Bovine babesiosis: An insight into the global perspective on the disease distribution by systematic review and meta-analysis

Siju Susan Jacob[a],*, Pinaki Prasad Sengupta[a], Krishnamoorthy Paramanandham[a], Kuralayanapalya Puttahonnappa Suresh[a], Jayantha Kumar Chamuah[b], Gudepalya Renukaiah Rudramurthy[a], Parimal Roy[a]

[a] ICAR- National Institute of Veterinary Epidemiology and Disease Informatics, Yelahanka, Bengaluru, Karnataka, 560064, India
[b] ICAR-National Research Centre on Mithun, Medziphema-797 106, Nagaland, India

ARTICLE INFO

ABSTRACT

Bovine babesiosis is continuing as a great threat to the livestock sector causing havoc production losses with significant morbidity and mortality. Being a tick-borne disease, the great complexity in the agent-host- vector relationship has severely hampered the sincere efforts towards the development of an effective vaccine against bovine babesiosis. In these circumstances, assessing the global scenario of disease prevalence is a prerequisite to strategize the available control measures. Keeping this in view, the objective of this study was to estimate the pooled prevalence of bovine babesiosis globally. The literature search was conducted to identify all relevant published articles reporting the prevalence of bovine babesiosis and a total of 163 studies were found eligible for final systematic review and meta-analysis. Meta-analysis was conducted using meta package of R software and summary estimates of the prevalence were calculated. Meta analysis of 81099 samples from 62 countires representing six continents revealed global pooled prevalence of bovine babesiosis as 29% (95% CI = 24%–34%) with estimated prevalence of active infection as 16% (95% CI = 13%–20%) and seroprevalence as 50% (95% CI = 45%–56%) using random effects model. Continent wise highest prevalence of bovine babesiosis in South America 64% (95% CI = 49%–77%) and lowest in Asia 19% (95% CI = 14%–25%). Highest prevalence was estimated with *B. bigemina* 22% (95% CI = 18%–27%) and least prevalence was recorded with *B. divergens* 12% (95% CI = 2%–46%). The pooled prevalence estimates generated in the study is revealing an increase in disease trend and the need for immediate planning of mitigation strategies paralleled with the development of early diagnostic methods to reduce the impact of disease throughout the world.

1. Introduction

Thenceforward the discovery of piroplasm in cattle blood in Romania (Babes, 1888), different species of *Babesia* are continue to emerge across the world with the enduring public health impact of babesiosis and considerable economic burden to the livestock sector in temperate to tropical countries. Bovine babesiosis, a tick-borne parasitic disease caused by intra-erythrocytic apicomplexan haemoprotozoan of the genus *Babesia* (Uilenberg, 1995), is imposing a significant burden on the global livestock sector with underestimated economic losses. In essence, bovine babesiosis is recognized as the second most common haemoprotozoan parasitic disease with wide geographic distribution of tick vectors augmented by focused change in the niche of ticks (Telford et al., 1993; Homer et al., 2000; Hunfeld et al., 2008).

Globally, bovine babesiosis (tick fever, cattle fever, Texas fever, red water disease, piroplasmosis) is caused by six species of the parasites; ie. *B. bigemina, B.bovis, B.divergens B.major, B. occultans* and *B. argentina*; *B.bigemina* (African red water) being the widely prevalent and *B.bovis* (Asiatic red water) being the highly pathogenic species (Ibrahim et al., 2013; Elsify et al., 2015). *B. bovis* and *B. bigemina* are distributed in Asia, Africa, Australia, Central and South America and Southern Europe (Criado-Fornelio et al., 2003; Altay et al., 2008; Silva et al., 2009), the important tick vector being *Rhipicephalus* (formerly *Boophilus*) *annulatus* and *Rh.* (*Bo.*) *microplus*, whereas *Rh.* (*Bo.*) *decoloratus* transmits only *B. bigemina* (Taylor et al., 2007). *B.divergens* is prevalent in central and northern Europe, Ireland, Great Britain and northern Africa (L'Hostis & Chauvin, 1999; Zintl et al., 2003; Edelhofer et al., 2004) with *Ixodus ricinus* (M' Fadyean & Stockman, 1911) as the vector with zoonotic

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* Corresponding author at: ICAR-National Institute of Veterinary Epidemiology and Disease Informatics (ICAR-NIVEDI), Ramagondanahalli, Yelahanka, Bengaluru, 560064, Karnataka, India.
E-mail address: drsiju291@gmail.com (S.S. Jacob).

	Literature search through PubMed, Science Direct, BioMed Central, Google Scholar and Scopus
Identification	

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	A total of 210 articles pertaining to prevalence of bovine babesiosis were selected for initial scrutiny!

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	38 articles were excluded after reading the abstracts (Exclusion criteria: reviews, case studies, outbreak investigation, non-availability of full-text articles) and further 9 after reading the full article (Exclusion criteria: Non-mentioning of sample size and selection of non-confirmatory diagnostic approaches)!
Screening and eligibility	

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	A total of 163 articles were reviewed full and were included in the final quantitative synthesis
Inclusion for meta-analysis	

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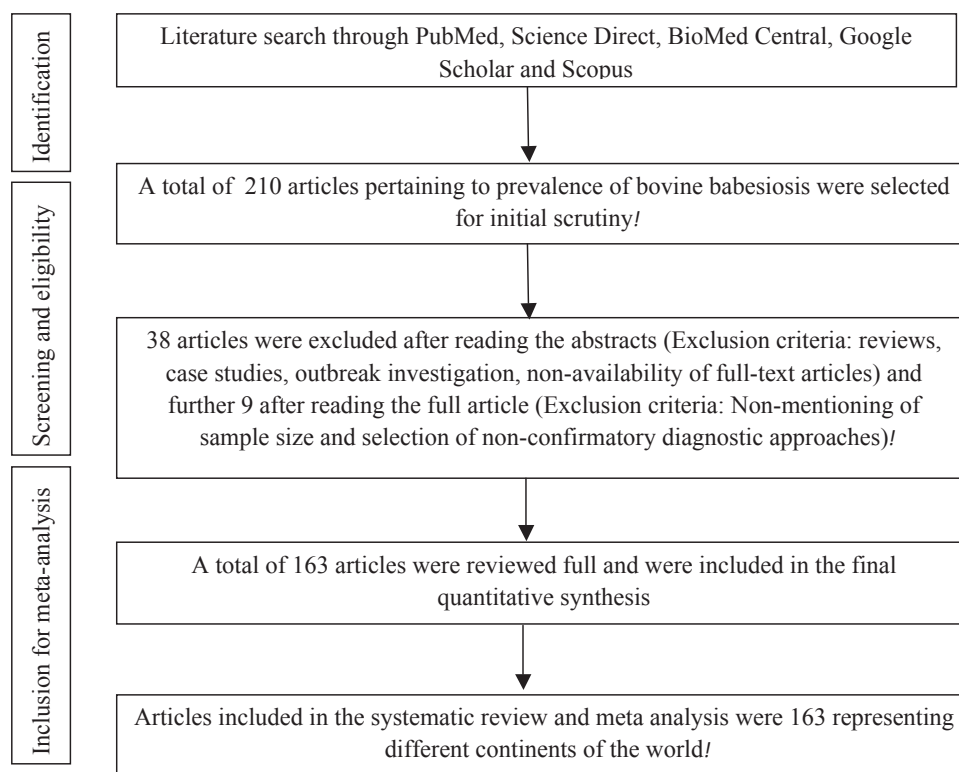|	Articles included in the systematic review and meta analysis were 163 representing different continents of the world!

Fig. 1. Schematic diagram representing the literature search with exclusion/inclusion process for meta-analysis.

importance (Fitzpatrick et al., 1968). *Babesia major* is reported from European countries (L'Hostis & Seegers, 2002; Zintl et al., 2003; Garcia-Sanmartin et al., 2006) and is less documented due to its low pathogenicity with the vector *Haemaphysalis punctata*. The disease is manifested by haemolytic anemia and fever, with occasional hemoglobinuria and death. Besides, acute infection with *B. bovis* may result in respiratory and neurological symptoms via sequestration of infected RBCs in the capillary beds (Everitt et al., 1986). Delayed treatment of bovine babesiosis often renders in poor prognosis.

Historically in the year 1888, Victor Babes investigated disease outbreaks in cattle with hemoglobinuria in Romania and was the first to detect piroplasm in the blood of cattle. After 5 years, elegant studies by Smith and Kilborne (1893) revealed that *B. bigemina* transmitted by *R. annulatus* is responsible for bovine babesiosis in susceptible cattle. M'Fadyean & Stockman M'Fadyean & Stockman (1911) first described *B. divergens* in the cattle blood who named it as *Piroplasma divergens*. The zoonotic potential of *Babesia* is noteworthy with the first confirmed case of human babesiosis was reported in 1956 with *B. divergens* as the causative organism (Skrabalo and Deanovic, 1957).

The journey towards the development of an effective vaccine against bovine babesiosis is obstacled by the ever-increasing complexity of the agent-vector-host-environment association accelerated by global climate change. Control of bovine babesiosis by adopting tick control measures is challenged by the concerns regarding the rapid emergence of acaricidal resistance and the threat of acaricide residues in the food chain. This dreadful situation demands a thorough understanding of the disease status in different geographical areas that will help to allocate the available resources to high-risk areas thereby the emergence of acaricide resistance that might have occurred due to extensive and indiscriminate application of acaricides can be slow down. Keeping in view of this, in the present study efforts are being taken to estimate the status of the disease in different countries in terms of pooled prevalence by systematic review coupled with meta-analysis.

2. Materials and Methods

2.1. Data sources and search strategy

The Prisma protocol (PRISMA, http://www.prisma-statement.org) was followed in conducting the study (Supplemenary file 1). The literature search was conducted to identify all published studies reporting the prevalence of bovine babesiosis across the globe using comprehensive combinations of keywords. The literature search was performed using the electronic databases including PubMed, Science Direct, BioMed Central, Google Scholar and Scopus. Further, reviews and the reference lists from the retrieved articles were manually searched to identify additional pertinent studies. The literature search was independently conducted by two experienced researchers. Those studies reporting the prevalence of bovine babesiosis were included for the final systematic review and meta-analysis. The literature pertaining to the bovine babesiosis was restricted to 1967 to 2019 based on the literature availability and the retrieval language was limited to English.

2.2. Eligibility criteria

The studies were restricted to cross-sectional and longitudinal studies in cattle and buffalo about the prevalence of bovine babesiosis across the world. The collected literatures were checked rigorously for duplicates and were removed. The inclusion criteria for consideration of meta-analysis for each study was those mentioning a) the number of animals screened b) the number of animals infected (either organism or antibodies) c) the use of standard methods like blood smear examination and molecular methods to detect the organism and/or serological techniques like ELISA, IFAT and capillary tube agglutination test for detection of antibodies and d) the year of study. The literature mentioning outbreak investigations, case reports, reviews and clinical trials were excluded from the study.
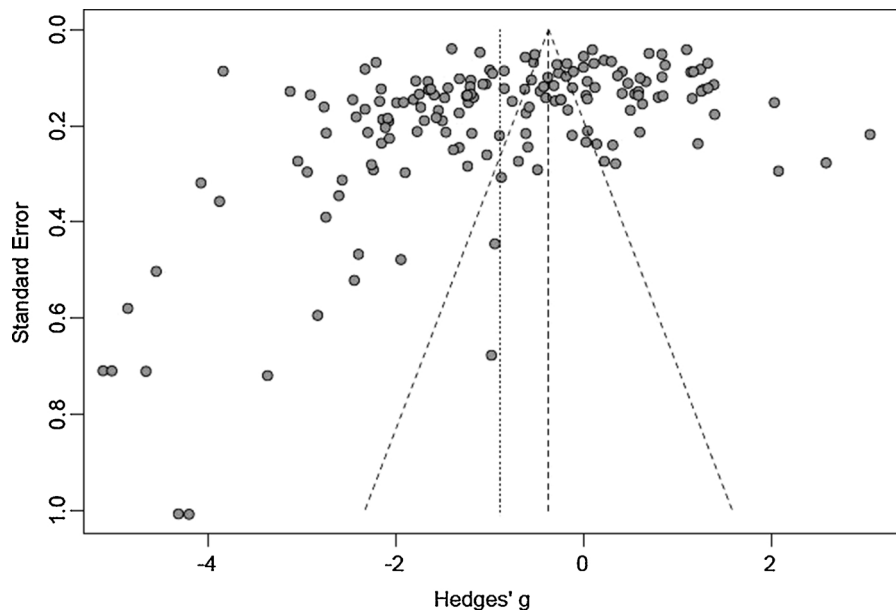
Fig. 2. Forest plot showing the details of the studies with the prevalence estimates.

Study	Events	Total	Weight (fixed)	Weight (random)	IV, Fixed + Random, 95% CI
Abdela et al., 2017, Ethiopia	49	408	0.3%	0.6%	0.12 [0.09; 0.16]
Abdullahi et al., 2014, Nigeria	4	50	0.0%	0.6%	0.08 [0.02; 0.19]
AbouLaila et al., 2010, Japan	51	145	0.3%	0.6%	0.35 [0.27; 0.44]
Acici et al., 2016, Turkey	99	256	0.5%	0.6%	0.39 [0.33; 0.45]
Agoulon et al., 2012, France	102	711	0.7%	0.6%	0.14 [0.12; 0.17]
Ajayi and Dipeolu, 1986, Nigeria	217	500	1.0%	0.6%	0.43 [0.39; 0.48]
Akinboade and Dipeolu, 1984, Nigeria	186	200	0.1%	0.6%	0.93 [0.89; 0.96]
Aktas and Ozubek, 2015, Turkey	13	100	0.1%	0.6%	0.13 [0.07; 0.21]
Al-Hosary, 2016, Egypt	20	76	0.1%	0.6%	0.26 [0.17; 0.38]
Alim et al., 2011, Bangladesh	51	648	0.4%	0.6%	0.08 [0.06; 0.10]
AlKhalifa et al., 2009, Saudi Arabia	7	116	0.1%	0.6%	0.06 [0.02; 0.12]
Almeria et al., 2001, Spain	9	131	0.1%	0.6%	0.07 [0.03; 0.13]
Andersson et al., 2017, Sweden	38	71	0.1%	0.6%	0.54 [0.41; 0.65]
Applewhaite et al., 1981, Guyana	382	477	0.6%	0.6%	0.80 [0.76; 0.84]
Atlay et al., 2008, Turkey	3	389	0.0%	0.6%	0.01 [0.00; 0.02]
Awad et al., 2011, Sudan	41	692	0.3%	0.6%	0.06 [0.04; 0.08]
Ayaz et al., 2013, Pakistan	237	2400	1.7%	0.6%	0.10 [0.09; 0.11]
Aziz et al., 2014, Egypt	117	296	0.6%	0.6%	0.40 [0.34; 0.45]
Banerjee et al., 1983, Bangladesh	26	179	0.2%	0.6%	0.15 [0.10; 0.21]
Barros et al., 2005, Brazil	659	848	1.2%	0.6%	0.78 [0.75; 0.80]
Bawm et al., 2016, Myanmar	192	713	1.1%	0.6%	0.27 [0.24; 0.30]
Bhutto et al., 2012, Pakistan	21	100	0.1%	0.6%	0.21 [0.13; 0.30]
Brito et al., 2013, Brazil	467	489	0.2%	0.6%	0.96 [0.93; 0.97]
Buling et al., 2007, Spain	5	40	0.0%	0.6%	0.12 [0.04; 0.27]
Byaruhanga et al., 2016, Uganda	12	240	0.1%	0.6%	0.05 [0.03; 0.09]
Camus and Montenegro, 1994, Antigua	26	73	0.1%	0.6%	0.36 [0.25; 0.48]
Camus and Montenegro, 1994, Barbados	15	51	0.1%	0.6%	0.29 [0.17; 0.44]
Camus and Montenegro, 1994, Dominica	39	83	0.2%	0.6%	0.47 [0.36; 0.58]
Camus and Montenegro, 1994, Grenada	20	60	0.1%	0.6%	0.33 [0.22; 0.47]
Camus and Montenegro, 1994, Guadeloupe	41	71	0.1%	0.6%	0.58 [0.45; 0.69]
Camus and Montenegro, 1994, Martinique	162	235	0.4%	0.6%	0.69 [0.63; 0.75]
Camus and Montenegro, 1994, Montserrat	3	11	0.0%	0.6%	0.27 [0.06; 0.61]
Camus and Montenegro, 1994, Saint Kitts and Nevis	19	50	0.1%	0.6%	0.38 [0.25; 0.53]
Camus and Montenegro, 1994, Saint Lucia	7	25	0.1%	0.6%	0.28 [0.12; 0.49]
Camus and Montenegro, 1994, Saint Vincent	31	53	0.1%	0.6%	0.58 [0.44; 0.72]
Cao et al., 2012, Thailand	42	200	0.3%	0.6%	0.21 [0.16; 0.27]
Carrique Mas et al., 2000, Bolivia	251	380	0.7%	0.6%	0.66 [0.61; 0.71]
Cassini et al., 2012, Italy	193	425	0.8%	0.6%	0.45 [0.41; 0.50]
Cesi et al., 2014, Italy	63	1500	0.5%	0.6%	0.04 [0.03; 0.05]
Chaudhry et al., 2010, Pakistan	29	100	0.2%	0.6%	0.29 [0.20; 0.39]
Chowdhury et al., 2006, Bangladesh	2	60	0.0%	0.5%	0.03 [0.00; 0.12]
Choramo and Ibrahim, 2017, Ethiopia	50	390	0.3%	0.6%	0.13 [0.10; 0.17]
Corrier et al., 1978, Colombia	2277	3035	4.5%	0.6%	0.75 [0.73; 0.77]
Criado-Fornelio et al., 2009, France	1	68	0.0%	0.5%	0.01 [0.00; 0.08]
Cringoli et al., 2002, Italy	117	506	0.7%	0.6%	0.23 [0.20; 0.27]
da Silva et al., 2013, Brazil	326	542	1.0%	0.6%	0.60 [0.56; 0.64]
Dreyer et al., 1998, South Africa	94	151	0.3%	0.6%	0.62 [0.54; 0.70]
Durrani and Kamal, 2008, Pakistan	20	100	0.1%	0.6%	0.20 [0.13; 0.29]
Duzlu et al., 2015, Turkey	45	300	0.3%	0.6%	0.15 [0.11; 0.20]
Ellefy et al., 2014, Egypt	50	489	0.4%	0.6%	0.10 [0.08; 0.13]
Eygelaar et al., 2015, Botswana	28	120	0.2%	0.6%	0.23 [0.16; 0.32]
Fakhar et al., 2012, Iran	136	6469	1.0%	0.6%	0.02 [0.02; 0.02]
Farhan et al., 2017, Egypt	127	301	0.6%	0.6%	0.42 [0.37; 0.48]
Gachohi et al., 2010, Kenya	84	440	0.5%	0.6%	0.19 [0.16; 0.23]
Garcia-Sanmartin et al., 2006, Spain	24	263	0.2%	0.6%	0.09 [0.06; 0.13]
Georges et al., 2001, Italy	34	187	0.2%	0.6%	0.18 [0.13; 0.24]
Gonzalez et al., 2018, Colombia	162	202	0.3%	0.6%	0.80 [0.74; 0.85]
Guswanto et al., 2017, Indonesia	340	487	0.8%	0.6%	0.70 [0.66; 0.74]
Guswanto et al., 2017, Indonesia	550	991	1.9%	0.6%	0.55 [0.52; 0.59]
Guven et al., 2012, Turkey	100	287	0.5%	0.6%	0.35 [0.29; 0.41]
Hadani et al., 1983, Argentina	108	213	0.4%	0.6%	0.51 [0.44; 0.58]
Hamsho et al., 2015, Ethiopia	65	384	0.4%	0.6%	0.17 [0.13; 0.21]
Hashemitrasadi et al., 2018, Iran	341	921	1.7%	0.6%	0.37 [0.34; 0.40]
He et al., 2012, China	32	304	0.2%	0.6%	0.11 [0.07; 0.15]
Herrera et al., 2017, Philippines	33	213	0.2%	0.6%	0.15 [0.11; 0.21]
Hilemariam et al., 2017, Ethiopia	55	392	0.4%	0.6%	0.14 [0.11; 0.18]
Hostis and Chavin, 1999, France	142	236	0.4%	0.6%	0.60 [0.54; 0.66]
Hugh-Jones et al., 1988, Saint Lucia	175	250	0.4%	0.6%	0.70 [0.64; 0.76]
Hussain et al., 2017, Pakistan	5	60	0.0%	0.6%	0.08 [0.03; 0.18]
Ibrahim et al., 2013, Egypt	56	247	0.3%	0.6%	0.23 [0.18; 0.28]
Isa et al., 2007, Turkey	2	337	0.0%	0.5%	0.01 [0.00; 0.02]
Iseki et al., 2010, Thailand	531	700	1.0%	0.6%	0.76 [0.73; 0.79]
Jaimes-Duenez et al., 2018, Colombia	591	1584	2.9%	0.6%	0.37 [0.35; 0.40]
James et al., 1985, Venezuela	294	376	0.5%	0.6%	0.78 [0.74; 0.82]
Jirapattharasate et al., 2016, Thailand	66	279	0.4%	0.6%	0.24 [0.19; 0.29]
Jirapattharasate et al., 2016, Thailand	61	329	0.4%	0.6%	0.19 [0.14; 0.23]
Johnston, 1967, Commonwealth of Australia	639	1277	2.5%	0.6%	0.50 [0.47; 0.53]
Jongejan et al., 1988, Gambia	1245	1784	3.0%	0.6%	0.70 [0.68; 0.72]
Kalkan et al., 2010, Turkey	152	240	0.4%	0.6%	0.63 [0.57; 0.69]
Kamani et al., 2010, Nigeria	102	637	0.7%	0.6%	0.16 [0.13; 0.19]
Katsande et al., 1999, Zimbabwe	1187	2266	4.4%	0.6%	0.52 [0.50; 0.54]
Kaya et al., 2006, Turkey	2	104	0.0%	0.5%	0.01 [0.00; 0.07]
Khamesipour, 2015, Iran	11	155	0.1%	0.6%	0.07 [0.04; 0.12]
Khan et al., 2004, Pakistan	2	307	0.0%	0.5%	0.01 [0.00; 0.02]
Khattak et al., 2017, Pakistan	23	380	0.2%	0.6%	0.06 [0.04; 0.09]
Kivaria et al., 2012, Sudan	425	805	1.8%	0.6%	0.53 [0.49; 0.56]
Knowles et al., 1982, Saint Lucia	62	96	0.2%	0.6%	0.65 [0.54; 0.74]
Kubelova et al., 2012, Angola	1	76	0.0%	0.5%	0.01 [0.00; 0.07]
Kuttler et al., 1988, Gambia	120	184	0.3%	0.6%	0.65 [0.58; 0.72]
Lemma et al., 1996, Ethiopia	92	400	0.6%	0.6%	0.23 [0.19; 0.27]
L'Hotis et al., 1994, France	375	424	0.3%	0.6%	0.88 [0.85; 0.91]
Li et al., 2015, Caribbean island	274	352	0.5%	0.6%	0.78 [0.73; 0.82]
Lolli et al., 2016, Uganda	776	3935	4.9%	0.6%	0.20 [0.18; 0.21]
Lorusso et al., 2016, Nigeria	73	704	0.5%	0.6%	0.10 [0.08; 0.13]
Mahmud et al., 2015, Bangladesh	8	395	0.1%	0.6%	0.02 [0.01; 0.04]
Malak et al., 2012, Sudan	175	343	0.7%	0.6%	0.51 [0.46; 0.56]
Martins et al., 2008, Mozambique	104	117	0.1%	0.6%	0.89 [0.82; 0.94]
Marufu et al., 2010, South Africa	66	144	0.3%	0.6%	0.46 [0.38; 0.54]
Matheus et al., 2019, Namibia	143	392	0.7%	0.6%	0.36 [0.32; 0.41]
Mattioli et al., 1997, Gambia	324	648	1.3%	0.6%	0.50 [0.46; 0.54]
Mazyad and Khalaf, 2002, Egypt	13	135	0.1%	0.6%	0.10 [0.05; 0.16]
Mghirbi et al., 2008, Tunisia	31	278	0.2%	0.6%	0.11 [0.08; 0.15]
Miller et al., 1984, Mali	129	274	0.5%	0.6%	0.47 [0.41; 0.53]
Moghazy et al., 2014, Egypt	60	167	0.3%	0.6%	0.36 [0.29; 0.44]
Moumouni et al., 2015, Kenya	98	192	0.4%	0.6%	0.51 [0.44; 0.58]
Moumouni et al., 2018, Benin	66	207	0.4%	0.6%	0.32 [0.26; 0.39]
Mtshali and MtShali, 2014, South Africa	278	430	0.8%	0.6%	0.65 [0.60; 0.69]
Mtshali et al., 2014, South Africa	204	268	0.4%	0.6%	0.76 [0.71; 0.81]
Murat et al., 2010, Turkey	84	191	0.4%	0.6%	0.44 [0.37; 0.51]
Musinguzi et al., 2016, Zambia	76	472	0.5%	0.6%	0.16 [0.13; 0.20]
Nayel et al., 2012, Egypt	33	405	0.2%	0.6%	0.08 [0.06; 0.11]
Ndi et al., 1991, Cameroon	248	524	1.0%	0.6%	0.47 [0.43; 0.52]
Niu et al., 2015, China	194	646	1.1%	0.6%	0.30 [0.27; 0.34]
Ochirkhuu et al., 2015, Philippines	209	339	0.6%	0.6%	0.62 [0.56; 0.67]
Ortiz et al., 2018, Argentina	169	263	0.5%	0.6%	0.64 [0.58; 0.70]
Osaki et al., 2002, Brazil	149	232	0.4%	0.6%	0.64 [0.58; 0.70]
Ozfem and Sevinc, 2009, Turkey	331	770	1.5%	0.6%	0.43 [0.39; 0.47]
Padietta et al., 2018, Argentina	79	186	0.4%	0.6%	0.42 [0.35; 0.50]
Payne and Osorio, 1990, Paraguay	970	1228	1.8%	0.6%	0.79 [0.77; 0.81]
Rajabi et al., 2017, Iran	40	450	0.3%	0.6%	0.09 [0.06; 0.12]
Ramos et al., 1992, Mexico	531	925	1.8%	0.6%	0.57 [0.54; 0.61]
Ringo et al., 2018, Tanzania	43	245	0.3%	0.6%	0.18 [0.13; 0.23]
Rizk et al., 2017, Egypt	65	439	0.4%	0.6%	0.15 [0.12; 0.18]
Roy et al., 2018, Bangladesh	4	384	0.0%	0.6%	0.01 [0.00; 0.03]
Saad et al., 2015, Pakistan	37	73	0.1%	0.6%	0.51 [0.39; 0.63]
Sahibi et al., 1998, Morocco	78	475	0.5%	0.6%	0.16 [0.13; 0.20]
Salih et al., 2007, Sudan	10	600	0.1%	0.6%	0.02 [0.01; 0.03]
Salih et al., 2008, Sudan	46	90	0.2%	0.6%	0.51 [0.40; 0.62]
Sevgili et al., 2010, Turkey	84	191	0.4%	0.6%	0.44 [0.37; 0.51]
Sevinc et al., 2001, Turkey	147	277	0.5%	0.6%	0.53 [0.47; 0.59]
Shams et al., 2013, Pakistan	165	600	0.9%	0.6%	0.28 [0.24; 0.31]
Shebish et al., 2012, Costa Rica	265	449	0.9%	0.6%	0.59 [0.54; 0.64]
Silva et al., 2009, Portugal	321	406	0.5%	0.6%	0.79 [0.75; 0.83]
Silva et al., 2010, Portugal	57	1104	0.4%	0.6%	0.05 [0.04; 0.07]
Silva et al., 2013, Brazil	365	800	1.8%	0.6%	0.46 [0.42; 0.49]
Silveria et al., 2016, Brazil	14	308	0.1%	0.6%	0.05 [0.03; 0.08]
Simking et al., 2013, Thailand	162	1824	1.2%	0.6%	0.09 [0.08; 0.10]
Sivakumar et al., 2012, Srilanka	95	316	0.5%	0.6%	0.30 [0.25; 0.35]
Sivakumar et al., 2017, Thailand	30	54	0.1%	0.6%	0.56 [0.41; 0.69]
Sivakumar et al., 2017, Vietnam	78	101	0.1%	0.6%	0.77 [0.68; 0.85]
Smeenk et al., 2000, Zimbabwe	33	94	0.2%	0.6%	0.35 [0.26; 0.46]
Sserugga et al., 2003, Commonwealth of Australia	616	874	1.4%	0.6%	0.70 [0.67; 0.73]
Staniec et al., 2018, Poland	20	192	0.1%	0.6%	0.10 [0.06; 0.16]
Swai et al., 2007, Tanzania	465	1329	2.4%	0.6%	0.35 [0.32; 0.38]
Taha et al., 2018, Egypt	14	148	0.1%	0.6%	0.09 [0.05; 0.15]
Tayebwa et al., 2018, Uganda	36	209	0.2%	0.6%	0.17 [0.12; 0.23]
Tembo et al., 2018, Zambia	33	299	0.2%	0.6%	0.11 [0.08; 0.15]
Terkawi et al., 2011, South Africa	549	719	1.0%	0.6%	0.76 [0.73; 0.79]
Terkawi et al., 2011, Thailand	68	305	0.4%	0.6%	0.22 [0.18; 0.27]
Terkawi et al., 2012, Syria	83	207	0.4%	0.6%	0.40 [0.33; 0.47]
Tonnessen et al., 2006, South Africa	1217	1822	3.2%	0.6%	0.67 [0.65; 0.69]
Torina et al., 2007, Italy	72	311	0.4%	0.6%	0.23 [0.19; 0.28]
Weerasooriya et al., 2016, Vietnam	69	307	0.4%	0.6%	0.22 [0.18; 0.28]
Wesonga et al., 2016, Kenya	171	421	0.8%	0.6%	0.41 [0.36; 0.45]
Wodajnew et al., 2015, Ethiopia	105	402	0.6%	0.6%	0.26 [0.22; 0.31]
Yamada et al., 2009, Zambia	16	71	0.1%	0.6%	0.23 [0.13; 0.34]
Yang et al., 2015, China	589	2364	3.5%	0.6%	0.25 [0.23; 0.27]
Ybanez et al., 2013, Philippines	104	408	0.6%	0.6%	0.25 [0.21; 0.30]
Yu et al., 2013, Philippines	27	250	0.2%	0.6%	0.11 [0.07; 0.16]
Zhou et al., 2016, Turkey	22	196	0.2%	0.6%	0.11 [0.07; 0.16]
Ziam and Benaouf, 2004, Algeria	3	54	0.0%	0.5%	0.06 [0.01; 0.15]
Ziapour et al., 2011, Iran	121	575	0.8%	0.6%	0.21 [0.18; 0.25]
Zulfiqar et al., 2012, Pakistan	27	144	0.2%	0.6%	0.19 [0.13; 0.26]
Total (fixed effect, 95% CI)		81099	100.0%	—	0.41 [0.40; 0.41]
Total (random effects, 95% CI)			—	100.0%	0.29 [0.25; 0.34]
Prediction interval					[0.02; 0.88]

Heterogeneity: Tau² = 2.1474; Chi² = 16826.87, df = 162 (P = 0); I² = 99%

data from the selected literature were the year of study, study area, sample size, number of animals positive for *Babesia* species, diagnostic method used, species of *Babesia* detected, author's name, article title and year of publication. The overall prevalence estimate of bovine babesiosis for each study was determined by selecting the highest prevalence when different diagnostic methods were employed.

2.4. Meta-analysis

Meta-analysis for prevalence studies aid in generating a weighted average proportion of prevalence of various studies. This will help to obtain a more precise estimate of prevalence from multiple studies thereby providing a better direction for future work. The meta-analysis on bovine babesiosis was conducted by using R Open Source Software version 3.2.5. The R packages used for meta-analysis were Metafor and Meta. The effect model was chosen depending on the percentage of heterogeneity (I^2). Because substantial heterogeneity was expected, random effect model was used to arrive at a pooled estimate of prevalence of bovine babesiosis. The possibility of publication bias was assessed by graphical analysis funnel plot with the y-axis showing the Standard Error (SE) of each study, with larger studies (which thus have a smaller SE) plotted on top of the y-axis; and the x-axis showing the effect size (Hedges' g) of each study. In the absence of publication bias, the studies with high precision concentrates along the line of average, whereas those with low precision distribute evenly on either sides of the average line, creating generally a funnel shaped scatter (Egger et al., 1997). Deviance from this shape indicates publication bias. Further, funnel plot asymmetry was checked by the Rank correlation method, linear regression test and Egger's test. Based on the P-value of each test Null hypothesis was either accepted or rejected. The Trim-and-fill method was used to adjust for funnel plot asymmetry. To determine the percentage of variation across studies that are due to heterogeneity rather than chance, Cohran Q test (chi-square test for heterogeneity) as well as the heterogeneity I^2 (Higgins I^2) statistic was calculated. To quantify the heterogeneity, 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 H value was also calculated to summarize the impact of heterogeneity. Since H statistic that has no upper limit, it will allow tracking changes in heterogeneity with high authenticity when the number of studies is less. The Forest plot was utilized for making the graphical representation of the data. The method used for the study was inverse with the logit transformation. Restricted maximum-likelihood estimator was used to determine between study variance τ^2. The prevalence estimates for bovine babesiosis was expressed as percentage with Confidence Interval (CI) and Prediction Interval (PI) at 95% level. The Clopper-Pearson confidence interval was employed for individual studies. Subgroup analysis was conducted based on species affected, diagnostic method used, continents of the world, and animal wise for determining the heterogeneity in each group and their comparison. Besides, prevalence based on antigen/organism detection (blood smear examination and molecular techniques) termed as infection prevalence (status of active infection) and based on antibody detection (seroprevalence) was estimated for 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, 210 articles were retrieved for further appraisal. Of these, 38 were excluded after reading the abstracts and further 9 after reading the full article. This resulted in a total of 163 studies to perform a systematic review and meta-analysis. The inclusion and exclusion criteria followed for meta-analysis of the prevalence of bovine babesiosis is depicted in

2.3. Data extraction

The relevant literature were retained based on the mentioned criteria and the results from the individual studies were extracted independently to a predesigned data extraction excel sheet. The extracted

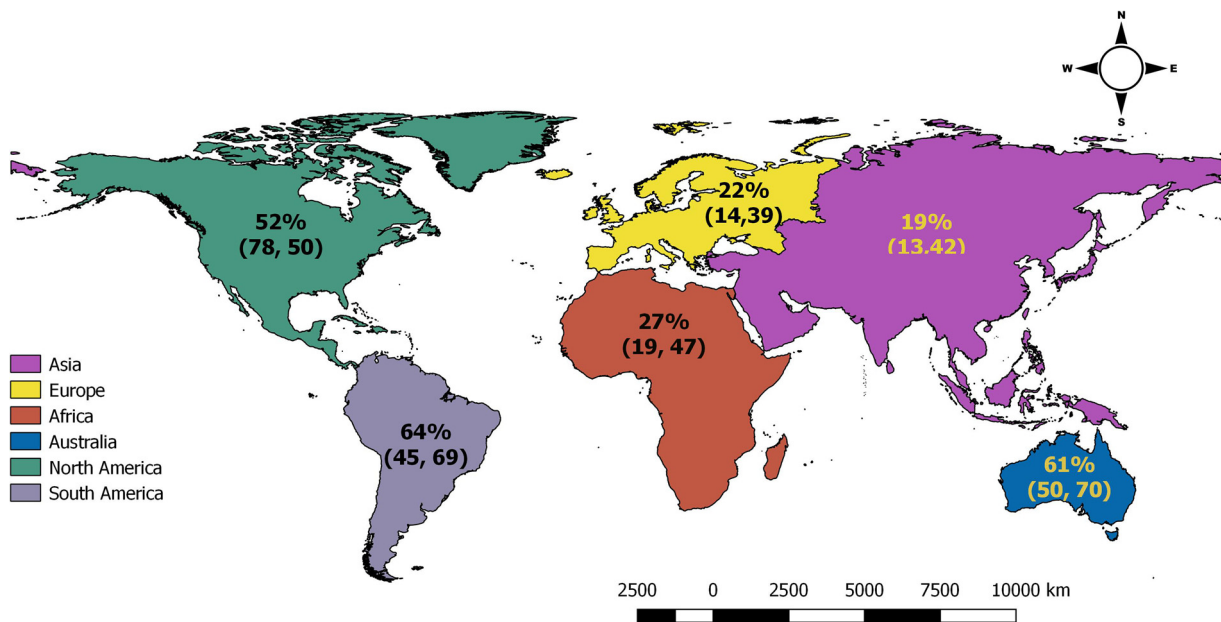**Fig. 3.** Funnel plot representing publication bias.

Fig. 4. Continent-wise prevalence estimates of bovine babesiosis in the world. The pooled prevalence estimate with status of active infection and seroprevalence are provided in the bracket for each continent.

Fig.1. The study was conducted based on the systematic review of the prevalence of bovine babesiosis from 1967 to 2019.

3.2. Meta-analysis of prevalence of bovine babesiosis

The study covered six continents (Asia, Africa, Australia, Europe, North America and South America) and 62 countries. The total number of studies included for meta-analysis was 163 with 81,099 samples for the period 1967-2019. The meta-analysis indicated that variability was high between studies ($\tau^2 = 2.1474$; heterogeneity $I^2 = 99\%$ with heterogeneity chi square = 16826.87, degree of freedom = 162, H = 10.19 with P < 0.001). Individual study prevalence estimates ranged from 1% to 96% with the overall random pooled prevalence of 29% (95% CI: 25-34%, PI: 2-88%). The random pooled infection prevalence was found to be 16% (95% CI: 13-20%, PI 10-65%) based on

114 studies whereas the seroprevalence was 50% (95% CI: 45-56%, PI: 13-87%) based on 72 studies. Studies weighted approximately equal with weights on individual studies ranging from 0.4% to 0.6%. Fig. 2 represents the forest plot derived from meta-analysis. Funnel plot asymmetry was determined by rank correlation test (z value: –3.005, P = 0.003), Linear regression test (t value: – 3.7681, P = 0) and Eggers test (Intercept = –5.549, P = 0) which indicated substantial asymmetry in the funnel plot (null hypothesis is rejected) which in turn reveals the likely presence of publication bias (Fig. 3).

3.2.1. Subgroup meta-analysis

Subgroup analyses were conducted for different periods (1967-2000, 2001-2010, 2011-2015 and 2016-2019), six continents, animals affected (cattle and buffalo), species of parasite (*B.bigemina, B.bovis, B.divergens, B.major* and *B.occultans*), diagnostic method used (blood

Table 1
Infection and sero-prevalence of bovine babesiosis.

SI. No	Authors	Prevalence							
		Country	Total	Infection	Sero-prevalence	Continent	Total	Infection	Sero prevalence
1.	Abdullah-al-Mahmud et al., 2015	Bangladesh	4%	3%	15%	Asia	19%	13%	42%
2.	Alim et al., 2011								
3.	Banerjee et al., 1983								
4.	Chawdhury et al., 2006								
5.	Roy et al., 2018								
6.	He et al., 2012	China	21%	19%	25%				
7.	Niu et al., 2015								
8.	Yang et al., 2015								
9.	Guswanto et al., 2017[a]	Indonesia	63%	70%	63%				
10.	Guswanto et al., 2017[b]								
11.	Fakhar et al., 2012	Iran	11%	11	–				
12	Hasheminasab et al., 2018								
13.	Khamesipour, 2015								
14.	Rajabi et al., 2017								
15.	Ziapour et al., 2011								
16.	AbouLaila et al., 2010	Japan	35%	35%	–				
17.	Bawm et al., 2016	Myanmar	27	27	–				
18.	Ayaz et al., 2013	Pakistan	15	15	–				
19.	Bhutto et al., 2012								
20.	Chaudhry et al., 2010								
21.	Durrani and Kamal, 2008								
22.	Hussain et al., 2017								
23.	Khan et al., 2004								
24.	Khattak et al., 2017								
25.	Saad et al., 2015								
26.	Shams et al., 2013								
27.	Zulfiqar et al., 2012								
28.	Herrera et al., 2017	Philippines	25	25	–				
29.	Ochirkhuu et al., 2015								
30.	Ybanez et al., 2013								
31.	Yu et al., 2013								
32.	Al-Khalifa et al., 2009	Saudi Arabia	6	6	–				
33.	Sivakumar et al., 2012	Sri Lanka	35	–	35				
34.	Terkawi et al., 2012	Syria	32	25	40				
35.	Cao et al., 2012	Thailand	29	18	58				
36.	Iseki et al., 2010								
37.	Jirapattharasate et al., 2016a								
38.	Jirapattharasate et al., 2016b								
39.	Simking et al., 2013								
40	Sivakumar et al., 2018								
41.	Terkawi et al., 2011								
42.	Acici et al., 2016	Turkey	17	7	33				
43.	Aktas and Ozubek, 2015								
44.	Atlay et al., 2008								
45.	Duzlu et al., 2015								
46.	Guven et al., 2012								
47.	Ica et al., 2007								
48.	Kalkan et al., 2010								
49.	Kaya et al., 2006								
50.	Murat et al., 2010								
51.	Ozlem and Sevinc, 2009								
52.	Sevgili et al., 2010								
53.	Sevinc et al., 2001								
54.	Zhou et al., 2016								
55.	Sivakumar et al., 2018	Vietnam	50	33	77				
56.	Weerasooriya et al., 2016								

Table 1 (*continued*)

SI. No	Authors	Prevalence							
		Country	Total	Infection	Sero-prevalence	Continent	Total	Infection	Sero prevalence
57.	Ziam and Benaouf, 2004	Algeria	6	6	–	Africa	27%	19%	47%
58.	Kubelova et al., 2012	Angola	1	1	–				
59.	Moumouni et al., 2018	Benin	32	32	–				
60.	Eygelaar et al., 2015	Botswana	23	23	–				
61.	Ndi et al., 1991	Cameroon	47	47	–				
62.	Al-Hosary, 2016	Egypt	19	16	29				
63.	Aziz et al., 2015								
64.	Elsify et al., 2014								
65.	Fereig et al., 2017								
66.	Ibrahim et al., 2013								
67.	Mazyad and Khalaf, 2002								
68.	Moghazy et al., 2014								
69.	Nayel et al., 2012								
70.	Rizk et al., 2017								
71.	Taha et al., 2018								
72.	Abdela et al., 2017	Ethiopia	17	17	–				
73.	Choramo and Ibrahim, 2017								
74.	Hamsho et al., 2015								
75.	Hilemariam et al., 2017								
76.	Lemma et al., 1996								
77.	Wodajnew et al., 2015								
78.	Kuttler et al., 1988	Gambia	21	1	57				
79.	Mattioli et al., 1997								
80.	Gachohi et al., 2010	Kenya	36	51	29				
81.	Moumouni et al., 2015								
82.	Wesonga et al., 2016								
83.	Miller et al., 1984	Mali	47	–	47				
84.	Sahibi et al., 1998	Morocco	18	14	22				
85.	Martins et al., 2008	Mozambique	89	89	–				
86.	Matheus et al., 2018	Namibia	36	–	36				
87.	Abdullahi et al., 2014	Nigeria	16	12	76				
88.	Ajayi and Dipeolu, 1986								
89.	Akinboade and Dipeolu, 1984								
90.	Kamani et al., 2010								
91.	Lorusso et al., 2016								
92.	Dreyer et al., 1998	South Africa	66	71	64				
93.	Marufu et al., 2010								
94.	Mtshali and MtShali, 2014								
95.	Mtshali et al., 2014								
96.	Terkawi et al., 2011								
97.	Tonnensen et al., 2006								
98.	Awad et al., 2011	Sudan	21	3	52				
99.	Kivaria et al., 2012								
100.	Malak et al., 2012								
101.	Salih et al., 2007								
102.	Salih et al., 2008								
103.	Ringo et al., 2018	Tanzania	26	18	35				
104.	Swai et al., 2007								
105.	M'ghirbi et al., 2008	Tunisia	11	11	–				
106.	Byaruhanga et al., 2016	Uganda	13	13	–				
107.	Lolli et al., 2016								
108.	Tayebwa et al., 2018								
109.	Jongejan et al., 1988	Zambia	26	16	70				
110.	Musinguzi eta l., 2016								
111.	Tembo et al., 2018								
112.	Yamada et al., 2009								
113.	Katsande et al., 1999	Zimbabwe	44	35	52				
114.	Smeenk et al., 2000								
115.	Camus and Montenegro, 1994	Antigua	36	–	36	North America	52	78	50
116.	Camus and Montenegro,1994	Barbados	29	–	29				
117.	Shebish et al., 2012	Costa Rica	19	3	59				
118.	Camus and Montenegro, 1994	Dominica	47	–	47				
119.	Camus and Montenegro, 1994	Grenada	33	–	33				
120.	Camus and Montenegro, 1994	Guadeloupe	58	–	58				
121.	Camus and Montenegro, 1994	Martinique island	69	–	69				
122.	Camus and Montenegro, 1994	Montserrat	27	–	27				
123.	Ramos et al., 1992	Mexico	39	24	57				
124.	Camus and Montenegro, 1994	Saint Kitts and Nevis	38	–	38				
125.	Camus and Montenegro, 1994	Saint Lucia	56	–	56				
126.	Hugh-Jones et al., 1988								
127.	Knowles et al., 1982								
128.	Camus and Montenegro, 1994	Saint Vincent	58	–	58				
129.	Li et al., 2015	Caribbean island	78	78	–				

Table 1 (*continued*)

SI. No	Authors	Prevalence							
		Country	Total	Infection	Sero-prevalence	Continent	Total	Infection	Sero prevalence
130.	Hadani et al., 1983	Argentina	53	42	58	South America	64%	45%	69%
131.	Ortiz et al., 2018								
132.	Paoletta et al., 2018								
133.	Carrique et al., 2000	Bolivia	66	–	66				
134.	Barros et al., 2005	Brazil	59	50	63				
135.	Brito et al., 2013,								
136.	da Silva et al., 2013								
137.	Osaki et al., 2002								
138.	Silva et al., 2013								
139.	Silveria et al., 2016								
140.	Corrier et al., 1978	Colombia	66	25	77				
141.	Gonzalez et al., 2018								
142.	Jaimes-Duenez et al., 2018								
143.	Applewhaite et al., 1981	Guyana	80	–	80				
144.	James et al., 1985	Venezuela	35	7	78				
145.	Payne and Osorio, 1990	Paraguay	79	–	79				
146.	Agoulon et al., 2012	France	32	27	33	Europe	22%	14%	39%
147.	Criado-Fornelio et al., 2009								
148.	L'Hostis and Chavin, 1999								
149.	L'Hotis et al., 1994								
150.	Cassini et al., 2012	Italy	10	2	35				
151.	Ceci et al., 2014								
152.	Cringoli et al., 2002								
153.	Georges et al., 2001								
154.	Torina et al., 2007								
155.	Silva et al., 2009	Portugal	31	27	79				
156.	Silva et al., 2010								
157.	Staniec et al., 2018	Poland	10	10	–				
158.	Almeria et al., 2001	Spain	9	9	–				
159.	Buling et al., 2007								
160.	Garcia-Sanmartin et al., 2006								
161.	Andersson et al., 2017	Sweden	54	54	–				
162.	Johnston, 1967	Commonwealth of Australia	61	50	70	Australia	61%	50%	70%
163.	Sserugga et al., 2003								

smear examination, molecular and serological methods) and for different countries. Continent wise analysis revealed highest prevalence of bovine babesiosis in South America 64% (95% CI = 49%–77%), followed by Australia 61% (95% CI = 4%–78%), North America 52% (95% CI = 43%–61%), Africa 27% (95% CI = 21%–35%), Europe 22% (95% CI = 11%–39%) and Asia 19% (95% CI = 14%–25%) with highest number of studies reported from Africa (n = 58) followed by Asia (n = 56) (Fig.4). The pooled prevalence estimate was high during the 1967-2000 period 55% (95% CI = 47%–63%) with 33 studies compared to 2001-2019 period 23% (95% CI = 14%–32%) with 132 studies which is also showing a decreasing trend in prevalence. However, the subgroup analysis involving recent years (2016-2019) was showing an increase in the prevalence 25% (95% CI = 18%–32%) that may be a threat in the future. Subgroup analysis based on species of parasite revealed the highest prevalence with *B. bigemina* 22% (95% CI = 18%–27%), followed by *B. bovis* 20% (95% CI = 16%–25%), *B. occultans* 16% (95% CI = 7%–33%), *B. major* 15% (95% CI = 2%–55%) and lowest with *B. divergens* 12% (95% CI = 2%–46%). The overall prevalence of babesiosis in cattle was higher 29% (95% CI = 24%–34%) compared to that of buffaloes 22% (95% CI = 13%–35%). On analysis of different diagnostic techniques employed, the highest prevalence was estimated with serology 50% (95% CI = 45%–56%) followed by nucleic acid-based techniques 19% (95% CI = 15%–24%) and blood smear examination 11% (95% CI = 8%–15%). The summarized results on meta-analysis of bovine babesiosis are mentioned in Tables 1 and 2 (References are enlisted in supplementary file 2).

4. Discussion

Bovine babesiosis impedes the development and sustainability of

the livestock sector worldwide. Meta-analysis is an essential tool to combine the results from two or more studies conducted by different individuals to provide a single numerical value of the estimatewith high statistical power. This report was from the analysis of data obtained through a systematic review of scientific publications on the prevalence of bovine babesiosis between 1967 and 2019. The meta-analysis showed high heterogeneity with I^2 values more than 90% which indicates that 90% of the total variability among effect sizes is caused not by sampling error, but by true heterogeneity between studies (Higgins and Thompson, 2002). The asymmetry of the funnel plot was suggestive of publication bias with higher heterogeneity. The observed heterogeneity could be attributed to different study settings and study populations. Heterogeneity was, however, still very high within the subgroups, hence these results should be interpreted cautiously.

In the present study, meta-analysis revealed a high pooled prevalence estimate during 1967-2000 (55%) which further showed a decrease in trend during 2001-2010 (21%) and during the last five years (2016-2019) the prevalence was gradually increased to 25%. This trend indicates the effective acaricidal usage followed by a period of emergence of acaricide resistance that might have hindered the tick control programs. It is noteworthy that bovine babesiosis has been eradicated from the U.S. by eliminating the *R.annulatus* and *R.microplus* (cattle fever ticks) populations through efforts of the Cattle Fever Tick Eradication Program (CFTEP) established in 1906 and the U.S. was declared free of cattle fever ticks in 1943. It is worth mentioning that the bovine babesiosis is a potentially eradicable disease that can only be achieved by wiping out the tick vectors from a targeted geographical region. The increase in prevalence may also be due to the extension of the niche of tick-borne diseases due to the accelerated rate of global warming. The seasonality in occurrence of bovine babesiosis is worth mentioning with the peak incidence being during summer. It has been

Table 2

: Summary of meta-analysis of prevalence of bovine babesiosis

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		
					I^2 Value (%) with range	Tau square value	H value with range	Chi square heterogeneity statistics	DF	P Value
Bovine babesiosis in World	163	81099	29 (25-34)	2-88	99.0 (99.0-99.1)	2.1474	10.19 (9.92-10.48)	16826.87	162	0
Infection Prevalence	114	53043	16 (13-20)	10-65	98.5 (98.4-98.7)	1.9822	8.29 (7.98-8.61)	7763.88	113	0
Seroprevalence	72	36109	50 (45-56)	13-87	98.5 (98.4-98.7)	0.8759	8.22 (7.84-8.62)	4797.64	71	
Subgroup analysis by period										
Period I (1967-2000)	33	16289	55 (47-63)	15-90	98.1 (97.8-98.4)	0.8682	7.25 (6.71-7.84)	1682.46	32	0
Period II (2001-2010)	39	14824	21 (13-32)	1-92	98.8 (98.6-98.9)	3.3277	9.01 (8.47-9.58)	3081.75	38	0
Period III (2011-2015)	50	31157	24 (18-32)	2-85	99.1 (99-99.2)	2.0349	10.75 (10.24-11.28)	5660.36	49	0
Period IV (2016-2019)	42	18360	25 (18-32)	3-80	98.2 (98.0-98.4)	1.5380	7.47 (6.99-7.99)	2290.58	41	0
Subgroup analysis by continents										
Asia										
Total Prevalence	56	29846	19(14-25)	1-81	98.8 (98.6-98.9)	2.0578	9.0 (8.55-9.48)	4458.6	55	0
Infection Prevalence	40	22223	13 (9-18)	1-65	98.2(97.9- 98.4)	1.5298	7.37 (6.88-7.90)	2118.76	39	0
Seroprevalence	16	7623	42 (28-56)	5-91	98.5(98.1-98.8)	1.4504	8.12 (7.31-9.02)	989.46	15	< 0.01
Africa										
Total Prevalence	58	28881	27 (21-35)	2-85	98.9 (98.8-99.0)	1.8010	9.48 (9.03-9.95)	5122.45	57	0
Infection Prevalence	37	17758	19 (13-26)	2-77	98.8(98.6-98.9)	1.6614	9.11 (8.55-9.70)	2985.02	36	0
Seroprevalence	21	11123	47 (36-57)	10-88	98.1(97.8-; 98.5)	0.9746	7.35 (6.67-8.10)	1079.86	20	< 0.01
Australia										
Total Prevalence	2	2151	61(4-78)	-	98.9 (97.7-99.4)	0.3730	9.35	87.43	1	< 0.01
Infection Prevalence	1	1277	50 (47-53)	-	-	-	-	-	-	-
Seroprevalence	1	874	70 (67-73)	-	-	-	-	-	-	-
Europe										
Total Prevalence	16	6575	22 (11-39)	1-91	99.1 (98.9-99.2)	2.6158	10.32 (9.44-11.29)	1598.20	15	0
Infection Prevalence	10	3980	14 (5-33)	0-91	99.0(98.7-99.2)	2.9492	9.95 (8.84-11.20)	891.50	9	< 0.01
Seroprevalence	6	2595	39 (20-62)	2-96	99.0(98.6- 99.3)	1.3638	9.98 (8.53-11.69)	498.31	5	< 0.01
North America										
Total Prevalence	15	2784	52 (43-61)	20-82	90.3 (85.7-93.4)	0.4255	3.21 (2.64-3.90)	144.29	14	< 0.01
Infection Prevalence	1	352	78 (73-82)	-	-	-	-	-	-	-
Seroprevalence	14	2432	50 (42-58)	21-79	86.2(78.4-91.1)	0.3333	2.69 (2.15-3.36)	94.12	13	< 0.01
South America										
Total Prevalence	16	11163	64(49-77)	10-97	98.9 (98.7-99.1)	1.5956	9.51 (8.65-10.45)	1355.27	15	< 0.01
Infection Prevalence	4	2567	45 (7-90)	0-100	99.1(98.7- 99.4)	6.1855	10.80 (8.91- 13.09)	349.95	3	< 0.01
Seroprevalence	12	8596	69 (62-76)	39-89	97.4(96.6-98.1)	0.2889	6.24 (5.39- 7.22)	428.19	11	< 0.01
Subgroup analysis by species of animal										
Cattle										
Total Prevalence	158	78625	29 (24-34)	2-89	99.0 (99.0-99.1)	2.2790	10.29 (10.01-10.58)	16614.59	157	0

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	H value with range	Chi square heterogeneity statistics	DF	P Value
Infection Prevalence	114	43546	16 (12-20)	1-75	98.5 (98.4-98.7)	1.9822	8.29 (7.98; 8.61)	7763.88	113	0
Seroprevalence	70	36173	48 (41-54)	8-90	98.7 (98.6-98.8)	1.3022	8.90 (8.49- 9.32)	5459.85	69	0
Buffalo										
Total Prevalence	12	2834	22 (13-35)	02-77	97.1 (96.1-97.9)	1.1233	5.88 (5.05-6.83)	379.85	11	< 0.01
Infection Prevalence	9	1187	17 (9-28)	2-70	92.0 (87.1-95.1)	0.9289	3.55 (2.79- 4.51)	100.62	8	< 0.01
Seroprevalence	3	1647	42 (22-65)	0-100	98.1(96.5-99.0)	0.6908	7.23(5.33- 9.81)	104.62	2	< 0.01
Subgroup analysis by diagnostic method										
Blood smear examination	45	29064	11 (8-15)	1-60	98.7 (98.5-98.8)	1.5252	8.69 (8.19-9.21)	3319.24	41	0
Molecular methods	82	27106	19 (15-24)	1-78	98.2 (98-98.3)	1.8676	7.4 (7.05-7.76)	4435.39	81	0
Serology	72	36109	50 (45-56)	13-87	98.5 (98.4-98.7)	0.8759	8.22 (7.84-8.62)	4797.64	71	0
Subgroup analysis by country										
Turkey										
Total Prevalence	13	3748	17 (7-37)	0-94	96.7 (95.5-97.6)	3.5189	5.51 (4.74-6.40)	363.76	12	< 0.01
Infection Prevalence	10	2871	7 (3-15)	0-69	96.4(94.8- 97.5)	1.9665	5.27(4.40-6.30)	249.58	9	< 0.01
Seroprevalence	7	2235	33 (14-61)	1-97	93.7(89.4- 96.2)	2.2639	3.98(3.07- 5.15)	94.98	6	< 0.01
Thailand										
Total Prevalence	7	3691	29 (15-50)	2-91	99.3 (99.1-99.5)	1.3539	12.16 (10.72-13.79)	886.65	6	< 0.01
Infection Prevalence	6	2787	18 (12-26)	4-52	94.7(91.0-96.9)	0.2719	4.35 (3.32-5.68)	94.47	5	< 0.01
Seroprevalence	4	1160	58 (31-81)	1-100	98.7(97.9-99.1)	1.3107	8.66 (6.93-10.83)	225.12	3	< 0.01
South Africa										
Total Prevalence	6	3534	66(57-74)	32-89	92.5 (86.4-95.9)	0.2172	3.65 (2.71-4.92)	66.74	5	< 0.01
Infection Prevalence	2	698	71 (8-80)	-	90.1(63.5- 97.3)	0.1389	3.17	10.05	1	< 0.01
Seroprevalence	4	2836	64 (51-75)	12-96	94.7(89.4- 97.3)	0.2874	4.34(3.08- 6.11)	56.39	3	< 0.01
Pakistan										
Total Prevalence	10	4264	15(7-27)	1-75	96.3 (94.6-97.4)	1.4058	5.16 (4.31-6.19)	240.02	9	< 0.01
Infection Prevalence	10	4264	15(7-27)	1-75	96.3 (94.6-97.4)	1.4058	5.16 (4.31-6.19)	240.02	9	< 0.01
Seroprevalence	-	-	-	-	-	-	-	-	-	-
Uganda										
Total Prevalence	3	4384	13 (5-27)	0-100	92.6 (81.7-97.0)	0.6311	3.68 (2.34- 5.8)	27.11	2	< 0.01
Infection Prevalence	3	4384	13 (5-27)	0-100	92.6 (81.7-97.0)	0.6311	3.68 (2.34- 5.8)	27.11	2	< 0.01
Seroprevalence	-	-	-	-	-	-	-	-	-	-
Bangladesh										
Total Prevalence	5	1666	4 (2-11)	0-66	91.1 (82.1-95.5)	1.1493	3.35 (2.37-4.74)	44.82	4	< 0.01
Infection Prevalence	4	1487	3 (1-7)	0-68	89.0(74.6- 95.3)	0.7477	3.02(1.98- 4.59)	27.35	3	< 0.01
Seroprevalence	1	179	15 (10-21)	-	-	-	-	-	-	-
Sudan										
Total Prevalence	5	2530	21 (5-60)	1-100	99.0 (98.7-99.3)	3.7807	10.26 (8.63-12.20)	420.89	4	< 0.01
Infection Prevalence	2	1292	3 (1-11)	-	92.6(75.0- 97.8)	0.7976	3.67	13.50	1	< 0.01
Seroprevalence	3	1238	52 (49-55)	35-69	0.0(0.0-40.2)	0	1.00 (1.00- 1.29)	0.35	2	0.84
Philippines										
Total Prevalence	4	1210	25 (10-51)	0-99	98.5 (97.6-99.0)	1.2676	8.10 (6.42-10.23)	196.98	3	< 0.01
Infection Prevalence	4	1210	25 (10-51)	0-99	98.5 (97.6-99.0)	1.2676	8.10 (6.42-10.23)	196.98	3	< 0.01
Seroprevalence	-	-	-	-	-	-	-	-	-	-
Egypt										

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		
					I^2 Value (%) with range	Tau square value	H value with range	Chi square heterogeneity statistics	DF	P Value
Total Prevalence	10	2703	19 (13-29)	3-63	96.3 (94.8-97.4)	0.6536	5.23 (4.37-6.26)	246.51	9	< 0.01
Infection Prevalence	9	2402	16 (10-24)	3-56	95.7 (93.7-97.1)	0.5737	4.85 (3.97-5.92)	187.92	8	< 0.01
Seroprevalence	4	1002	29 (21-40)	4-78	90.8 (79.5-95.9)	0.1998	3.29(2.21- 4.92)	32.56	3	< 0.01
Iran										
Total Prevalence	5	8570	11 (4-27)	0-91	99.6 (99.4-99.7)	1.6020	15.31 (13.42-17.46)	937.55	4	< 0.01
Infection Prevalence	5	8570	11 (4-27)	0-91	99.6 (99.4-99.7)	1.6020	15.31 (13.42-17.46)	937.55	4	< 0.01
Seroprevalence	-	-	-	-	-	-	-	-	-	-
Ethiopia										
Total Prevalence	6	2376	17 (13-22)	6-39	89.0 (78.7-94.3)	0.1377	3.02 (2.17-4.2)	45.5	5	< 0.01
Infection Prevalence	6	2376	17 (13-22)	6-39	89.0 (78.7-94.3)	0.1377	3.02 (2.17-4.2)	45.5	5	< 0.01
Seroprevalence	-	-	-	-	-	-	-	-	-	-
China										
Total Prevalence	3	3314	21 (11-36)	0-100	95.0 (88.6-97.8)	0.4344	4.46 (2.96-6.7)	39.73	2	< 0.01
Infection Prevalence	2	950	19 (6-45)	-	97.5(93.7- 99.0)	0.8164	6.29	39.61	1	< 0.01
Seroprevalence	1	2364	25 (23-27)	-	-	-	-	-	-	-
Nigeria										
Total Prevalence	5	3091	16 (8-29)	1-78	98.4(97.5- 98.9)	0.6816	7.83 (6.36- 9.63)	245.04	4	< 0.01
Infection Prevalence	4	2591	12 (10-16)	5-30	72.0(20.7- 90.1)	0.0472	1.89 (1.12- 3.18)	10.73	3	0.01
Seroprevalence	2	700	76 (16-98)	-	99.0(97.9- 99.5)	4.0252	9.79	95.77	1	< 0.01
Vietnam										
Total Prevalence	2	408	50 (8-92)	0	98.8(97.4-99.4)	2.9868	8.98	80.65	1	< 0.01
Infection Prevalence	2	408	33 (14-59)	-	95.2(85.6- 98.4)	0.5750	4.55	20.66	1	< 0.01
Seroprevalence	1	101	77 (68-85)	-	-	-	-	-	-	-
Colombia										
Total Prevalence	3	4821	66 (37-86)	0-100	99.7 (99.5-99.8)	1.0567	17.54 (14.82-20.75)	615.17	2	< 0.01
Infection Prevalence	2	1786	25 (10-51)	-	97.0(92.2- 98.8)	0.6427	5.77	33.27	1	< 0.01
Seroprevalence	2	3237	77 (72-81)	-	63.1(0.0- 91.5)	0.0282	1.65	2.71	1	0.1
Brazil										
Total Prevalence	6	3219	59 (23-87)	0-100	99.0 (98.6-99.2)	3.9016	9.78 (8.33-11.48)	478.34	5	< 0.01
Infection Prevalence	2	797	50 (1-100)	-	99.7 (99.5-99.8)	18.542	17.43	303.92	1	< 0.01
Seroprevalence	4	2422	63 (48-75)	9-97	98.3(97.2-98.9)	0.3411	7.58 (5.95- 9.67)	172.52	3	< 0.01
St. Lucia										
Total Prevalence	3	371	56 (31-78)	0-100	86.6 (61.4-95.3)	0.7467	2.73 (1.61-4.63)	14.89	2	< 0.01
Infection Prevalence	-	-	-	-	-	-	-	-	-	-
Seroprevalence	3	371	56 (31-78)	0-100	86.6 (61.4-95.3)	0.7467	2.73 (1.61-4.63)	14.89	2	< 0.01
France										
Total Prevalence	4	1439	32 (3-86)	0-100	99.4 (99.1-99.6)	6.6081	12.55 (10.55-14.94)	472.87	3	< 0.01
Infection Prevalence	2	492	27 (0-99)	-	97.3(93.3-98.9)	18.948	6.12	37.51	1	< 0.01
Seroprevalence	2	947	33 (5-81)	-	99.4(98.9-99.7)	2.4041	12.89	166.08	1	< 0.01
Spain										
Total Prevalence	3	434	9 (7-12)	1-46	0 (0-84.1)	0	1 (1-2.51)	1.31	2	0.52
Infection Prevalence	3	434	9 (7-12)	1-46	0 (0-84.1)	0	1 (1-2.51)	1.31	2	0.52
Seroprevalence	-	-	-	-	-	-	-	-	-	-
Italy										
Total Prevalence	5	2929	19 (8-38)	1-91	98.8 (98.3-99.2)	1.1257	9.15 (7.59-11.02)	334.53	4	< 0.01
Infection Prevalence	3	1769	7 (2-19)	0-100	96.1(91.7- 98.2)	0.9135	5.07 (3.47- 7.40)	51.37	2	< 0.01

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	H value with range	Chi square heterogeneity statistics	DF	P Value
Seroprevalence	3	1242	30 (18-45)	0-100	96.8(93.5- 98.4)	0.3350	5.62 (3.94- 8.02)	63.13	2	< 0.01
Zambia										
Total Prevalence	4	2626	26 (9-56)	0-99	99.5 (99.2-99.6)	1.6872	13.51 (11.45-15.94)	547.36	3	< 0.01
Infection Prevalence	3	842	16 (11-22)	0-97	72.1(5.8- 91.8)	0.1117	1.89 (1.03- 3.48)	7.18	2	0.02
Seroprevalence	1	1784	70 (68-72)	-	-	-	-	-	-	-
Kenya										
Total Prevalence	3	1053	36 (19-57)	0-100	97.3 (94.6-98.6)	0.5682	6.04 (4.3-8.49)	73.02	2	< 0.01
Infection Prevalence	1	192	51 (44-58)	-	-	-	-	-	-	-
Seroprevalence	2	861	29 (12-53)	-	97.8(94.8- 99.1)	0.5541	6.79	46.12	1	< 0.01
Argentina										
Total Prevalence	3	662	53 (40-65)	0-100	90.8 (75.8- 96.5)	0.1838	3.29 (2.03-5.32)	0.1838	2	< 0.01
Infection Prevalence	1	186	42 (35-50)	-	-	-	-	-	-	-
Seroprevalence	2	476	58 (44-70)	-	88.7(57.0-97.0)	0.1383	2.97	8.82	1	0
Indonesia										
Total Prevalence	2	1478	63 (48-76)	-	96.4(90.0- 98.7)	0.1838	5.25	27.58	1	< 0.01
Infection Prevalence	1	487	70 (66-74)	-	-	-	-	-	-	-
Seroprevalence	2	1478	63 (48-76)	-	96.4(90.0- 98.7)	0.1838	5.25	27.58	1	< 0.01
Gambia										
Total Prevalence	2	2126	21 (1-87)	-	99.3(98.9-99.5)	8.0386	11.89	282.70	1	0
Infection Prevalence	1	1294	1 (1-2)	-	-	-	-	-	-	-
Seroprevalence	2	832	57 (42-71)	-	92.4(74.1- 97.8)	0.1825	3.62	13.11	1	0
Tanzania										
Total Prevalence	2	1574	26 (12-46)	-	96.3(89.9-98.7)	0.4144	5.22	27.30	1	< 0.01
Infection Prevalence	1	245	18 (13-23)	-	-	-	-	-	-	-
Seroprevalence	1	1329	35 (32-38)	-	-	-	-	-	-	-
Commonwealth of Australia										
Total Prevalence	2	2151	61 (40-78)	-	98.9(97.7-99.4)	0.3730	9.35	87.43	1	< 0.01
Infection Prevalence	1	1277	50 (47-53)	-	-	-	-	-	-	-
Seroprevalence	1	874	70 (67-73)	-	-	-	-	-	-	-
Portugal										
Total Prevalence	2	1510	31 (1-97)	-	99.8(99.7-99.9)	8.9697	23.20	538.44	1	< 0.01
Infection Prevalence	2	1510	27 (1-94)	-	99.8(99.7- 99.9)	7.2158	21.79	475.01	1	< 0.01
Seroprevalence	1	406	79 (75-83)	-	-	-	-	-	-	-
Zimbawe										
Total Prevalence	2	2360	44 (28-61)	-	90.4(65.1-97.3)	0.2276	3.22	10.39	1	0
Infection Prevalence	1	94	35 (26-46)	-	-	-	-	-	-	-
Seroprevalence	1	2266	52 (50-54)	-	-	-	-	-	-	-
Subgroup analysis by species of parasite										
B.bigemina										
Total Prevalence	128	61423	22 (18-27)	1-86	98.8 (98.8-98.9)	2.3566	9.28 (8.98-9.59)	10939.70	127	0
Infection Prevalence	78	34630	10 (7-13)	1-64	98.0(97.8-98.2)	1.9464	7.09 (6.74-7.46)	3873.83	77	0
Seroprevalence	65	31846	41 (35-48)	8-86	98.4(98.2- 98.5)	1.1218	7.84 (7.44-8.26)	3929.72	64	0
B.bovis										
Total Prevalence	108	45971	20 (16-25)	1-85	98.9 (98.7-98.9)	2.4850	9.27 (8.94-9.61)	9188.75	107	0

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	H value with range	Chi square heterogeneity statistics	DF	P Value
Infection Prevalence	66	26047	9 (6-13)	0-70	98.2(98.0-98.4)	2.3948	7.48 (7.09-7.89)	3635.48	65	0
Seroprevalence	52	24380	38 (31-45)	7-84	98.8(98.7- 98.9)	1.1350	9.20 (8.73-9.70)	4319.45	51	0
B.divergens										
Total Prevalence	9	4754	12 (2-46)	0-99	99.1 (98.9-99.3)	7.2598	10.65 (9.45-12.01)	907.80	8	< 0.01
Infection Prevalence	6	3549	7 (1-48)	0-100	99.3(99.1- 99.5)	9.8367	12.12(10.55-13.92)	734.29	5	< 0.01
Seroprevalence	3	1205	34 (13-64)	0-100	98.8(98.0- 99.3)	1.1971	9.21 (7.10-11.96)	169.79	2	< 0.01
B.major										
Total Prevalence	8	4567	15 (2-55)	0-100	99.2(99-99.4)	7.8796	11.14 (9.84-12.61)	868	7	< 0.01
Infection Prevalence	5	3362	8 (0-65)	0-100	99.4 (99.2-99.6)	12.049	13.12 (11.33-15.19)	688.54	4	< 0.01
Seroprevalence	3	1205	34 (13-64)	0-100	98.8 (98-99.3)	1.1971	9.21 (7.10-11.96)	169.79	2	< 0.01
B.occultans										
Total Prevalence	2	312	16 (7-33)	-	88.9 (58.3-97.1)	0.4117	3.01	9.04	1	< 0.01
Infection Prevalence	2	312	16 (7-33)	-	88.9 (58.3-97.1)	0.4117	3.01	9.04	1	< 0.01
Seroprevalence	-	-	-	-	-	-	-	-	-	-

observed that atmospheric temperature has a profound effect on tick activity evidenced by increased tick population during high temperature (El Moghazy et al., 2014). This fact possesses an alarming threat to the scientific community in the era of global warming. It is anticipated that the disease prevalence may continue to increase in the future until and unless we can control the ticks or the disease effectively.

The continent wise analysis revealed a higher prevalence in South America (64%). It has been estimated that the majority of the cattle population in South America is in tick infested areas with established enzootic stability in most of the regions (Montenegro-James, 1992). However, the highest prevalence in South America may be attributed to the high tick population and the favourable agroclimatic conditions prevailing in this region (Payne and Osorio, 1990). The pooled prevalence estimate was least in Asia (19%) which may be due to the high number of studies (n = 56) considered for meta-analysis with less seroprevalence studies. The studies from South Africa demonstrated that wide distribution of *B. bigemina* whereas the patchy distribution of *B.bovis* solely depend on the vector distribution (Bryant and Norval, 1985)

The diagnosis of bovine babesiosis mainly depends on the microscopic examination of Giemsa stained blood smear as the detection of piroplasms is the gold standard for the diagnosis, especially during the acute stage of the disease. However, in bovine babesiosis, a low parasitemia carrier state is usually developed after recovery of infection wherein the survived animals serve as a reservoir of the parasite and the blood smear examination is less sensitive to detect the carrier state (Mahoney, 1969). Further, in endemic countries where enzootic stability along with premmunity persist among cattle; the absence of infection by blood smear examination may not be reliable, rather antibody detection methods will aid in determining the level of endemicity of the disease (Akinboade and Dipeolu, 1984). Keeping in view of this, the seroprevalence will be on the higher side compared to the infection prevalence and this may result in erroneous pooled prevalence estimate. To address this issue, in the present paper, meta-analysis for

infection prevalence (active infection) and seroprevalence has been calculated that generated more clarity in the analysis.

In bovine babesiosis, endemic stability is noteworthy wherein host, parasite, vector, and environment remained in a balanced way so that clinical disease occurs rarely (Perry et al., 1998). *Bos Taurus* is highly susceptible to tick-borne diseases compared to *Bos indicus* that remains as a major constraint in the rearing of high yielding exotic breeds of cattle. The crossbred cattle are also highly susceptible to tick-borne diseases whereas buffalo and zebu cattle often act as carrier of infection (Jithendran, 1997). Although *B. bigemina* is more widespread, causing mortality rates up to 30% in animals without treatment, *B. bovis* is the most virulent generating mortality rates between 70–80%, as a result of the related neurological signs.

Despite its overwhelming effects on the health of livestock, adequate emphasis on the control of bovine babesiosis has not been given across the globe. Ideally, control of bovine babesiosis relies on an integrated approach with vector control, chemotherapy and immunoprophylaxis along with exploitation for the scope of endemic stability. Besides, grazing management wherein the ecological system has made unfavourable for the growth and propagation of ticks is also found promising (Teel et al., 1997).

The study showed the wide distribution of bovine babesiosis across the globe with the involvement of six continents. Since widely accepted cost-effective vaccines are not available in the market, the threat will continue to increase and will spread across the remaining part of the world soon. In this study, analysis in all the subgroups based on antigen detection methods (infection prevalence) and antibody detection methods (seroprevalence) has been carried out to avoid the overestimation of total pooled prevalence. This will help to understand the prevalence realistically as serology is unable to demarcate between past and present infection and will represent cumulative exposure to infection.

5. Conclusion

To the best of our knowledge, this study represents the first systematic review and meta analysis providing an overview of seroprevalence and active disease prevalence estimates of bovine babesiosis in a global perspective. The pooled prevalence estimates generated in the study is revealing an increase in disease trend and the need for immediate planning of mitigation strategies paralleled with the development of early diagnostic methods to reduce the impact of disease throughout the world.

Funding

CRediT authorship contribution statement

Siju Susan Jacob: Conceptualization, Methodology, Writing - original draft, Visualisation. **Pinaki Prasad Sengupta:** Writing - review & editing, Supervision. **Krishnamoorthy Paramanandham:** Methodology, Data curation. **Kuralayanapalya Puttahonnappa Suresh:** Formal analysis. **Jayantha Kumar Chamuah:** Writing - review & editing. **Gudepalya Renukaiah Rudramurthy:** Writing - review & editing. **Parimal Roy:** Writing - review & editing, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

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