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A systematic review on the seroprevalence and global distribution pattern of paratuberculosis in small ruminant and deer herds

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ABSTRACT

Paratuberculosis, also known as Johne's disease, is a chronic wasting disease caused by *Mycobacterium avium subs paratuberculosis* (MAP) in ruminants. Paratuberculosis causes a significant reduction of milk production in the affected dairy sheep or goats and increase the cost of diagnosis, treatment, and culling of the infected animals. Paratuberculosis is currently recognised as a disease of major economic significance in cattle, sheep, goats, and wild ruminants globally. Recent reports also suggest that paratuberculosis affects wild ruminants and farmed deer. Despite the widespread occurrence of MAP, there are variations in the seroprevalence and global distribution patterns of disease among small ruminants and deer herds due to the influence of interacting epidemiological variables in different places. This systematic review aims to provide insights on the current global seroprevalence status and distribution pattern of paratuberculosis among small ruminants and deer herds. The review compiled, analyzed, and narratively synthesized 36 eligible research articles published between January 1, 2010, and January 31, 2024, from the SCOPUS and PubMed databases based on the 22-point Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist. The average global seroprevalence of paratuberculosis in sheep was 14.02% (0.7-66.8), with the highest rate in Canada (66.8%) and the lowest in Austria (0.7%). Comparatively, the average global seroprevalence in goats was 18.44% (0.3-83), with the highest rate in Canada (83%) and the lowest in the West Indies (0.3%). The average global prevalence of paratuberculosis in deer was 14.76% (3.7-30.2), with the highest rate in Spain (30.2%) and the lowest rate in the Czech Republic (3.7%). This review revealed that Canada is a hot spot for both caprine and ovine paratuberculosis and there was a higher global seroprevalence rates in goats than sheep and deer. The lack of data on the seroepidemiology of paratuberculosis among small ruminant stock in Southeast Asia and other regions is a gap in our current knowledge of its distribution. Therefore, seroprevalence surveys of paratuberculosis among the small ruminant and deer livestock are required to furnish information for planning suitable interventions in these areas.

Introduction

Paratuberculosis (also known as Johne's disease) is a chronic, contagious disease of the intestinal tract caused by *Mycobacterium avium subs paratuberculosis* (MAP) in domestic and wild ruminant (Barrero-Domínguez *et al*., 2019). The organism is a small gram-positive and acid-fast staining bacteria which causes chronic granulomatous gastroenteritis and regional lymphadenitis in the host tissues (Stau *et al* 2012). It is shed in the faeces and persists in the environment for several months, impeding prevention and control efforts (Stonos *et al*., 2017). Infection of animals occurs via the oral route by ingestion of contaminated colostrum and milk from the infected dam (Smith *et al*., 2013) or contaminated feed in older animals (Selim *et al*., 2021). Zoonotic transmission from animal to human hosts occurs via water and foodborne routes, with a higher risk of foodborne exposure in children and immunocompromised patients (Garvey, 2018). Paratuberculosis has a chronic course and generally takes up to two years before animals show clinical symptoms of progressive weight loss, exercise intolerance, diarrhoea, and diminished milk production (Barrero-Domínguez *et al*., 2019).

Outbreaks of paratuberculosis are associated with significant economic losses due to diminished milk production and high cost of controlling disease (Sardaro *et al*., 2017; Garvey, 2020). Moreover, paratuberculosis further presents challenges due to unreliability of diagnostic tests for early detection of subclinical infections because of low sensitivity (Idris *et al*., 2022). Despite the global spread of MAP among cattle and the potential for cross-sepecies transimission to small ruminants (Garvey, 2018), sheep and goats are rarely screened for MAP. Additionally, prevalence and incidence data systematic reviews are gaining importance because they provide situation analysis on disease exposure among herds and help to inform policy makers in decisions towards effective control efforts. Therefore, this literature review appraised the current global seroprevalence status and distribution of MAP among small ruminant and deer population, inorder to gain further insights on its global impact and stimulate policy towards effective control. The research question addressed by this review is: "what is the current global seroprevalence and distribution pattern of paratuberculosis among sheep, goat, and deer populations?".

Materials and methods

Study design

This study was designed following the updated Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline for reporting systematic reviews 2020 (Page *et al*., 2021). All accessible original peer reviewed research articles published in the English Language on the seroprevalence of MAP in sheep, goats, or deer populations from January 1, 2010 to January 31, 2024 were considered eligible for inclusion in this systematic review. The scope of review included all cross-sectional epidemiological studies that used probability sampling, in sheep, goats, or deer population, which employed standard serological screening tests such as ELISA, CFT, AGID, or Haeameagglutination, to detect MAP antigens or antibodies.

Search strategy, inclusion criteria, and data quality control

A strategic search was conducted in the SCOPUS and PubMed databases based on the Condition, Context, and Population (CoCoPop) search terms, to identify relevant literatures (Munn *et al*., 2015, 2018). Based on this strategy, studies involving all age groups, gender and breeds of sheep, goat, or deer were considered. Seroprevalence was defined as the proportion of sheep, goats, or deer in a herd testing positive for paratuberculosis based on serological detection techniques.

In total 1200 research articles matching the search criteria were initially dowloaded for the databases. Preliminary screening of the titles revealed that there were 401 duplicates which were eliminated. Further

Table 1. Global seroprevalence of MAP among sheep, goats, and deer livestock.

Species	Country	% Seropositive	Reference
Sheep	Austria	0.7	Ebani *et al*. (2023).
	Canada	66.8	Bauman *et al*. (2016).
	Colombia	8	Hernández-Agudelo *et al*. (2021).
	Cyprus	9.9	Liapi *et al*. (2011).
	Germany	15	Stau *et al*. (2012).
	Iran	15.4	Pourmahdi Borujeni *et al*. (2021).
	Italy	6.2	Rita *et al*. (2011).
	Italy	2.8	Iarussi *et al*. (2019).
	Italy	15.1	Rita *et al*. (2011).
	Mexico	7.48	Morales-Pablos *et al*. (2020).
	Morocco	29.2	Benazzi *et al*. (1996).
	Portugal	3.7	Coelho *et al*. (2007).
	Saudi Arabia	11.1	Shabana and Aljohani (2020).
	Saudi Arabia	19.5	Elsohaby *et al*. (2021).
	South Africa	3	Michel *et al*. (2017).
	Spain	8.1	Jiménez-Martín *et al*. (2022).
	Tunisia	3.25	Khamassi Khbou *et al*. (2020).
	Turkey	6.2	Buyuk *et al*. (2014).
	Turkey	48	Celik and Turutoglu (2017).
	West Indies	2.3	Kumthekar *et al*. (2013).
Goats	Austria	2	Ebani *et al*. (2023).
	Brazil	0.82	Freitas *et al*. (2015).
	Canada	83	Bauman *et al*. (2016).
	Cyprus	7.9	Liapi *et al*. (2011).
	France	2.9	Mercier *et al*. (2010).
	Germany	21	Stau *et al*. (2012).
	India	63.5	Singh *et al*. (2013).
	Iran	15.9	Pourmahdi Borujeni *et al*. (2021).
	Italy	6.8	Galiero *et al*. (2017).
	Italy	10	Cecchi *et al*. (2019).
	Italy	15.7	Iarussi *et al*. (2019)
	Korea	0.8	Kim *et al*. (2015).
	Mexico	20	Martínez-Herrera *et al*. (2012).
	Portugal	50	Mendes *et al*. (2004).
	Saudi Arabia	13.8	Shabana and Aljohani (2020).
	Saudi Arabia	17.1	Elsohaby *et al*. (2021).
	Spain	22.5	Barrero-Domínguez *et al*. (2019).
	Spain	20	Jiménez-Martín *et al*. (2022).
	Tanzania	10.9	Mpenda and Buza (2014).
	Thailand	13.3	Rerkyusuke *et al*. (2018).
	Turkey	24	Celik and Turutoglu (2017).
	USA	1.9	Pithua and Kollias (2012).
	West Indies	0.3	Kumthekar *et al*. (2013).
Deer	China	17.6	Meng *et al*. (2015).
	Czech Republic	3.7	Kopecna *et al*. (2008).
	India	6.3	Budhe *et al*. (2014).
	Mexico	16	Lozano-Cavazos *et al*. (2021).
	Spain	30.2	Reyes-García *et al*. (2008).

assessment of the titles and abstracts for the remaining 799 records was conducted to carefully filter and select only cross sectional epidemiological studies reporting the seroprevalence of MAP in small ruminants or deer. At this stage, we excluded 701 studies and proceeded with further assessment of full texts of the selected 98 articles for completeness by following the 22-point Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist (Cuschieri, 2019) and the Joan Briggs Institute's critical appraisal checklist for studies reporting prevlence data (Munn *et al*., 2015). We further excluded studies based on non serological detection methods (n=21), descriptive studies (n=33), reviews (3), case reports (n=4), and book chapter (n=1). Two independent investigators were involved in screening and selecting research articles to minimise selection bias. Information extracted by the first investigator was further scrutinized for data entry errors, and all discrepancies in entries were resolved following a consensus between the two investigators.

Data extraction and processing

Since there were no articles with comparable numerical values to permit a quantitative analysis, the literatures were synthesised narratively. The required information including geographical location, size of the study population, sample size, study period, target population (sheep, goat, or deer), diagnostic tests, and the prevalence rate was extracted from eligible papers and stored in a Microsoft Excel spreadsheet Program 2024. Summarized seroprevalence data was presented descriptively as proportions reported using evidence tables and the global distribution was presented on a point distribution map constructed using Maptive® web-based mapping software.

Results

Characteristics of the eligible studies

A total of 36 research articles were included in this systematic review. All the articles were cross-sectional epidemiological studies that reported the seroprevalence of paratuberculosis based on the results of serological tests using serum or faecal samples from small ruminants and deer herds. The thirty-three studies considered in this review were carefully selected from a pool of published research on paratuberculosis based on a predetermined set of selection criteria (Figure 1).

Global distribution on seroprevalence of MAP in small ruminants and deer

Geographically, the occurrence of paratuberculosis in small ruminants was reported in 27 countries form Africa (Egypt, Morocco, Tanzania, Tunisia), Asia (China, India, Iran, Korea, Saudi Arabia, Thailand), Europe (Austria, Brazil, Cyprus, France, Germany, Italy, Portugal, Spain, and Türkiye), North America (Canada, US, Mexico, West Indies), and South America (Brazil and Colombia) (Figure 2). However, only China, Czech Republic, India, Mexico, and Spain have reported the occurrence of paratuberculosis among deer globally.

Prevalence and distribution of paratuberculosis among small ruminants and dear

The global seroprevalence status of MAP among sheep, goats, and deer livestock is presented in Table 1. Among the 36 articles that met the inclusion criteria for this study, 20 articles from 16 countries reported the seroprevalence of MAP among sheep flocks, 24 articles from 19 countries reported the seroprevalence of MAP among goat flocks, while 5 articles from 5 countries reported the seroprevalence of MAP among deer livestock. The global average seroprevalence of MAP in sheep was found to be 14.02% (0.7-66.8) with the highest prevalence rate in Canada (66.8%) and the lowest in Austria (0.7%). The average global seroprevalence of MAP in goats was found to be 18.44% (0.3-83), with the highest seroprevalence in Canada (83%) and the lowest in the West Indies (0.3%). The average global seroprevalence of MAP in deer herds was found to be 14.76% (3.7-30.2) with the highst seroprevalence in red deer from Spain (30.2%) and the lowest in the Czech Republic (3.7%).

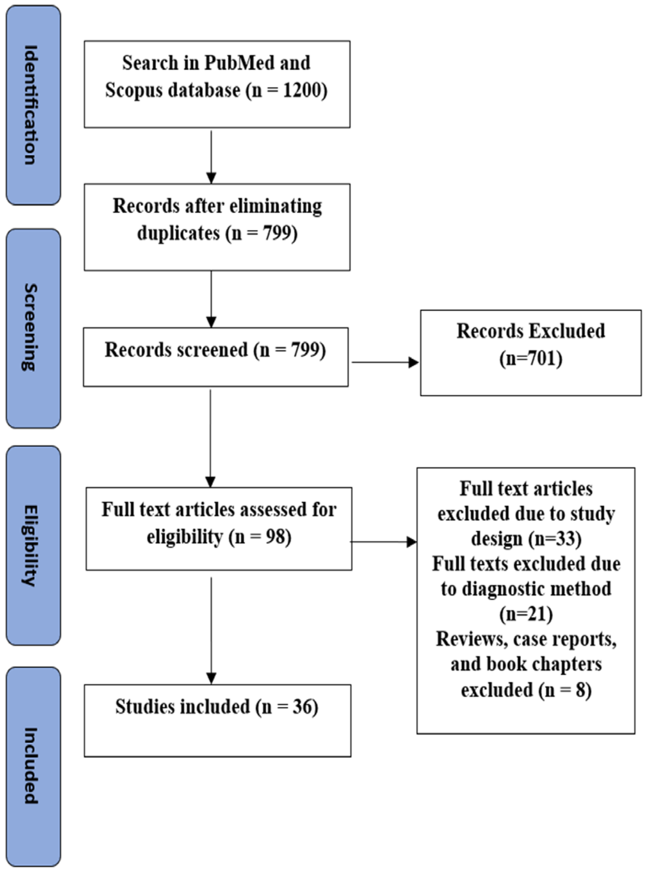

Figure 1. Flow diagram of inclusion criteria and selection of studies in the review.

Figure 2. Global distribution map of paratuberculosis in small ruminants.

Discussion

This literature review appraised the current global seroprevalence status and distribution of MAP among small ruminant and deer population, inorder to provide further insights on its global impact and stimulate policy towards effective control. The review addresssed the research question: "what is the current global seroprevalence and distribution pattern of paratuberculosis among sheep, goat, and deer populations?." In attempting to answer the research question, we found that the average global seroprevalence of MAP was 18.44, 14.02, and 14.76 among goats, sheep, and deer, respectively. The results further showed the highest recorded prevalence rates were 83%, 66.8%, and 30.2% in goat, sheep, and deer. This review has shown that paratuberculosis is distributed at high prevalence rates wherever sheep, goats, and deer are raised (Benazzi *et al*., 1995; Hailat *et al*., 2010; Rasmussen *et al*., 2021). Since the first outbreak of paratuberculosis among European dairy cows in 1895 (Dhand *et al*., 2013), it gained rapid global recognition as a major disease of great economic importance to sheep and goat producers. The presence of high seroprevalence of MAP among the various livestock species may have several economic consequesnces to livestock producers and consumers. Major economic losses due to paratuberculosis are linked to decreased milk production, progressive wasting, and the cost of controlling disease due to culling, trade restrictions, and carcass condemnation at slaughter (Sardaro *et al*., 2017; Garvey, 2020). Although all domestic and wild ruminants are susceptible to MAP infection, it has been observed that goats are naturally more susceptible to disease than sheep and cattle (Idris *et al*., 2022). Thus, the higher seropositivity observed in the goats may be related to their behavioural and physical peculiarities. The high seroprevalence of MAP in both the dairy goat and sheep farms in Canada was attributed to a lack of voluntary paratuberculosis control program for sheep and goats in the country (Bauman *et al*., 2016). A significant positive association between animals that tested positive for SRLV and animals positive for MAP by fecal culture was also identified among Canadian goat flocks, suggesting that the prevalence of SRLV may increase the risk of MAP infection among Canadian livestock (Stonos *et al*., 2017).

Although very few studies have reported the seroprevalence of paratuberculosis in farmed deer globally, the current average global seroprevalence rate of 14.76% (3.7-30.2) is epidemiologically significant. According to a joint report published by the Center for Food Security and Public Health (CFSPH) and The United States Department of Agriculture, Animal and Plant Health Inspection Service (USDA APHIS), the host range of MAP now includes a wide range of wild ruminants such as the moose, reindeer, bison, bighorn sheep, Rocky Mountain goats, various species of deer, antelope and elk. The potential role of deer as reservoirs of MAP for other susceptible species of farm animals should be investigated in certain countries such as Argentina, Austria, Italy, Mexico, Slovenia, South Africa, United Kingdom, and Venezuela, where notification is not required for camelids and deer (Whittington *et al*., 2019).

This study revealed that there was no specific published research on the serological status of MAP among small ruminants and deer livestock in most of Southeast Asian countries. However, isolated cases have been documented by the Veterinary Research Institute as part of routine disease monitoring activity of the Department of Veterinary Services Malaysia. According to a study based on the surveillance data of various livestock species, out of 168 suspected cases (with an average one case per year) recorded over a 17-year period (from 2001-2018), the highest number was in 2001 (n = 94), followed by 2003 (n = 42), and 2004 (n = 15), among which only 2 (0.11% (0.01 to 1%) were confirmed positive for paratuberculosis by PCR (Chin *et al*., 2014; Roselizar *et al*., 2019). One possible reason for the lack of data on paratuberculosis may be because the region is not a major small ruminant producer compared to neighbouring New Zealand and Australia. Another reason may be due to the cryptic nature of the MAP organism, which is a slow-growing bacterium and may take up to 2 years of incubation period before clinical manifestations. Moreover, routine diagnosis by bacterial isolation and identification technique usually yields only 10 - 50% success rates due to dormancy phase of MAP, which makes it unreliable in diagnosis (Sonawane and Tripathi, 2019). The advanced molecular detection of the IS900 gene by PCR which yields 80-85% sensitivity (Sonawane and Tripathi, 2019) and up to 90-100% (Gwóźdź *et al*., 1997) are very expensive. These challenges are major drawbacks in screening and surveillance efforts against paratuberculosis among the small ruminant population in many low and midle income countries.

Generally paratuberculosis has a notifiable status regardless of the animal species in Australia, Finland, Norway and Sweden and in all of the farmed species present in 32 other countries worldwide (Whittington *et al*., 2019). From results of this literature review, it is essential to conduct a holistic screening to determine the seroprevalence of paratuberculosis the ruminant and deer populations in all countries with ruminant livestock as main commodities. Because MAP infects a wide spectrum of animals including cattle, sheep, goats, deer, camelids, and wild ruminants, cross-contamination may occur between domestic and wild ruminants. Therefore, serological data on wildlife is required for implementing sustainable control to avoid spillover of infection from wild animals into the domestic animal population.

Conclusion

This systematic review reveals a deficit in research data on the seroprevalence status of MAP infection among small ruminant and deer livestock. Special emphasis must be given for Southeast Asian countries due to a complete lack of published data.

Conflict of interest

The authors declare that they have no conflict of interest.

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