



REVIEW ARTICLE

Bovine anaplasmosis: A systematic review with meta-analysis on the global prevalence

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ABSTRACT

Bovine anaplasmosis, caused by *Anaplasma marginale*, is a significant infectious disease affecting cattle populations globally. However, the prevalence and distribution of bovine anaplasmosis vary across regions, making it crucial to assess its global burden systematically. This study aims to provide a comprehensive understanding of the global prevalence of bovine anaplasmosis and synthesized data from diverse geographic regions. A literature search was conducted to identify all relevant published articles reporting the prevalence of bovine anaplasmosis and a total of 164 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 129,851 samples from 42 countries was conducted and the overall estimated prevalence of bovine anaplasmosis was found to be 38% (100% CI = 33% - 42%). The prevalence was found to be higher in cattle (39.9%) in comparison to yaks (6.4%). Diagnosis using serology (40.2%) yielded a higher prevalence compared to molecular testing (38.3%) and blood smears (22.4%) methods. Additionally, there were significant differences in the prevalence of bovine anaplasmosis between different countries ($p < 0.05$). This study will inform evidence-based strategies for control and prevention of bovine anaplasmosis on a global scale by discovering the true extent of the disease and identifying high-prevalence areas.

Keywords: Bovine anaplasmosis; *Anaplasma*; systematic review; meta-analysis; global prevalence.

INTRODUCTION

Bovine anaplasmosis caused by the obligate intracellular bacterium *Anaplasma marginale* is a significant health concern affecting cattle populations worldwide (Hanzlicek *et al.*, 2016). The disease is primarily transmitted through tick vectors, with variations in prevalence observed across different geographic regions including Africa, Asia, Europe, and the Americas (Aubry & Geale, 2011). The disease can pose significant challenges to beef and dairy production if not treated promptly (Kocan *et al.*, 2010). The lack of evident symptoms in persistently infected animals makes it difficult for some producers to determine the infection status of their herd. This lack of knowledge about the infection can hinder the efforts of cattle producers and veterinarians in developing effective control programs for anaplasmosis (Spare *et al.*, 2020).

Bovine anaplasmosis is characterized by persistent parasitemia, which leads to anemia, reduced productivity, weight loss, and increased susceptibility to other infections (M'Ghirbi *et al.*, 2016). Historically, the disease was first described in South Africa in late 1800s, where it was known as "gall sickness". It was not until the 1930s that it was identified as a bacterial infection, and the causative organism was named *A. marginale* (Ashford, 2001; Kocan *et al.*, 2010).

The development of vaccines against bovine anaplasmosis began in the mid-20th century, when it was first recognized as a major problem for the cattle industry. The first vaccines were based on whole-cell preparations of *A. marginale*, which were inactivated by chemical or physical methods to make them safe for use in cattle (Kocan *et al.*, 2000). In the 1950s, researchers began experimenting with live vaccines, which contained the weakened forms of *A. marginale*. These vaccines provided longer-lasting immunity than the killed vaccines but carried a small risk of causing disease in some animals (Kocan *et al.*, 2003). Today, a variety of vaccines are available for the prevention of bovine anaplasmosis, including killed, live, and subunit vaccines. These vaccines are administered by injection and provide varying degrees of protection against the disease. In addition to vaccination, control of bovine anaplasmosis also involves measures to control tick populations and limit the spread of the disease through blood transfusions and contaminated medical equipment (Quiroz-Castañeda *et al.*, 2016; Paramanandham *et al.*, 2019).

While bovine anaplasmosis has been extensively studied in various regions, there is a need for a comprehensive understanding of its global prevalence to facilitate effective control and prevention strategies. Systematic reviews and meta-analyses play a crucial role in synthesizing existing knowledge by systematically identifying,

appraising, and summarizing relevant studies (Higgins *et al.*, 2019; Morgan & Florez, 2022). These analyses provide a reliable estimate of the prevalence of bovine anaplasmosis and identification of potential risk factors associated with its occurrence by combining data from multiple studies.

Understanding the global prevalence of bovine anaplasmosis is vital for assessing its impact on cattle health, productivity, and global livestock industry. A previous systematic review and meta-analysis on the worldwide prevalence of bovine anaplasmosis has been conducted specifically in dairy animals (Paramanandham *et al.*, 2019) while the present study focused on the disease's occurrence in a wider perspective of bovine species namely the cattle, buffalo, and yak. Thus, this study aims to provide valuable insights into the global prevalence of the disease, the bovine species that are highly affected by bovine anaplasmosis and the effective diagnostic method for the detection of *Anaplasma* spp. A systematic review and meta-analysis of the global prevalence of bovine anaplasmosis will enhance the understanding of the disease's burden worldwide. The discoveries will aid in the development of evidence-based approaches for managing diseases, thus, providing valuable guidance for controlling bovine anaplasmosis.

MATERIALS AND METHOD

Data sources and search strategy

The PRISMA protocol (Moher *et al.*, 2009) was followed to identify the prevalence of bovine anaplasmosis across the globe. The literature search was conducted using a comprehensive combination of keywords such as "bovine anaplasmosis", "*Anaplasma marginale*", "*Anaplasma centrale*", "*Anaplasma* spp.", "anaplasmosis", "cattle", "bovine haemoparasites" and "haemoparasites". The keywords were used alone or in combination to ensure that all relevant studies were identified. Electronic databases such as PubMed, Science Direct, and Scopus were used to search for relevant studies.

For the final systematic review and meta-analysis, only studies that reported the prevalence of bovine anaplasmosis were included. The literature search was limited from the year 1911 to January 2023 and the search was restricted to English language publications and open access articles only (Figure 1).

Eligibility criteria

The research focused on the prevalence of bovine anaplasmosis in cattle and buffalo worldwide, using only cross-sectional and longitudinal studies. The collected literature were subjected to a rigorous check for duplicates and those meeting the inclusion criteria for meta-analysis that reported the number of animals screened, number of infected animals based on detection of the organism

or antibodies, use of standard methods such as blood smear examination and molecular methods for detecting the organism, and/or serological techniques namely ELISA, IFAT, and capillary tube agglutination test for antibody detection. Additionally, year of publication was also included in the criteria. Any literature pertaining to outbreak investigations, case reports, reviews, and clinical trials were excluded from this study.

Data extraction

Based on the specified criteria, the relevant literatures were selected and the findings from each study were independently extracted and populated into a pre-designed Excel sheet. The extracted information included the study location, the size of the sample, the number of animals found positive for *Anaplasma* spp., the diagnostic method used, the name of the author, the title of the article, and the year of publication. For studies that applied different diagnostic methods, the method with the highest prevalence rate was chosen to be analysed.

Meta-analysis

The use of meta-analysis in prevalence studies enables the calculation of a weighted average proportion of prevalence based on various studies. By doing so, a more accurate estimate of the prevalence of a particular condition can be obtained from multiple studies, which can provide valuable insights for future research. In this study, a meta-analysis was carried out using R OpenSource Software version 4.2.1. The R packages used for the analyses were Meta, dplyr and ggplot2. The rworldmap package was utilized to visually analyze the global prevalence of bovine anaplasmosis.

In order to determine the appropriate effect model for the meta-analysis, the percentage of heterogeneity (I^2) was taken into consideration. As a significant level of heterogeneity was anticipated ($I^2 > 50\%$), a random effects model was selected to generate a pooled estimate of the prevalence of bovine anaplasmosis. To assess the possibilities of publication bias, a funnel plot was performed with the y-axis showing the standard error (SE) of each study and the x-axis showing the proportion of event which refers to the prevalence of bovine anaplasmosis in this study. The presence of asymmetry in the funnel plot was assessed using a linear regression test and the null hypothesis of the test was either accepted or rejected based on its corresponding p-value. In cases where funnel plot asymmetry was detected, the trim-and-fill method was utilized to correct it by inputting missing studies and re-estimating the effect size.

Subgroup analyses were carried out to explore various factors affecting the prevalence of bovine babesiosis. These factors included years (1966-2023), species of infected animals (cattle, buffalo, yaks), diagnostic methods employed (blood smear examination, molecular and serological methods), and countries where the studies were conducted.

RESULTS

Details of studies

Following a preliminary review of article titles related to the prevalence of bovine anaplasmosis and removal of irrelevant titles, 2,027 articles were initially selected for evaluation. After reviewing the abstracts, 1,574 articles were excluded, and an additional 289 articles were excluded after reviewing the full articles. The remaining 164 studies were included in the systematic review and meta-analysis.

Meta-analysis of bovine anaplasmosis prevalence

A meta-analysis was conducted on 164 studies, covering 42 countries, from 1966 to 2023. These studies involved a total of 129,851 samples, of which 27,318 were positive. The results of the meta-analysis showed a high level of variability between the studies ($T^2 = 0.0805$; heterogeneity, $I^2 = 100\%$). Additionally, the p-value

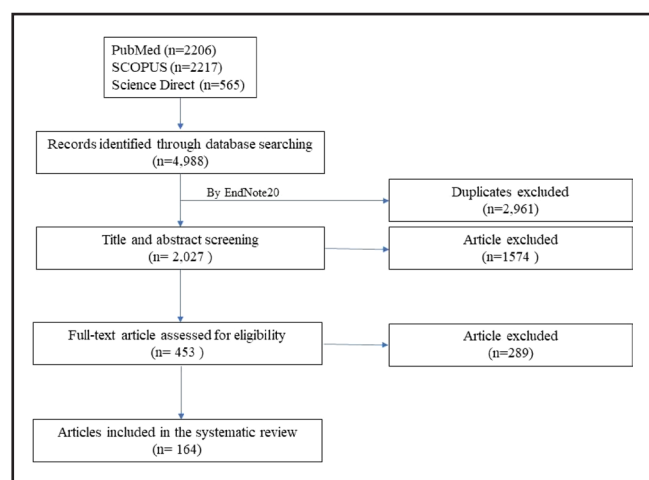


Figure 1. Schematic diagram on exclusion and inclusion process for meta-analysis.

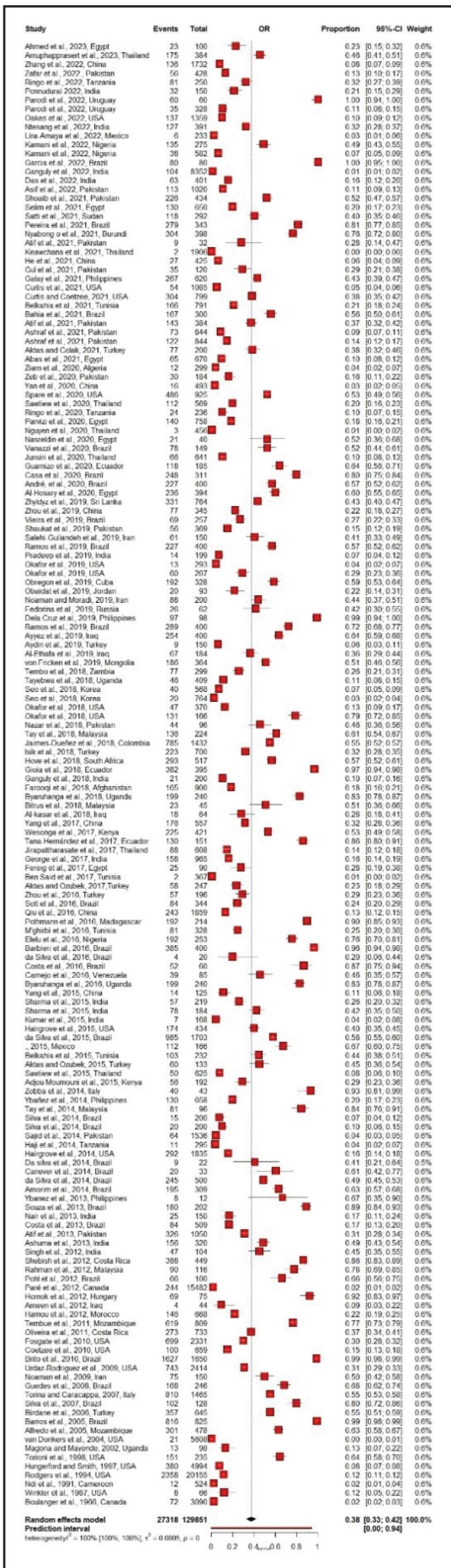


Figure 2. Forest plot on prevalence estimates and heterogeneity details for each study.

of 0 indicated that the observed heterogeneity was statistically significant. The prevalence estimates for individual studies ranged from 0.1% to 100%. Based on the random pooled analysis of 164 studies, the overall prevalence was estimated to be 38% (100% CI [33%-42%], PI: 0-94%). Figure 2 represents the forest plot derived from the meta-analysis.

There was a significant asymmetry in the funnel plot determined by linear regression test ($t(162)=5.95, p<0.0001$) and Egger's test ($=0.0220$) suggesting that publication bias or other forms of bias may be present in the included studies (Figure 3).

Subgroup meta-analysis

Subgroup analysis shows that 164 studies have been conducted on bovine anaplasmosis with a total of 129,851 samples involved and 27,318 infections. The I^2 value is 99.9%, indicating high heterogeneity. The estimated between-study variance is $\tau^2 = 0.0805$ (95% CI [0.0651-0.1009]). The estimated standard deviation of the random effects' distribution is $\tau = 0.2836$ (95% CI [0.2551 - 0.3177]) (Table 1).

The prevalence of bovine anaplasmosis was significantly higher ($p<0.0001$) in cattle (39.9%), followed by the combination of prevalence in cattle and buffalo (34.5%), buffalo (19.4%), and yaks (7.9%) (Table 2). The prevalence estimates varied depending on the diagnostic methods used, with serology tests yielding a higher prevalence (38.3%) than molecular assays (40.2%) or blood smears (22.4%). However, there was no significant difference between the diagnostic subgroups ($p=0.257$). Significant differences were observed in the prevalence of bovine anaplasmosis among the countries ($p<0.001$). Hungary and Madagascar had the highest prevalence rate, 92.0% and 89.7%, respectively, while the lowest prevalence was observed in Canada (1.9%) (Figure 4).

DISCUSSION

PRISMA protocol (Moher et al., 2009) is a widely accepted guideline for conducting and reporting systematic reviews and meta-analyses in healthcare research. It helps to ensure that the review is comprehensive and transparent, and that the results are reliable and replicable (Pati & Lorusso, 2018). Thus, it has the potential to provide valuable insights for guiding future researches and policy-making related to bovine anaplasmosis. Anaplasmosis caused by *A. marginale* is a common outbreak in cattle that leads to noticeable clinical signs such as anaemia and jaundice (OIE, 2018). Although the disease has not been reported in humans, it causes substantial losses in the ruminant industry by reducing cattle production, reproduction, and draught ability. As a result, this negatively affects cattle farming profitability and increases the cost of infection management and treatment. While sporadic fatalities are typical, bovine anaplasmosis can cause significant morbidity if herd immunity is compromised (Ola-Fadunsin et al., 2018, Pamanandham et al., 2019).

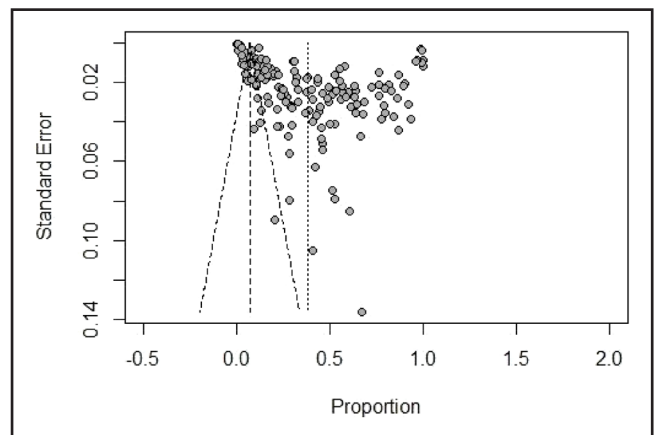


Figure 3. Funnel plot on publication bias.

Table 1. Summary of subgroups analysis

| Subgroup parameters | S | O | E | Heterogeneity analysis | | | | | | | |
|---------------------|-----|--------|-------|---------------------------|----------------------------|----------------------------|-------|-----------------------|-----|---|--|
| | | | | Quantifying heterogeneity | | | | Test of heterogeneity | | | |
| | | | | I ² | tau ² | tau | H | Q test | df | p | |
| Species of animal | | | | | | | | | | | |
| Diagnostic method | 164 | 129851 | 27318 | 99.9 | 0.0805 (0.0651; 0.1009) | 0.2836 (0.2551; 0.3177) | 40.77 | 270976.11 | 163 | 0 | |
| Country | | | | | | | | | | | |
| Year | | | | | | | | | | | |

S=Number of studies, O=Number of observations, E=Number of events, I²=Total variation across studies that is due to heterogeneity rather than chance, tau²=Estimate between-study variance, tau=Estimated standard deviation of the random effects' distribution, H=Heterogeneity, df=Degree of freedom, p=P-value.

Table 2. Summary of subgroup random effect model meta-analysis of the prevalence of bovine anaplasmosis

| Parameter | Total | Proportion | 95%-CI | tau ² | tau | Test for subgroup differences | | | | |
|---------------------------|-------|------------|------------------|------------------|--------|-------------------------------|---------|---------|---------|--|
| | | | | | | Q | df | P-value | | |
| Animal type | | | | | | | | | | |
| Cattle | 140 | 0.3986 | [0.3502; 0.4469] | 0.0841 | 0.29 | | | | | |
| Yaks, Cattle | 1 | 0.0785 | [0.0659; 0.0912] | 0 | 0 | | | | | |
| Buffalo | 10 | 0.194 | [0.0631; 0.3250] | 0.0442 | 0.2101 | Between groups | 185.93 | 4 | <0.0001 | |
| Cattle, Buffalo | 12 | 0.3448 | [0.2315; 0.4582] | 0.0397 | 0.1993 | | | | | |
| Yaks | 1 | 0.0635 | [0.0403; 0.0867] | 0 | 0 | | | | | |
| Diagnostic methods | | | | | | | | | | |
| Molecular | 99 | 0.3826 | [0.3269; 0.4382] | 0.0788 | 0.2807 | | | | | |
| Serology | 54 | 0.4015 | [0.3281; 0.4749] | 0.0749 | 0.2736 | Between groups | 2.71 | 2 | 0.2568 | |
| Blood smearing | 11 | 0.2236 | [0.0252; 0.4220] | 0.1123 | 0.3352 | | | | | |
| Country | | | | | | | | | | |
| Egypt | 7 | 0.297 | [0.1589; 0.4351] | 0.0332 | 0.1823 | | | | | |
| Thailand | 7 | 0.1339 | [0.0260; 0.2539] | 0.0235 | 0.1532 | | | | | |
| China | 7 | 0.1356 | [0.0617; 0.2094] | 0.0097 | 0.0982 | | | | | |
| Pakistan | 13 | 0.2322 | [0.1505; 0.3140] | 0.0217 | 0.1472 | | | | | |
| Tanzania | 3 | 0.1526 | [0.0000; 0.3217] | 0.0219 | 0.1478 | | | | | |
| India | 13 | 0.2188 | [0.1334; 0.3042] | 0.024 | 0.1548 | | | | | |
| Uruguay | 2 | 0.5534 | [0.0000; 1.0000] | 0.3988 | 0.6315 | | | | | |
| USA | 17 | 0.2596 | [0.1524; 0.3667] | 0.0504 | 0.2246 | | | | | |
| Mexico | 2 | 0.3493 | [0.0000; 0.9852] | 0.2099 | 0.4581 | | | | | |
| Nigeria | 3 | 0.4377 | [0.0413; 0.8342] | 0.1222 | 0.3495 | | | | | |
| Brazil | 27 | 0.6003 | [0.4934; 0.7072] | 0.0789 | 0.2808 | | | | | |
| Sudan | 1 | 0.4041 | [0.3478; 0.4604] | – | – | | | | | |
| Burundi | 1 | 0.7638 | [0.7221; 0.8055] | – | – | | | | | |
| Philippines | 4 | 0.568 | [0.2256; 0.9104] | 0.1177 | 0.3431 | Between groups | 7007.71 | 42 | 0 | |
| Tunisia | 4 | 0.2247 | [0.0490; 0.4005] | 0.0317 | 0.178 | | | | | |
| Turkey | 7 | 0.3267 | [0.2079; 0.4456] | 0.0249 | 0.1578 | | | | | |
| Algeria | 1 | 0.0401 | [0.0179; 0.0624] | – | – | | | | | |
| Ecuador | 3 | 0.8242 | [0.6346; 1.0000] | 0.0274 | 0.1654 | | | | | |
| Sri Lanka | 1 | 0.4332 | [0.3981; 0.4684] | – | – | | | | | |
| Iran | 3 | 0.4478 | [0.3981; 0.4976] | 0.0004 | 0.0212 | | | | | |
| Cuba | 1 | 0.5854 | [0.5320; 0.6387] | – | – | | | | | |
| Jordan | 1 | 0.2151 | [0.1316; 0.2986] | – | – | | | | | |
| Russia | 1 | 0.4194 | [0.2965; 0.5422] | – | – | | | | | |
| Iraq | 4 | 0.3451 | [0.1215; 0.5687] | 0.0504 | 0.2244 | | | | | |
| Mongolia | 1 | 0.511 | [0.4596; 0.5623] | – | – | | | | | |
| Zambia | 1 | 0.2575 | [0.2080; 0.3071] | – | – | | | | | |
| Uganda | 4 | 0.476 | [0.0761; 0.8759] | 0.1659 | 0.4073 | | | | | |
| Korea | 2 | 0.0474 | [0.0041; 0.0907] | 0.0009 | 0.0301 | | | | | |
| Malaysia | 4 | 0.6915 | [0.5469; 0.8361] | 0.0195 | 0.1398 | | | | | |
| Colombia | 1 | 0.5482 | [0.5224; 0.5740] | – | – | | | | | |
| South Africa | 1 | 0.5667 | [0.5240; 0.6094] | – | – | | | | | |
| Afghanistan | 1 | 0.1883 | [0.1581; 0.2086] | – | – | | | | | |
| Kenya | 2 | 0.4141 | [0.1761; 0.6520] | 0.0286 | 0.1692 | | | | | |

| | | | | | | | | | |
|-------------|----|--------|------------------|---------|--------|----------------|---------|----|---|
| Madagascar | 1 | 0.8972 | [0.8565; 0.9379] | - | - | | | | |
| Venezuela | 1 | 0.4588 | [0.3529; 0.5648] | - | - | | | | |
| Italy | 2 | 0.7398 | [0.3700; 1.0000] | 0.0704 | 0.2652 | | | | |
| Costa Rica | 2 | 0.6184 | [0.1365; 1.0000] | 0.1206 | 0.3473 | | | | |
| Canada | 2 | 0.0191 | [0.0118; 0.0265] | <0.0001 | 0.0049 | | | | |
| Hungary | 1 | 0.92 | [0.8586; 0.9814] | - | - | | | | |
| Morocco | 1 | 0.2186 | [0.1872; 0.2499] | - | - | | | | |
| Mozambique | 2 | 0.6984 | [0.5657; 0.8311] | 0.0088 | 0.0939 | | | | |
| Cameroon | 1 | 0.0229 | [0.0101; 0.0357] | - | - | | | | |
| Year | | | | | | | | | |
| 2023 | 2 | 0.3454 | [0.1242; 0.5665] | 0.0243 | 0.1558 | | | | |
| 2022 | 15 | 0.276 | [0.1134; 0.4386] | 0.103 | 0.3209 | | | | |
| 2021 | 19 | 0.318 | [0.2128; 0.4232] | 0.054 | 0.2324 | | | | |
| 2020 | 15 | 0.3317 | [0.1959; 0.4675] | 0.0712 | 0.2668 | | | | |
| 2019 | 19 | 0.3894 | [0.2777; 0.5010] | 0.0608 | 0.2465 | | | | |
| 2018 | 17 | 0.3969 | [0.2582; 0.5357] | 0.0842 | 0.2902 | | | | |
| 2017 | 8 | 0.3166 | [0.1309; 0.5023] | 0.0712 | 0.2668 | | | | |
| 2016 | 11 | 0.537 | [0.3434; 0.7306] | 0.1058 | 0.3253 | | | | |
| 2015 | 11 | 0.3406 | [0.2189; 0.4622] | 0.0415 | 0.2038 | | | | |
| 2014 | 12 | 0.3741 | [0.1914; 0.5567] | 0.1023 | 0.3199 | | | | |
| 2013 | 6 | 0.4413 | [0.2057; 0.6769] | 0.0836 | 0.2891 | | | | |
| 2012 | 8 | 0.4993 | [0.2509; 0.7477] | 0.1273 | 0.3568 | | | | |
| 2011 | 2 | 0.5689 | [0.1841; 0.9538] | 0.0768 | 0.2772 | | | | |
| 2010 | 3 | 0.4794 | [0.0000; 0.9831] | 0.1981 | 0.4451 | Between groups | 4428.49 | 26 | 0 |
| 2009 | 2 | 0.3998 | [0.2116; 0.5880] | 0.0176 | 0.1326 | | | | |
| 2008 | 1 | 0.6829 | [0.6248; 0.7411] | - | - | | | | |
| 2007 | 2 | 0.6726 | [0.4336; 0.9117] | 0.029 | 0.1704 | | | | |
| 2006 | 1 | 0.5535 | [0.5151; 0.5919] | - | - | | | | |
| 2005 | 2 | 0.8101 | [0.4579; 1.0000] | 0.0643 | 0.2536 | | | | |
| 2004 | 1 | 0.0037 | [0.0021; 0.0053] | - | - | | | | |
| 2002 | 1 | 0.1327 | [0.0655; 0.1998] | - | - | | | | |
| 1998 | 1 | 0.6426 | [0.5813; 0.7038] | - | - | | | | |
| 1997 | 1 | 0.0761 | [0.0687; 0.0834] | - | - | | | | |
| 1994 | 1 | 0.117 | [0.1126; 0.1214] | - | - | | | | |
| 1991 | 1 | 0.0229 | [0.0101; 0.0357] | - | - | | | | |
| 1987 | 1 | 0.1212 | [0.0425; 0.2000] | - | - | | | | |
| 1966 | 1 | 0.0233 | [0.0180; 0.0286] | - | - | | | | |

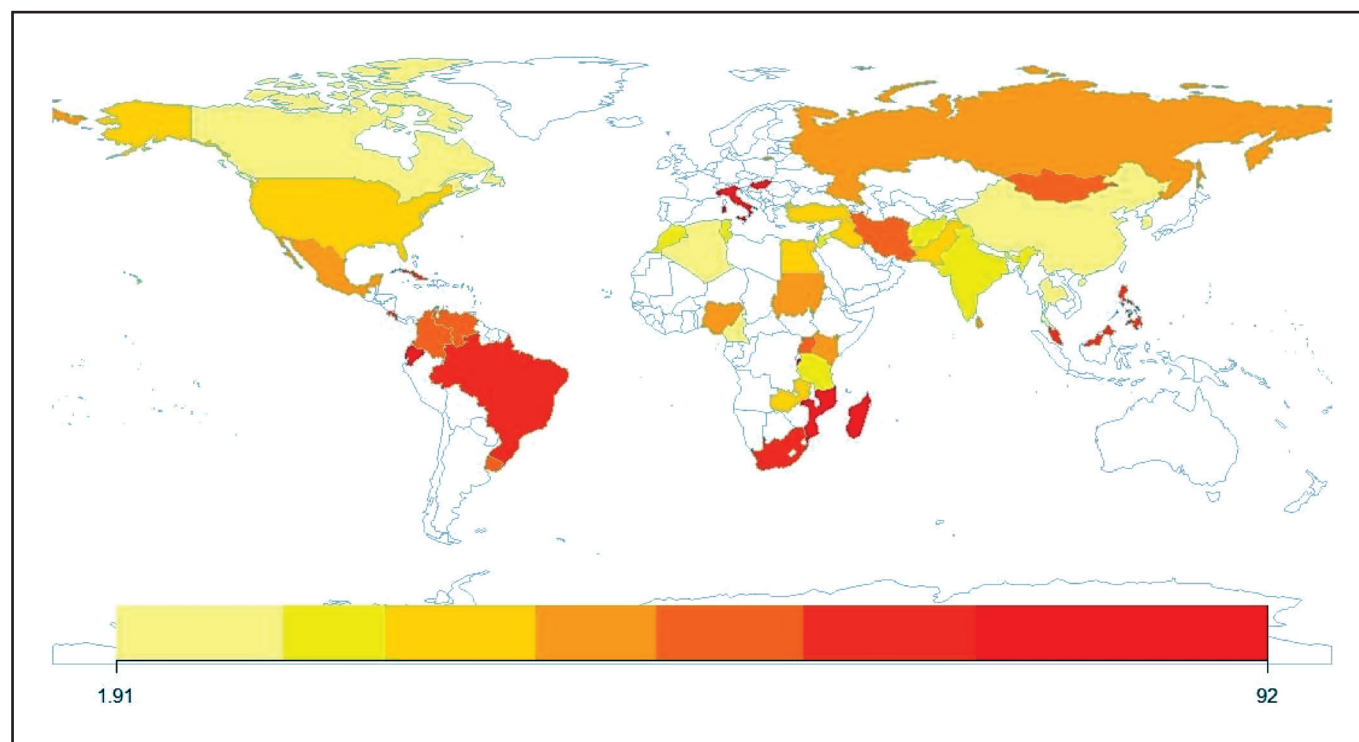


Figure 4. Estimation of bovine anaplasmosis global prevalence. The color scheme used indicates higher prevalence rates with red and lower rates with pale yellow.

The meta-analysis study involves the integration of findings from multiple studies conducted by different researchers to generate a single estimate that possesses strong statistical power. This analytical tool is crucial for obtaining a numerical value that accurately reflects the collective results of the studies (Wiernik & Dahlke, 2020). The data used in this study was obtained through a systematic review of scientific publications on the prevalence of bovine anaplasmosis spanning from 1911 to 2023. The meta-analysis demonstrated significant heterogeneity, as evidenced by I^2 values of 100%. This suggests that the majority of the variation among effect sizes is due not to sampling error, but rather by true heterogeneity between the studies (Higgins & Thompson, 2002). In an ideal scenario, a meta-analysis should pool together the findings of numerous studies that share similar characteristics in terms of study design, patient population, and intervention. These individual studies display comparable patterns in their outcomes but may not possess enough statistical power to provide a conclusive outcome (Melsen *et al.*, 2014). In reality, the studies involved in meta-analysis may not necessarily have similar characteristics, making it challenging to draw conclusive outcomes. Heterogeneity in meta-analysis studies were caused by various factors including study design, the population included in the study, the treatment strategies used, and the outcomes measured. The variability of factors can potentially affect the study result and caused a high heterogeneity in the meta-analysis study (Hoaglin, 2014; Melsen *et al.*, 2014). The significant heterogeneity observed in this meta-analysis study is likely attributed to the differences in study design, animal species, and diagnostic techniques utilized across the various studies.

In general, subgroup analyses can be useful in identifying potential sources of heterogeneity and providing insights into the variability of the results across different studies. It is important to ensure that the subgroups are defined a priori and that the analyses are appropriately powered to detect differences between subgroups (Lesko *et al.*, 2018). In this current study, the subgroup meta-analysis revealed a high heterogeneity (99.9%) with the estimated variance of the true effect across studies suggesting that the high I^2 are due to heterogeneity rather than chance. This study reveals a high pooled prevalence of bovine anaplasmosis were detected in cattle (39.9%) and combination of prevalence in cattle and buffalo (34.5%).

Cattle are more frequently exposed to ticks as the vectors for *A. marginale*, as they are often raised in large herds, which increases the risk of disease transmission (Zabel & Agosto, 2018) hence may be more susceptible compared to the other bovine species. In addition, the tick vectors for *A. marginale* are more commonly found in the tropical and subtropical regions where cattle are raised (Abdisa, 2019).

Factors such as breed, age, and immune status can all affect an animal's susceptibility to the disease (Smith, 2015; Das *et al.*, 2022). Some breeds of cattle may be more susceptible to infection than others, and younger animals may be more vulnerable to the disease (Abdisa, 2019). The severity of the disease may also vary between bovine species. Recent findings show that co-infection of *A. marginale* with the other haemoparasite species such as *Babesia bigemina* and *Theileria orientalis* affected the milk yield and body weight of Mafriwal cattle (Nur-Sabrina *et al.*, 2023). While all infected animals may show some symptoms, cattle may develop more severe and persistent anaemia as a result of *A. marginale* infection (Aubry & Geale, 2011). This can lead to reduced productivity and even death, making bovine anaplasmosis a significant concern for the cattle industry.

Unlike the systematic review and meta-analysis study previously conducted by Jacob *et al.* (2020), this study performed a systematic review and meta-analysis on individual basis for each country. In this study, country subgroup analysis shows the highest prevalence of bovine anaplasmosis in Hungary with the prevalence of 92.0%. Nonetheless, the country with a higher number of studies may have

a lower pooled prevalence due to the potential of mixed results from a greater number of studies. This is because the results of individual studies can vary depending on factors such as sample size, study design, and population characteristics. From the review, Brazil is the leading country on publication of bovine anaplasmosis (27/164), with the pooled prevalence of 60.0%. Brazil has a tropical and subtropical climate that is suitable for the survival and reproduction of ticks, which are the primary vectors for *A. marginale*, the pathogen that causes bovine anaplasmosis (Souza *et al.*, 2013). The humid and warm climate in many parts of Brazil also creates favourable conditions for the growth of vegetation, which provides an ideal habitat for ticks. Moreover, Brazil is one of the largest producers of beef and dairy products in the world, and cattle are often raised in large herds on extensive grazing systems (Berndt & Tomkins, 2013; Hairgrove *et al.*, 2014; Greenwood, 2021). This type of production system exposes cattle to a higher risk of tick infestation and, therefore, an increased risk of anaplasmosis.

Based on the meta-analysis, the diagnosis methods of bovine anaplasmosis are mainly molecular, accounting for 60.36% (99/164) of all publication. However, a higher prevalence of bovine anaplasmosis can be observed through a serological method as these tests detect antibodies produced by the animal's immune system in response to infection with *A. marginale*. When an animal is infected with bovine anaplasmosis, its immune system produces specific antibodies to fight the infection. These antibodies can be detected in the animal's blood using serological tests, such as the indirect fluorescent antibody test (IFAT) or enzyme-linked immunosorbent assay (ELISA) (Aubry & Geale, 2011). Serological tests are useful for screening large populations of animals for the presence of the disease, as they are relatively quick, simple, and cost-effective. However, it is important to note that seropositivity (positive serological test results) does not always indicate active infection (Gwida *et al.*, 2011; Solano-Gallego *et al.*, 2014). Animals that have been previously exposed to *A. marginale* may continue to produce antibodies even after the infection has been cleared, which can result in false positives. Therefore, while serological tests can provide valuable information about the prevalence of bovine anaplasmosis in a population, they should be used in conjunction with other diagnostic methods, such as molecular methods or clinical observation, to accurately diagnose active infections and monitor the disease's progression (Shabana *et al.*, 2018; Garcia *et al.*, 2022). Although microscopic examination using Giemsa stain is convenient for the detection of bovine anaplasmosis, it is not sensitive enough or sufficiently specific to detect chronic carriers of piroplasm infections, particularly when mixed infections occur (Madzimure *et al.*, 2011). A comprehensive approach to detect bovine anaplasmosis in both temperate and tropical countries would involve a combination of diagnostic methods to ensure accurate and reliable results. According to the data, diagnosis of bovine anaplasmosis in both temperate and tropical countries were mostly based on molecular method, while the least used method was blood smearing. Implementation of routine testing programs that combine microscopic examination on blood smears supported by findings from molecular assays such as polymerase chain reaction (PCR) and/or serology tests such as enzyme-linked immunosorbent assay (ELISA) are recommended to diagnose bovine anaplasmosis. It is important to note that the choice of diagnostic tool may vary based on factors such as the level of infection, available resources, expertise, and the purpose of testing (individual diagnosis, population surveillance).

Although bovine anaplasmosis has a significant impact on the health of livestock as well as causing production losses, it has not received sufficient attention globally in terms of control measures (Aubry & Geale, 2011). An integrated approach is ideally required for controlling bovine anaplasmosis, involving vector control, chemotherapy, and immunoprophylaxis, in addition to utilizing the potential of endemic stability. Moreover, managing grazing practices

to create an unfavourable ecological environment for the growth and spread of ticks has shown some promises (Zabel & Agosto, 2018).

The occurrence and spread of *Anaplasma* spp. are significantly influenced by the presence of vectors, carrier animals, and reservoir hosts. Vectors are organisms that transmit pathogens between hosts, carrier animals are individuals infected with a pathogen without showing symptoms, and reservoir hosts are species that naturally maintain a pathogen, serving as a source of infection for other species (Miller *et al.*, 2014, Tucker *et al.*, 2016). Understanding the roles of vectors, carriers, and reservoir hosts is crucial for controlling and preventing the spread of bovine anaplasmosis in the populations.

Bovine anaplasmosis is endemic in many regions across the world causing economic losses in bovine industries worldwide; however, treatment with therapeutic drugs like tetracycline compound along with supportive care leads to excellent recovery in the majority of clinical cases (Aubry & Geale, 2011; Kumar *et al.*, 2015; Paramanandham *et al.*, 2019). The identified carrier animals should be isolated or culled from the herd to reduce the potential source of infection (Teshome & Addis, 2019). Ticks and other biting arthropods can be routinely controlled by using pesticide dips and sprays, hence aiding to reduce the vector's population. Additionally, the cattle must be kept away from the reservoir particularly among the wildlife by providing a proper fencing around the farm.

Transmission through contaminated needles and surgical instruments must be avoided to control bovine anaplasmosis. Environmental management also plays a critical role in controlling bovine anaplasmosis by creating conditions less conducive to the disease such as routine cleaning of farm areas including hutches, stables, pens, feed and water troughs as well as proper manure managements to control the vector's population (Aubry & Geale, 2011; Paramanandham *et al.*, 2019).

Short-duration rotational grazing can be considered to prevent bovine anaplasmosis because of its potential cost-effectiveness and the ability to control vector loads especially in tropical region (Rapiya *et al.*, 2019). In addition, vaccination is an important tool in controlling and preventing bovine anaplasmosis. According to a study by Curtis *et al.* (2020), calves showed noticeably less clinical indications of anaplasmosis when the vaccine was administered using a combination of adjuvants rather than a single adjuvant in a single-dose delivery platform. Nonetheless, the optimal vaccine combination should be determined by further research.

Based on our knowledge, to this date, this is the first study that represents a systematic review and meta-analysis on anaplasmosis focusing on bovine species including cattle, buffalo, and yak. This systematic review and meta-analysis of bovine anaplasmosis provides an overview on the prevalence estimates in a global perspective. This review will contribute to the existing knowledge by synthesizing data from multiple studies and identifying research gaps. The pooled estimated prevalence revealed a lack of research in some regions including the ASEAN countries, South American, African and European countries. Thus warrants a need to study the prevalence of bovine anaplasmosis in those countries to understand the epidemiology of the disease at a precise global scale.

Conflict of interests

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.

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