The managemental practices followed should ensure that the target population is entirely free of the disease or there is endemic stability (Bakor 2008). The cattle and buffaloes can be protected from theileriosis infection by preventing transmission through infected needles or surgical instruments and also by the use of insecticide sprays and dips to control the tick population in the places where the dairy animals are kept.

The theileriosis prevalence estimates obtained in the present study may be considered with few limitations, as it does not provide the estimate for the association of the disease with various risk factors and also as reported earlier (Walker *et al*. 2008). Most of the prevalence studies included for meta-analysis mentioned the prevalence of theileriosis. Further, there may be many other factors that may lead to variations between the studies are breed, age, parity of the animal, lactation number, milk yield, managemental practices, climatic conditions, geographical area, and period of study (Krishnamoorthy *et al*. 2019a, b), which can also affect the prevalence of theileriosis in India. In the present study, the prevalence estimates identified various zones, states in India, and countries in the World as high-risk areas, which need to be concentrated for taking control and preventive measures to overcome the occurrence of theileriosis in the future. Thus, theileriosis prevalence data generated will help the livestock farmers to alter the farming practices, and for the policy and decision-makers to maneuver the prevention and control measures for theileriosis in India and the World. The resources which are usually scarce may be allocated for the implementation of effective control and preventive measures for theileriosis to those areas only where the disease is highly prevalent. The elements which act as an important role in theileriosis occurrence and transmission are the existence of vectors, availability of carrier, and susceptible animals in the farms. To reduce the vector population in the potential transmission of theileriosis is by controlling the ticks by using insecticide sprays and dips for animals. Despite *T. parva* and *T. annulata* having varying affinity to cells, the similarity was observed in the causation of disease and immunology of these two *T.* species. Live vaccines are available for theileriosis during the past four decades, but although they provide durable immunity, practical problems have restricted their use at the ground level. There are efforts to develop alternative vaccines by using parasite antigens with a focus on the sporozoite and intracellular schizont stages of the *Theileria* parasites. Experimental vaccination studies using viral vectors expressing *T. parva* schizont and *T. parva*, *T. annulata* sporozoites as a source of antigens along with suitable adjuvants have established immunity against challenge with infection in a section of vaccinated animals as discussed earlier (Nene and Morrison 2016). Regardless of the absolute efficacy of theileriosis vaccines by using live parasites, they have been used on a limited scale only, owing to lack of groundwork for vaccine manufacturing and supply, the market for the vaccines, as well as apprehensions of the introduction of vaccine strains of the parasite into the ticks in the new area. Even though subunit vaccines targeting sporozoite, schizont, and merozoite stages of the parasite have been tried, the protection levels achieved have not been sufficient to allow exploitation for vaccination. Further research in these areas is needed to fully discover the possibility of the target antigens for vaccine development with superior immunity. At present in India, the theileriosis vaccine has been discontinued due to a lot of practical problems in the field situation and less usage of vaccines by the farmers, who are already having resource constraints.

In the present study, the pooled prevalence estimates for theileriosis in cattle and buffaloes in India by employing meta-analysis for the first time to the best of our knowledge was done. The theileriosis prevalence estimates obtained helped in identifying the high-risk states and zones in India. This implied the necessity for scientific management methods to be adopted in dairy farms to minimize the prevalence of theileriosis in cattle and buffaloes in India. The present study provides information on the theileriosis prevalence studies in one place for easy access and further studies. The molecular methods are widely used nowadays because of their high sensitivity in detecting pathogens in the clinical samples than the conventional microscopic examination of blood smears. The antibody detection methods and molecular methods are highly sensitive for detection of theileriosis prevalence when compared to other methods and may be employed in future studies also. The serological diagnostic method, i.e. ELISA is required for population screening in cattle and buffaloes for theileriosis in endemic areas in India, to know the status of these diseases. The theileriosis prevalence in dairy cattle and buffaloes may result in low milk production over time and can trigger economic loss to dairy farmers. There is a need for scientific management practices of dairy farms, population screening tests, early diagnostics, and timely therapeutic interventions by field veterinarians, to control and prevent the occurrence of theileriosis in India, and thus improving the productivity of dairy animals and economic growth of the livestock farmers. Furthermore, to determine the theileriosis prevalence estimates across the zones in India, there is a need for more studies on theileriosis prevalence from the Central zone and North Eastern states in India for enhanced understanding. Thus, the prevalence estimates will help the policymakers, various stakeholders to develop cognisant judgement on theileriosis prevention and control strategies and also efficiently use the available limited resources in India.

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