Journal of Medical Microbiology and Infectious Diseases

JoMMID
ISSN: 2345-5349
eISSN: 2345-5330

Potential Zoonotic Disease Transmission from Macaques to Human in Ecotourism Areas: A Systematic Review

Sepriyoga Virdana[1], Rizaldi[1]*, Rita Maliza[1]

[1]Department of Biology, Faculty of Mathematics and Natural Sciences, Andalas University, Padang, 25163, Indonesia

ARTICLE INFO

Systematic Review

Keywords: Zoonotic diseases, Macaques, Pathogen transmission, Ecotourism, Human-wildlife interaction, Public health management

Received: 17 Sep. 2023
Received in revised form: 07 Oct. 2024
Accepted: 03 Nov. 2024
DOI: 10.61186/JoMMID.12.4.243

***Correspondence**
Email: rizaldi@sci.unand.ac.id
Tel/fax: +6285278222862

ABSTRACT

Introduction: Zoonotic diseases pose a significant public health threat, particularly in ecotourism areas where frequent human-macaque interactions increase the risk of pathogen transmission between species. Understanding these dynamics is crucial for safeguarding both human and animal health. This systematic review synthesizes research on the prevalence and transmission of zoonotic pathogens from macaques to humans in ecotourism settings. **Methods:** The review adhered to PRISMA guidelines, and a comprehensive literature search was conducted across PubMed, Web of Science, Scopus, Google Scholar, and Semantic Scholar to identify relevant publications. Seventeen studies published between 2000 and 2024 were rigorously evaluated. These studies investigated zoonotic disease transmission between macaques and humans in diverse ecotourism settings across eight countries. **Results:** The analysis revealed that viruses (42%) were the most frequently reported zoonotic pathogens transmitted from macaques to humans, followed by helminths (28%) and protozoa (26%). Transmission occurred through both direct and indirect pathways, including bites, scratches, physical contact, and exposure to contaminated surfaces or objects. **Conclusions:** The findings underscore the need for robust public health interventions, such as enhanced surveillance, vaccination programs, and hygiene protocols. Effective ecotourism management strategies should also incorporate educational programs for visitors on zoonotic risks, improved hygiene infrastructure, and strict regulations on human-macaque interactions, including maintaining safe distances and prohibiting feeding, to protect both human and animal health.

INTRODUCTION

Emerging infectious diseases represent a significant threat to global conservation efforts, particularly for vulnerable wildlife populations. An estimated 70-75% of these diseases originate in wildlife [1-3], with a substantial proportion, exceeding 60%, being zoonotic in nature [1, 4]. Non-human primates, particularly macaques, constitute a significant reservoir for zoonotic disease transmission. The increasing human population and the concomitant intensification of anthropogenic activities, such as deforestation, agriculture, and urbanization, within primate habitats elevate the probability of zoonotic pathogen spillover from primates to humans [5]. These primates represent significant reservoirs of pathogens that pose a notable risk to human health. This heightened risk is largely attributable to their considerable overlap with humans in genetic, physiological, and behavioral characteristics, including susceptibility to a range of shared pathogens. Furthermore, their propensity for close social interactions significantly facilitates pathogen transmission [6]. Importantly, approximately 25% of emerging infectious diseases in humans are estimated to have originated in primates, underscoring their critical role in zoonotic disease dynamics [7]. Ecotourism, characterized by close human-wildlife interactions, facilitates the transmission of zoonotic diseases. Macaques, owing to their high adaptability and frequent proximity to humans in ecotourism areas, represent a focal point of concern regarding potential zoonotic transmission. By way of illustration, African tick-bite fever (*Rickettsia africae*), the most prevalent tick-borne rickettsiosis, is a leading cause of post-travel fever in individuals returning from sub-Saharan Africa, second only to malaria [8]. Additionally, rabies transmission from non-human primates has been confirmed [9]. Conversely, research has demonstrated the bidirectional nature of pathogen transmission, with diseases also capable of being transmitted from humans to wildlife, a phenomenon termed reverse zoonosis or zooanthroponosis [10]. This phenomenon affects various vertebrate groups, with non-human primates being particularly susceptible [11]. Notable viral pathogens implicated in such reverse zoonotic transmission include rubella and measles [6].

Tourism-related activities, encompassing close encounters and physical interactions with macaques (*e.g*., feeding or provocation), significantly elevate the risk of interspecies pathogen transmission [12-15]. Ecotourists, particularly those originating from international or distant locales, pose a potential risk of introducing novel pathogens to macaques [11, 16]. Beyond rabies, a spectrum of other zoonotic pathogens have been identified in macaques and present a recognized risk to human health, notably including simian foamy virus (SFV), which has been identified in long-tailed macaques [16, 17]. SFV, though currently non-pathogenic in humans, has the potential to evolve into pathogenic variants, similar to the evolution of simian immunodeficiency virus (SIV) into HIV. While naturally acquired SFV infections in humans are currently considered non-pathogenic, a latent potential exists for SFV variants to evolve and acquire pathogenic properties in humans, paralleling the established evolutionary pathway of SIV to human immunodeficiency virus (HIV) [18]. Yong *et al*. (2013) provided compelling serological evidence of pathogen transmission from Tibetan macaques (*Macaca thibetana*) to humans. Their study was conducted at an ecotourism site on Mount Huangshan [19]. Serological analysis of 16 blood samples revealed the presence of antibodies against a panel of six viruses, with the following seroprevalence: Herpes B virus (6.3%), Hepatitis B virus (HBV; 12.5%), Simian foamy virus (SFV; 18.8%), Simian poxvirus (12.5%), Simian retrovirus (18.8%), and Simian T-cell lymphotrophic virus-1 (6.3%). This study unequivocally underscores the tangible potential for zoonotic pathogen spillover from macaques to humans within ecotourism environments.

The expansion of ecotourism, particularly activities involving close interactions with macaques, such as feeding, touching, or close proximity, significantly elevates the potential for zoonotic disease transmission. Macaques are recognized reservoirs for a range of zoonotic pathogens, including SIV, *Mycobacterium tuberculosis* (TB), and Herpes B virus (Cercopithecine herpesvirus 1). Transmission can occur via direct contact, such as bites and scratches, or through exposure to infected bodily fluids. Furthermore, the incidence of malaria caused by *Plasmodium knowlesi*, a zoonotic pathogen transmitted from macaques, has been notably increased in certain regions [20]. Additionally, enteroparasites and other gastrointestinal pathogens harbored by macaques represent a significant public health concern [21]. Collectively, these pathogens underscore the salient health risks inherent in close human-macaque interactions within ecotourism settings. Crucially, a comprehensive understanding of transmission dynamics is not only essential for mitigating human health risks but also for informing and implementing effective management strategies aimed at safeguarding the health and well-being of both human communities and macaques. However, while numerous studies have explored zoonotic disease transmission from diverse wildlife species within ecotourism settings, a comprehensive systematic review specifically focusing on macaque-to-human transmission in these contexts remains absent. Such a review is crucial for generating evidence-based recommendations for policymakers and ecotourism managers, offering actionable guidance on optimizing visitor behavior, enhancing hygiene protocols, and implementing effective macaque population management strategies to mitigate transmission risks. Consequently, this systematic review aims to synthesize and critically analyze the existing literature on the transmission of zoonotic diseases from macaques to humans within ecotourism environments. The findings of this review will significantly contribute to our understanding of the specific risks associated with human-macaque interactions in ecotourism and will inform the development and implementation of evidence-based strategies to minimize zoonotic disease transmission.

METHODS

Search strategy. A systematic literature search was conducted from March 7 to April 3, 2024, to identify relevant studies on zoonotic disease transmission from macaques to humans within ecotourism settings. The following electronic databases were searched: PubMed, Web of Science (Clarivate Analytics), Scopus (Elsevier), ScienceDirect (Elsevier), Google Scholar, and Semantic Scholar. The search strategy incorporated the following keywords and their combinations: 'zoonotic disease transmission from macaques to humans' AND 'human-macaque interface in ecotourism areas'. This review followed the PRISMA 2020 guidelines, including the use of a PRISMA flow diagram to document study selection and adherence to the four-phase process (identification, screening, eligibility, and inclusion) [22].

Eligibility criteria. The eligibility criteria for this systematic review were clearly defined to ensure the inclusion of studies specifically addressing zoonotic disease transmission between macaques and humans within ecotourism contexts. Studies were included if they were published between January 1, 2000, and December 31, 2024, and investigated zoonotic pathogens, including viruses, protozoa, helminths, and bacteria. Additionally, included studies employed observational or experimental research methodologies focusing on direct interactions (*e.g*., physical contact) or

[DOI: 10.61186/JoMMID.12.4.243]

indirect interactions (*e.g*., shared environments) between macaques and humans and were published in English. The geographical scope encompassed regions with macaque populations in ecotourism settings, such as Southeast Asia, South Asia, and other areas where macaques are present in national parks, nature reserves, zoological parks, urban areas with frequent human-macaque interactions (*e.g*., temple complexes or city parks), and cultural heritage sites.

Studies were excluded if they were conducted in laboratory settings without ecotourism-related contexts, involved captive macaques in settings unrelated to ecotourism (*e.g*., research facilities or private collections), or were non-primary research studies, such as reviews, opinions, or editorials. Studies not published in English were also excluded due to resource constraints and the widespread use of English in scientific literature.

Data extraction. All articles identified through the systematic search were imported into and subsequently de-duplicated within Microsoft Excel (version 2016). A standardized data extraction form was utilized to systematically extract the following information from each included study: study characteristics (author(s), publication year, article title, journal title, geographic location of the study, study design, data collection methods, sample size, sample type, and study period); the specific ecotourism context (*e.g*., type of protected area, level of human-macaque interaction, and implemented management practices); exposure variables, including the nature of human-macaque interactions (*e.g*., direct physical contact, bites, scratches, and potential environmental exposure routes); primary and secondary outcome measures, such as the type of zoonotic disease(s) identified, specific pathogens detected, reported incidence or prevalence rates, and other relevant epidemiological parameters; study quality assessment, including the specific quality assessment tool employed; and information regarding preventive measures, explicitly stating whether these measures were reported within the included studies or identified from external sources, along with detailed descriptions of the documented measures.

Data analysis. Descriptive statistical analyses were performed using Microsoft Excel based on the extracted data from the included studies. Data were extracted using a standardized form, including study design, sample size, geographical location, types of human-macaque interactions (*e.g*., feeding, touching), and prevalence of zoonotic diseases in both macaque and human populations. Study characteristics, such as study design, sample size, and geographical location, were summarized to contextualize the findings and identify patterns across studies. Extracted data were cross-checked by a second reviewer to ensure accuracy and consistency. A qualitative synthesis was conducted to categorize and summarize the identified zoonotic pathogens in macaques across various ecotourism settings, using thematic analysis. Ecotourism settings were defined as areas where tourism focuses on wildlife observation and conservation, including national parks, nature reserves, and cultural heritage sites. Visualizations, including bar charts and heat maps, were generated using Flourish Studio for its advanced data visualization capabilities, enabling the creation of interactive and publication-quality charts to illustrate the distribution and prevalence of zoonotic pathogens.

Ethics statement. This systematic review involved the analysis of publicly available, peer-reviewed literature and did not entail the collection of primary data from human participants or animals. Consequently, formal ethical approval was not deemed necessary for this study.

RESULTS

Study selection process and characteristics. The initial database searches yielded a total of 1902 records, which were screened for relevance based on title and abstract. Of these, 1000 were retrieved from CrossRef, 565 from Google Scholar, 141 from PubMed, 136 from Web of Science, 56 from ScienceDirect, and 4 from Semantic Scholar. Duplicates were identified and removed using reference management software, resulting in 213 unique articles for screening. After title and abstract screening, 213 articles were retained for further evaluation, of which 29 progressed to full-text review. A further six articles were excluded as they focused exclusively on behavioral interactions without identifying specific zoonotic pathogens (as detailed in Figure 1, PRISMA flow diagram). Comprehensive data on the types and prevalence of pathogens detected in each macaque species can be found in Table 1, which provide a detailed overview of the geographical distribution and pathogen diversity. Ultimately, 17 articles satisfied all inclusion criteria and were included in the final data extraction (see Table 2). This rigorous selection process ensured that only studies directly addressing zoonotic disease transmission between macaques and humans in ecotourism settings were included.

Description of included studies. A total of 17 studies met the inclusion criteria and were incorporated into the qualitative synthesis. The publication dates spanned from 2000 to 2024, with a distribution of three studies published between 2000 and 2010 and the remaining 14 published between 2011 and 2024, reflecting growing awareness of zoonotic risks in ecotourism areas. These 17 studies were conducted across eight countries, representing diverse ecological settings and anthropogenic settings (*e.g*., temples, national parks) with varying intensities of human-macaque interaction, ranging from occasional encounters to frequent physical contact. Thailand accounted for the highest number of studies (n=5), with research conducted in various settings, including temple complexes, national parks, and

[DOI: 10.61186/JoMMID.12.4.243]

urban areas, which are hotspots for close human-macaque interactions and potential pathogen spillover. China contributed four studies, predominantly focusing on national parks and zoological parks. Indonesia (n=2) and Nepal (n=2) each contributed studies conducted in national parks and prominent monkey temples, which attract large numbers of tourists and facilitate frequent human-macaque interactions. The remaining four countries each contributed a single study: Bangladesh (encompassing a sacred site frequented by tourists and an urban area with high human-macaque interaction), the Philippines (within a national park), Malaysia (at a cultural heritage site with high tourist visitation), and India (in a natural habitat adjacent to human settlements, where close interactions increase the risk of zoonotic spillover).

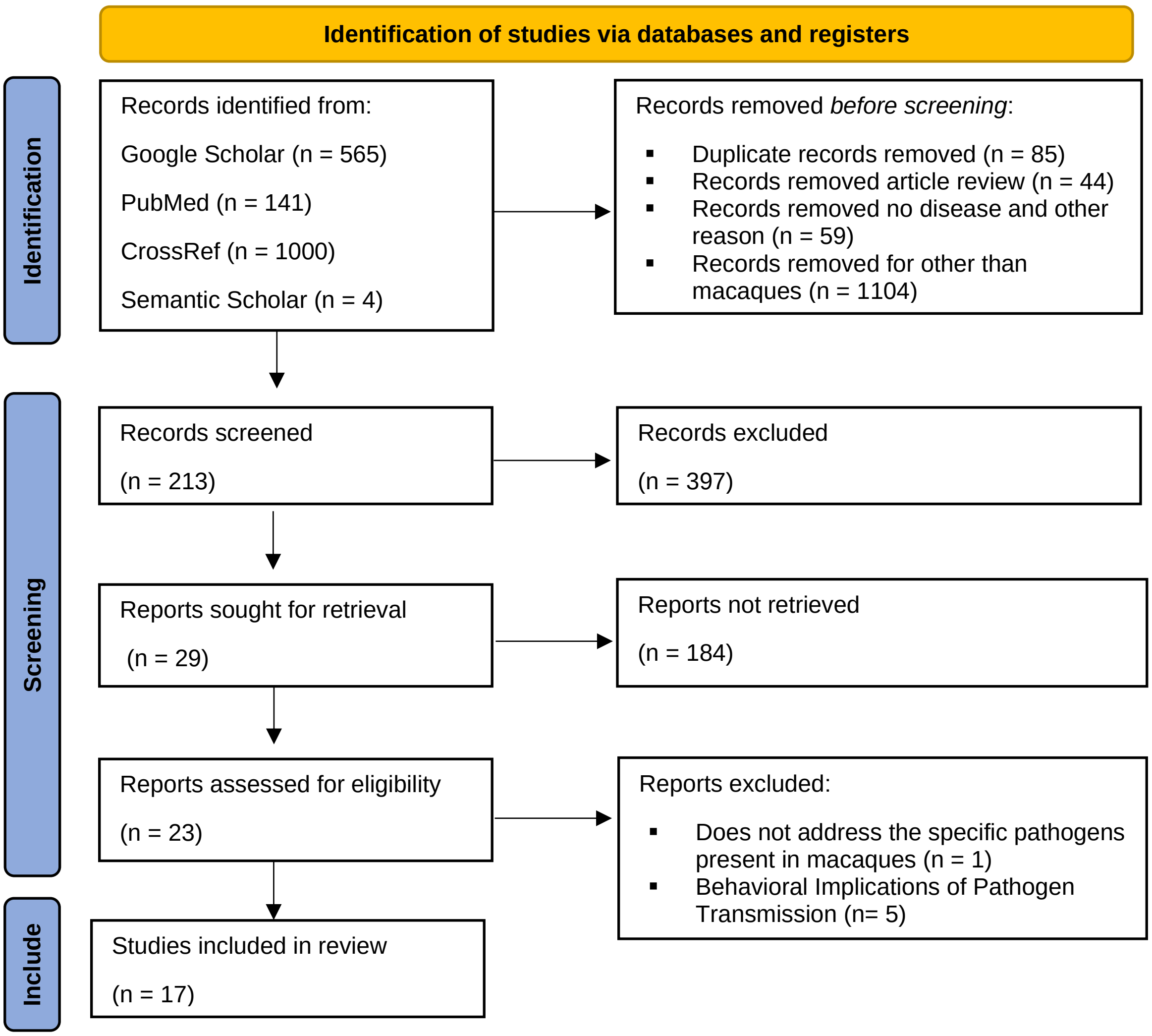

Fig. 1. PRISMA flow diagram illustrating the systematic literature search and study selection process for this systematic review

The research designs employed within the 17 included studies were diverse, including cross-sectional, observational, and experimental designs. Nine studies (53%) utilized a cross-sectional design to determine the prevalence of zoonotic pathogens in specific macaque species or populations through serological or molecular testing (see Table 2 for details). Two studies (12%) adopted observational designs to investigate macaque behavior related to human interactions and pathogen transmission in ecotourism settings, where close human-macaque interactions increase the risk of zoonotic spillover. The remaining six studies employed experimental or longitudinal designs to explore pathogen transmission dynamics. These diverse research designs provide a comprehensive understanding of zoonotic disease transmission risks in ecotourism areas.

The included studies encompassed research on nine distinct species within the genus *Macaca*: *M. fascicularis* (long-tailed macaque), *M. mulatta* (rhesus macaque), *M. thibetana* (Tibetan macaque), *M. nemestrina* (pig-tailed macaque), *M. fuscata* (Japanese macaque), *M. maura* (Moorish macaque), *M. assamensis* (Assamese macaque), *M. arctoides* (stump-tailed macaque), and *M. cyclopis* (Formosan rock macaque). Studies focusing on non-macaque primate species,

[DOI: 10.61186/JoMMID.12.4.243]

such as apes and lemurs, were excluded to maintain specificity. One study was excluded due to its focus on aspects unrelated to zoonotic disease transmission, such as behavioral ecology or conservation genetics, aligning with the defined scope of this review. While the primary focus of this review is on macaques, other primate taxa, such as apes, were acknowledged as potential reservoirs for zoonotic disease transmission but were excluded to maintain focus on macaques. For instance, a study conducted in Hlawga National Park, a site with high human-primate interaction, investigated behavioral patterns in apes, such as close proximity to humans that could facilitate zoonotic pathogen transmission [23].

The sample sizes across the included studies varied widely, reflecting differences in study design and logistical constraints. For macaque subjects, the sample sizes ranged from 16 to 649 individuals, while human subject sample sizes ranged from 11 to 82 participants. Biological samples, including blood, feces, rectal swabs, oropharyngeal swabs, and occasionally carcasses, were collected to identify zoonotic pathogens in macaques and humans. These samples were analyzed to identify a spectrum of potential zoonotic pathogens relevant to human health within ecotourism areas (Table 2). Nucleic acid amplification tests, such as polymerase chain reaction (PCR), were used to detect viral and bacterial pathogens with high sensitivity. Serological assays, including enzyme-linked immunosorbent assay (ELISA), were employed to detect antibodies against viral and bacterial pathogens. Microscopic analysis was utilized to identify helminth eggs and protozoan parasites in fecal samples. Furthermore, ELISA was used to detect antibodies against specific protozoan pathogens [24- 30]. The integration of multiple diagnostic methodologies, such as PCR, ELISA, and microscopic analysis, enhanced the accuracy and comprehensiveness of pathogen detection, providing a more robust understanding of pathogen prevalence and potential transmission pathways within these ecotourism settings. These findings provide critical insights into the prevalence and transmission dynamics of zoonotic pathogens in ecotourism areas, informing the development of mitigation strategies.

Prevalence of pathogens in macaques. The detection rates of the four primary pathogen categories-viruses, helminths, protozoa, and bacteria-varied across the included studies due to differences in sampling methods, diagnostic techniques, and geographical locations. Viral pathogens were the most frequently detected, identified in seven studies (42%), likely due to their high transmission rates and adaptability to diverse hosts. Protozoan infections were reported in five studies (28%) [21, 29-35]. Helminth infections were detected in four studies (26%). Bacterial infections, including *Mycobacterium tuberculosis*, were reported in only one study (6%) [28, 36]. These findings highlight the diversity of pathogens present in macaques, with notable variations in prevalence influenced by factors such as macaque species, geographical location, and human-macaque interaction intensity (Figure 2). The spectrum of pathogen types observed across different macaque species and geographical locations underscores the need for region-specific zoonotic disease management strategies.

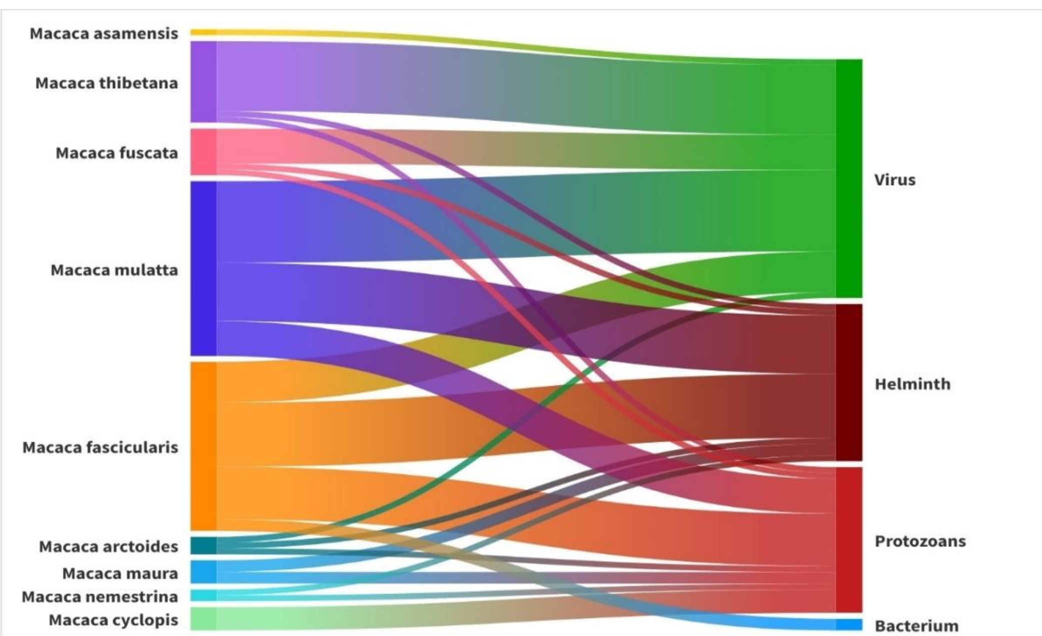

Fig. 2. Distribution of pathogen diversity, including viral, helminth, protozoan, and bacterial pathogens, across nine macaque species (*Macaca fascicularis***,** *Macaca mulatta***,** *Macaca thibetana*, *etc*.) examined in the included studies

[DOI: 10.61186/JoMMID.12.4.243]

As illustrated in Figure 2, which shows the distribution of pathogen diversity across macaque species, the types and prevalence of detected pathogens varied. *Macaca fascicularis* had the broadest range of pathogens, with evidence of viral, protozoan, helminth, and bacterial infections, as detected through molecular, serological, and microscopic techniques. *M. mulatta***,** *M. fuscata*, *M. thibetana*, and *M. arctoides* harbored viruses, helminths, and protozoa. Both *M. nemestrina* and *M. maura*, which are commonly found in ecotourism areas, presented with protozoan and helminth infections. In *M. assamensis*, only viral pathogens, such as *Simian foamy virus*, were detected, while *M. cyclopis*, a species with limited human interaction, was found to harbor only protozoan pathogens.

Human-macaque interactions and potential transmission pathways. Zoonotic pathogen transmission, including viruses, bacteria, and parasites, from macaques to humans can occur via direct contact (*e.g*., physical interaction) and indirect contact (*e.g*., exposure to contaminated environments). The most frequently reported modes of direct contact were feeding (64.29%), scratching (14.29%), biting (14.29%), and touching (7.14%). Feeding, the most prevalent form of direct interaction, often leads to closer proximity and increased risk of aggressive behaviors such as biting or scratching, thus facilitating pathogen transmission through direct exposure to macaque saliva or feces, or through the contamination of shared environments, such as picnic areas or temple grounds, where food items and surfaces may be contaminated with macaque feces [19, 24-25, 29, 30-33, 34-37].

Indirect contact was also identified as a relevant transmission pathway in several studies. Close proximity to macaques, which increases the risk of exposure to airborne pathogens or contaminated surfaces, was reported in 57.14% of the studies. Environmental contact, such as touching picnic tables, temple surfaces, or food items contaminated with macaque saliva or feces, was reported in 42.86% of the studies. These indirect interactions represent viable routes for pathogen transmission due to the persistence of pathogens in the environment and frequent human-macaque interactions. Several studies, including Kosoltanapiwat *et al*. (2022), have provided evidence supporting indirect transmission through contaminated environments [26]. For example, the sharing of water sources or foraging areas, where macaque feces or saliva can contaminate resources used by humans, and the handling of macaque feces during cleaning activities or objects contaminated with macaque saliva, such as food containers or toys, have been identified as potential mechanisms for indirect pathogen transmission (Table 2).

Geographical distribution of studies and pathogen detection in macaques. The majority of the included studies were conducted in Thailand (n=5; [24-28]) and China (n=4; [19, 29-31]), which are hotspots for ecotourism and human-macaque interactions. Research was also conducted in Indonesia [32, 33], Nepal [34, 35], Malaysia [36], India [37], Bangladesh [38], and the Philippines [21], regions with significant macaque populations and ecotourism activities. In Thailand, across the studies, four macaque species were found to harbor viruses, helminths, and bacteria [24-28]. In China, across the studies, seven macaque species were found to harbor viruses, helminths, and protozoa [19, 29-31].

Table 1. Distribution of pathogens detected in different macaque species across countries

Country	Macaque species studied	Pathogen type	References
Thailand	*M. fascicularis*	Virus	[27]
	M. assamensis, *M. fascicularis*, *M. mulatta*	Virus	[24]
	M. fascicularis, *M. nemestrina*, *M. arctoides*	Virus	[26]
	M. fascicularis	Helminths	[25]
	M. fascicularis	Bacterium	[28]
China	*M. thibetana*, *M. fuscata*, *M. mulatta*	Virus	[31]
	M. thibetana	Virus	[19]
	M. thibetana, *M. fascicularis*, *M. arctoides*, *M. mulatta*, *M. nemestrina*, *M. fuscata*	Protozoans and Helminths	[29]
	M. cyclopis	Protozoans	[30]
Indonesia	*M. fascicularis*	Virus	[32]
	M. maura	Protozoans and Helminths	[33]
Nepal	*M. mulatta*	Protozoans and Helminths	[35]
	M. mulatta	Virus	[34]
Malaysia	*M. fascicularis*	Bacterium	[36]
India	*M. mulatta*	Virus	[37]
Bangladesh	*M. mulatta*	Virus	[40]
Philippines	*M. fascicularis*	Protozoans and Helminths	[21]

Pathogen diversity across macaque species. Across the reviewed studies, a total of 14 distinct viral species, 14 protozoan species, 13 helminth species, and 2 bacterial species were identified as infecting agents in macaques. *M. mulatta*, a species commonly found in ecotourism areas, exhibited the highest viral diversity, with 11 distinct viral species detected, suggesting a greater potential for zoonotic transmission. In contrast, *M. arctoides* and *M. assamensis*, species with limited human interaction, each harbored only a single detected viral species. No viral pathogens were detected in *M. nemestrina*, *M. maura*, or *M. cyclopis* within the scope of

[DOI: 10.61186/JoMMID.12.4.243]

these studies, suggesting lower zoonotic risk in these species. A comparative analysis of pathogen species richness across macaque species is illustrated in Figure 3, highlighting the variability in pathogen diversity among the studied species. Figure 4 represents the global distribution of studies included in the systematic review.

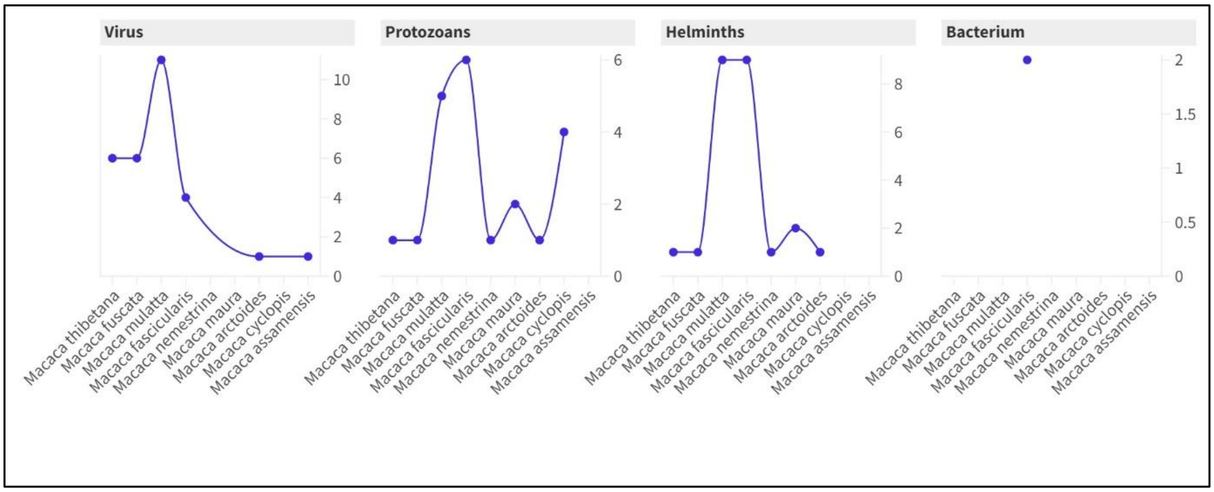

Fig 3. Comparative analysis of pathogen species richness across different macaque species included in this systematic review

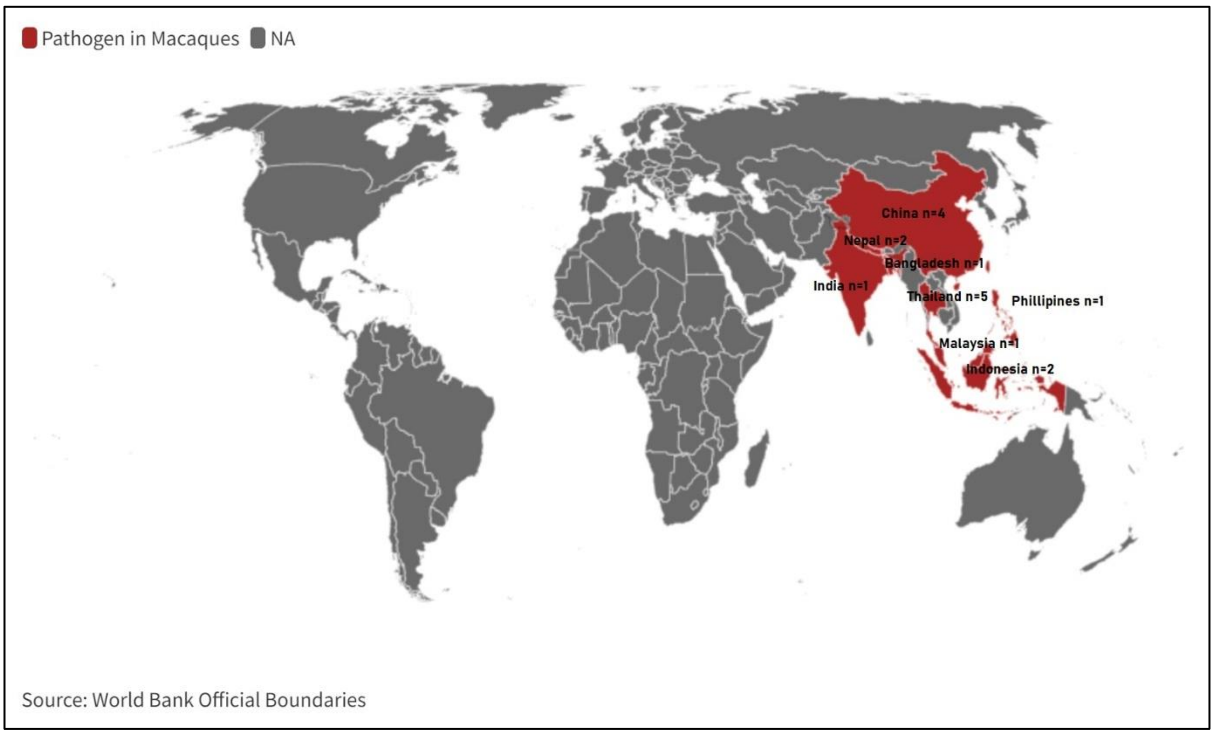

Fig 4. Global distribution of studies included in this systematic review investigating potential zoonotic pathogen transmission from macaques to humans in ecotourism areas

M. fascicularis exhibited the highest diversity of protozoan species, with six distinct species detected, while only a single protozoan species was identified in *M. assamensis*. Both *M. fascicularis* and *M. mulatta* harbored the highest number of helminth species, with nine species detected in each. No helminth pathogens were detected in *M. cyclopis* or *M. assamensis*, suggesting lower zoonotic risk in these species. Bacterial pathogens were exclusively found in *M. fascicularis*, with two species reported. These findings suggest that interactions with humans, such as feeding or physical contact, which increase the risk of pathogen spillover, are a significant factor contributing to the transmission of pathogens from macaques to humans. A comprehensive understanding of pathogen transmission, which requires evaluating ecological variables (*e.g*., habitat type), behavioral variables (*e.g.*, human feeding practices), and sampling methodologies (*e.g*., molecular, serological, and microscopic techniques), is essential for developing effective mitigation strategies.

[DOI: 10.61186/JoMMID.12.4.243]

Table 2. Potential zoonotic pathogen transmission from macaques to humans in ecotourism areas: a synthesis of findings from reviewed studies

Study area	Ecotourism setting	Macaque species	Study design	Sample size (n)	Sample type	Human-macaque interaction	Pathogen(s) detected	References
Bangladesh	Diverse settings (wild, urban, shrines, performing environments)	*Macaca mulatta*	Cross-sectional design	Macaque: 56	Blood	Indirect: close proximity	Measles virus	[40]
China	Huangshan Valley of the Wild Monkeys, Hefei Wildlife Zoo, Qimen Laboratory Rhesus Macaque Center	*Macaca thibetana*, *Macaca fuscata*, *Macaca mulatta*	Cross-sectional design	Macaque: 46	Blood	Direct: feeding, scratching; Indirect: close proximity	**Viruses:** Herpes B virus (HBV), Hepatitis A virus (HAV), Simian poxvirus (SPV), Simian foamy virus (SFV), Simian retrovirus (SRV), Simian T-cell lymphotropic virus 1 (STLV-1)	[31]
Philippines	Puerto Princesa Subterranean River National Park	*Macaca fascicularis*	Cross-sectional design	Macaque: 35	Fecal	Indirect: environmental contact	**Protozoa:** *Entamoeba coli*, *Entamoeba* spp., *Iodamoeba butschlii*, *Endolimax nana*, *Blastocystis* sp., *Chilomastix mesnili*, *Entamoeba polecki*, *Giardia intestinalis* **Helminths:** Hookworm larvae, hookworm *vs. strongylid* eggs, *Strongyloides* sp. larva, *Trichuris trichiura*, *Ascaris* sp., *Hymenolepis nana*, *Enterobius vermicularis*	[21]
China	Mt. Huangshan National Reserve	*Macaca thibetana*	Observational, cross-sectional design	Humans: 282, Macaque: 16	Behavioral observation, blood	Direct: scratching, biting	**Viruses:** Herpes B virus, Hepatitis A virus, Simian foamy virus, Simian poxvirus, Simian retrovirus, Simian T-cell lymphotropic virus 1	[19]
Thailand	Monkey temples	*Macaca assamensis*, *Macaca fascicularis and Macaca mulatta*	Cross-sectional design	Macaque: 118	Blood	Direct: feeding; Indirect: close proximity	**Viruses:** Simian Foamy Virus (SFV)	[24]
Thailand	Monkey temples	*Macaca fascicularis*, *Macaca nemestrina and Macaca arctoides*	Cross-sectional design	Macaque: 203	Fecal, Rectal swab	Indirect: close proximity	**Viruses:** Simian adenovirus	[26]
India	Natural habitat adjacent to human settlements	*Macaca mulatta*	Cross-sectional design	Data not available	Blood	Direct: touching, biting	**Viruses:** Simian foamy virus (SFV), Influenza A virus (IAV)	[37]
Thailand	Kosumpee Forest Park	*Macaca fascicularis*	Cross-sectional design	Macaque: 102, Human: 115	Fecal	Direct: feeding	**Helminths:** *Strongyloides* spp., *Ascaris* spp., *Trichuris* sp.	[25]
Thailand	Various urban areas	*Macaca fascicularis*	Cross-sectional design	Macaque: 649	Blood, oropharyngeal swabs	Indirect: close proximity, environmental contact	**Viruses:** Simian foamy virus (SFV), Hepatitis B virus (HBV) **Protozoa:** *Plasmodium* spp.	[27]
Indonesia	Bantimurung Bulusaraung National Park	*Macaca maura*	Cross-sectional design	Macaque: 18	Fecal	Indirect: environmental contact	**Protozoa:** *Entamoeba* spp., *Balantidium coli* **Helminths:** *Strongyloides* spp., *Trichuris* spp., Unidentified helminths	[33]
China	Zoological gardens (n=24)	*Macaca thibetana* *Macaca fascicularis* *Macaca arctoides* *Macaca mulatta* *Macaca nemestrina* *Macaca fuscata*	Cross-sectional design	Macaque: 152	Fecal	Direct: feeding; Indirect: environmental contact	**Protozoa:** *Trichuris* spp., *Entamoeba* spp.	[29]
Indonesia	Sangeh Monkey Temple	*Macaca fascicularis*	Cross-sectional design	Humans: 82, Macaque: 38	Blood	Direct: feeding	**Viruses:** Simian foamy virus (SFV)	[32]
China	Shoushan National Nature Park	*Macaca cyclopis*	Cross-sectional design	Macaque: 37	Fecal	Direct: feeding	**Protozoa:** *Entamoeba coli*, *Entamoeba chattoni*, *Entamoeba hartmanni*, *Entamoeba nuttalli*	[30]
Malaysia	World Heritage Listed Sites, Malaysia	*Macaca fascicularis*	Cross-sectional design	Macaque: 42	Tissue sample from carcasses	Direct: feeding; Indirect: close proximity	**Bacteria:** *Mycobacterium avium* complex (MAC)	[36]
Thailand	Kosumpee Forest Park	*Macaca fascicularis*	Cross-sectional design	Macaque: 30	Blood	Indirect: close proximity, environmental contact	**Bacteria:** *Leptospira* spp.	[28]
Nepal	Kathmandu Valley	*Macaca mulatta*	Cross-sectional design	Macaque: 121	Fecal	Direct: feeding; Indirect: close proximity, environmental contact	**Protozoa:** 5 unspecified species **Coccidia:** 1 unspecified species **Helminths:** 8 unspecified species	[35]
Nepal	Swoyambhu Temple in Kathmandu	*Macaca mulatta*	Cross-sectional design	Macaque: 39	Blood	Direct: feeding	**Viruses:** Rhesus cytomegalovirus, Simian virus 40, Cercopithecine herpesvirus 1, Simian foamy virus (SFV)	[34]

The prevalence of zoonotic diseases in ecotourism areas. This systematic review demonstrated a variable prevalence of zoonotic pathogens within macaques inhabiting ecotourism areas. While not all studies explicitly investigated zoonotic transmission, multiple studies identified the presence of pathogens with well-established zoonotic potential. Significant variability in pathogen prevalence was observed across different geographical regions and macaque species, with some exhibiting higher infection rates than others. The presence of viruses, protozoa, and helminths was commonly reported in the reviewed studies. However, the methodological approaches used to investigate and confirm zoonotic transmission pathways varied significantly. These discrepancies highlight the need for more focused research on elucidating the direct and indirect risks associated with zoonotic transmission in these specific ecotourism areas.

Table 3. Prevalence of pathogens in macaques and humans in ecotourism areas: findings from reviewed studies

Study area	Sample size (n)	Pathogen prevalence (%)	References
Bangladesh	Macaques: n = 56	**Measles virus:** • Performing environment: 50.00 • Urban area: 5.88 • Shrine: 4.76 • Wild area: 0.00	[38]
China	Macaques: n = 46	**Viruses:** • Herpes B virus (HBV): ○ *Macaca thibetana*: 6.30 ○ *Macaca fuscata*: 37.50 ○ *Macaca mulatta*: 27.30 • Hepatitis A virus (HAV): ○ *Macaca thibetana*: 12.50 ○ *Macaca fuscata*: 0.00 ○ *Macaca mulatta*: 13.60 • Simian poxvirus (SPV): ○ *Macaca thibetana*: 12.50 ○ *Macaca fuscata*: 12.50 ○ *Macaca mulatta*: 27.30 • Simian foamy virus (SFV): ○ *Macaca thibetana*: 18.80 ○ *Macaca fuscata*: 0.00 ○ *Macaca mulatta*: 9.10 • Simian retrovirus (SRV): ○ *Macaca thibetana*: 18.80 ○ *Macaca fuscata*: 25.00 ○ *Macaca mulatta*: 4.50 • Simian T-cell lymphotropic virus-1 (STLV-1): ○ *Macaca thibetana*: 6.30 ○ *Macaca fuscata*: 0.00 ○ *Macaca mulatta*: 0.00	[30]
Philippines	Macaques: n = 35	**Enteroparasites:** 85.71 **Protozoa:** • *Entamoeba coli*: 34.29 • *Entamoeba* spp.: 31.43 • *Iodamoeba butschlii*: 31.43 • *Endolimax nana*: 28.57 • *Blastocystis* sp.: 22.86 • *Chilomastix mesnili*: 20.00 • *Entamoeba polecki*: 20.00 • *Giardia intestinalis*: 8.57 **Helminths:** • Hookworm larva: 40.00 • Hookworm *vs. strongylids* ova: 34.29 • *Strongyloides* sp. larva: 28.57 • *Trichuris trichiura*: 20.00 • *Ascaris* sp.: 11.43 • *Hymenolepis nana*: 2.86 • *Enterobius vermicularis*: 2.86	[21]

China	Humans: n = 282, Macaques: n = 16	**Viruses (Macaques):** • Herpes B virus: 6.30 • Hepatitis A virus: 12.50 • Simian foamy virus: 18.80 • Simian poxvirus: 12.50 • Simian retrovirus: 18.80 • Simian T-cell lymphotropic virus-1: 6.30	[19]
Thailand	Macaques: n = 118	**Simian foamy virus (SFV):** 92.00	[24]
Thailand	Macaques: n = 203	**Simian adenovirus:** 33.30	[26]
India	Not reported	**Simian foamy virus (SFV):** Data not available **Influenza A virus (IAV):** Data not available	[37]
Thailand	Macaques: n = 102, Human: n = 115	**Gastrointestinal parasites:** • Macaques: 44.00 • Humans: 12.00	[25]
Thailand	Macaques: n = 649	**Viruses:** • Simian foamy virus (SFV): 56.50 • Hepatitis B virus (HBV): 0.30 **Protozoa:** • *Plasmodium* spp.: 2.20	[27]
Indonesia	Macaques: n = 18	**Gastrointestinal parasites**: 56.30	[33]
China	Macaques: n = 152	**Protozoa:** • *Trichuris* spp.: 31.75 • *Entamoeba* spp.: 4.76 **Protozoa:** • *Trichuris* spp.: 3.70 • *Entamoeba* spp.: 66.67 **Protozoa:** • *Entamoeba* spp.: 3.13 **Protozoa:** • *Trichuris* spp.: 23.08 **Protozoa:** • *Trichuris* spp.: 66.67	[29]
Indonesia	Human: n = 82, Macaques: n = 38	**Viruses:** Simian foamy virus (SFV): • Macaques: 89.00 • Humans: 1.00	[32]
China	Macaques: n = 37	**Gastrointestinal parasites**: 100.00 **Protozoa:** • *Entamoeba coli*: 19.00 • *Entamoeba chattoni*: 50.00 • *Entamoeba hartmanni*: 11.00 • *Entamoeba nuttalli*: 20.00	[30]
Malaysia	Macaques: n = 42	***Mycobacterium avium* complex (MAC):** 33.30	[36]
Thailand	Macaques: n = 30	***Leptospira* spp.:** 13.33	[28]
Nepal	Macaques: n = 121	**Gastrointestinal parasites:** 87.60	[35]
Nepal	Macaques: n = 39	**Rhesus cytomegalovirus (RhCMV):** 94.90 **Simian virus 40 (SV40):** 89.70 **Cercopithecine herpesvirus 1 (CHV-1):** 64.10 **Simian foamy virus (SFV):** 97.40	[34]

Table 3 unequivocally demonstrates that viruses constitute the most frequently detected category of pathogens in macaque blood samples, with Simian foamy virus (SFV) exhibiting the highest prevalence. SFV was identified in seven of the reviewed studies, with prevalence in macaques ranging from 9.1% to 92%. Notably, evidence of zoonotic transmission was observed through the detection of SFV in humans, with a 1% prevalence observed in a cohort of 82 individuals [32]. The prevalence of Hepatitis A virus (HAV) ranged from 12.5% to 13.6% across the studies where it was detected [19, 30]. Hepatitis B virus (HBV) was detected at a lower prevalence of 0.3%. The prevalence of HBV showed considerable variation, ranging from 6.3% to 64.1% [19, 30, 34]. Measles virus was detected in one study, exhibiting a prevalence of 5% [38]. Rhesus cytomegalovirus (RhCMV) showed a high prevalence of 94.9% in the study where it was identified. Finally, Simian adenovirus was detected with a prevalence of 33.3% in one study [26]. Simian pox virus (SPV) had a prevalence of 12.5% in the study where it was detected [19, 30]. Simian retrovirus (SRV) prevalence varied from 4.5% to 25% across the studies where it was detected. Simian T-cell lymphotropic virus 1 (STLV-1) was found at a prevalence of 6.3%. Simian virus 40 (SV40) exhibited a prevalence of 89.7% in one study. The prevalence of Influenza A virus was not reported in the studies included in this review. Furthermore, analysis of blood samples revealed the presence of bacteria, specifically *Leptospira spp.*, at a prevalence of 13.33% [19, 28, 30, 34, 37]. The protozoan parasite *Plasmodium spp*. was also identified in macaques, with a prevalence of 2.2% [27, 28]. Helminths and protozoa, detected in fecal or rectal samples, had prevalence rates in macaques ranging from 44% to 100%. In a separate study examining human fecal samples, gastrointestinal parasites were identified with a prevalence of 12% (14 out of 115 samples) [25].

DISCUSSION

This systematic review synthesizes and analyzes the potential for zoonotic pathogen transmission from macaques to humans within ecotourism settings globally, based on an analysis of 17 publications spanning the period from 2000 to 2024. The findings unequivocally highlight that direct physical interactions, such as feeding, touching, and handling, represent significant risk factors for pathogen transmission. Behaviors such as feeding, touching, handling, and close proximity for photographic purposes are consistently reported as high-risk activities. The documented presence of viral, protozoan, and helminth pathogens within macaques provides strong evidence for zoonotic spillover through these interactions [31]. A prevalent observation across multiple studies was the engagement of tourists in direct physical interactions with macaques, most notably feeding. Tourists frequently utilized food as a means to attract macaques for closer encounters, often to facilitate photographic opportunities. Instances of tourists directly hand-feeding macaques or placing food items into the mouths of macaques have been reported [25, 32, 39]. This practice constitutes a significant route for pathogen transmission, as direct contact with macaque saliva or food items contaminated with macaque saliva can readily facilitate the dissemination of zoonotic agents.

It is crucial to acknowledge the inconsistencies observed across the reviewed studies. For example, while some studies reported high prevalence rates of specific viruses within *M. fascicularis* populations in Thailand [24-28], studies employing similar methodologies in Indonesia did not detect these viruses in the same macaque species [32]. These discrepancies may be attributed to several factors. Firstly, ecological differences, including habitat structure, climate patterns, and other environmental factors, could significantly influence pathogen prevalence within macaques. Secondly, the frequency and type of human-macaque interactions across different ecotourism sites could influence pathogen transmission dynamics. Finally, methodological differences, such as the choice of sample types (*e.g*., blood *vs*. fecal samples) and the sensitivity of detection techniques (*e.g*., PCR-based methods *vs.* serological assays), could contribute to the observed variations. For instance, certain viral pathogens may be more readily detectable in blood samples, whereas others may exhibit higher prevalence in fecal samples. Similarly, PCR-based methods may offer superior sensitivity compared to serological assays for the detection of specific pathogens [19, 21, 24-35, 37, 40]. The adoption of standardized sampling and detection protocols across future studies is paramount to address these discrepancies and to facilitate a more robust and reliable understanding of pathogen prevalence and associated zoonotic disease risks across diverse geographical regions and macaque populations. This, in turn, will contribute to the development of more effective strategies for the prevention and management of zoonotic disease transmission within ecotourism areas.

Furthermore, the manifestation of aggressive behaviors by macaques towards humans was documented in several studies [19, 31, 37], encompassing instances of food snatching, chasing, and biting. This behavior is frequently attributed to human activities that disrupt macaque behavior, such as disregarding established guidelines and regulations of ecotourism sites. For instance, tourists who engage in feeding macaques, approach them at excessively close distances, or attempt to interact with infant macaques may inadvertently elicit aggressive responses. Such interactions can lead to physical injuries, including bites and scratches, which inherently present a risk of zoonotic disease transmission. Reports of bites and scratches sufficiently severe to induce bleeding among both tourists and workers within ecotourism areas have been documented [32]. These injuries create a direct pathway for pathogens to enter the human bloodstream, thereby elevating the risk of infection. Therefore, educating tourists about appropriate behavior around macaques and rigorously enforcing regulations to minimize aggressive interactions are essential measures. In the event of bites or scratches, the provision of prompt medical attention and appropriate post-exposure prophylaxis is crucial for the prevention of potential zoonotic infections.

The hands and feet of macaques may be contaminated with fecal matter, urine, or other substances that harbor a diverse array of microorganisms, including bacterial pathogens. While direct contact with macaques presents a potential route for the transmission of these pathogens, viral transmission frequently occurs through distinct mechanisms. For instance, viruses such as Herpesvirus simiae (Herpes B virus) and Simian Foamy Virus readily transmit through mucosal contact, including bites, scratches, or exposure to saliva or respiratory droplets [28].

[DOI: 10.61186/JoMMID.12.4.243]

These findings underscore the critical importance of educating tourists regarding the potential risks associated with close proximity to macaques and of promoting hygiene practices, such as thorough handwashing with soap and water, for effectively minimizing the risk of pathogen transmission within ecotourism areas.

Intestinal parasites, such as helminths and protozoans, are frequently detected within the digestive tracts of macaques and are subsequently shed in their feces [21, 25, 26, 30]. Tourists may accidentally contact contaminated feces, leading to the transfer of these parasites to their footwear and hands. Subsequent hand-to-mouth contact or contact with other mucous membranes can then result in pathogen transmission. This issue is not exclusive to macaque ecotourism sites and has been documented in multiple ecotourism and wildlife settings involving non-human primates, including Singapore, Indonesia, Bali, and Gibraltar [32, 34, 39, 40]. These findings underscore the importance of implementing robust hygiene measures within ecotourism areas to minimize the risk of fecal contamination and subsequent pathogen transmission. Ecotourism operators should provide readily accessible handwashing facilities and educate tourists about the importance of avoiding contact with macaque feces and practicing thorough handwashing with soap and water to mitigate these risks.

Moreover, the reviewed studies exhibited variations in their assessment of indirect transmission routes, such as environmental contamination [21, 27-29, 33, 35]. While some studies highlighted contaminated water sources or surfaces soiled with macaque feces as potential sources of zoonotic risk, others primarily focused on direct contact through bites, scratches, or handling as the predominant transmission route. Several factors may explain these discrepancies. Firstly, tourist activity levels, including visitor density and engagement in high-risk behaviors, as well as the presence of infrastructure and waste management practices, can influence the extent of environmental contamination and the potential for indirect transmission. Secondly, differences in tourist behavior, such as adherence to hygiene guidelines, feeding practices, and the frequency of close interactions with macaques, can also impact the risk of both direct and indirect transmission. Finally, ecological and infrastructural factors, such as the presence of natural water sources, macaque population density, and hygiene standards, can contribute to variations in transmission dynamics. While indirect transmission may be reported less frequently compared to direct contact, it still poses a significant risk, particularly in environments where humans and macaques share spaces and resources [24-28, 30-31, 34-36, 40]. Therefore, effective prevention strategies for zoonotic diseases in ecotourism areas must address both direct and indirect transmission routes by promoting responsible tourist behavior, implementing appropriate hygiene measures, and managing environmental contamination.

Environmental conditions, such as sanitation and water quality, exert a significant influence on the elevated risk of pathogen transmission within ecotourism areas. Poor sanitation and waste management, along with the presence of contaminated water sources, can create conducive conditions for the persistence and dissemination of pathogens, thereby increasing the risk of exposure for both humans and animals [21, 37, 40]. Consequently, maintaining environmental hygiene is crucial for mitigating the risk of zoonotic disease transmission. Proper sanitation and effective waste management practices can reduce the environmental burden of pathogens, minimizing the likelihood of human exposure. These findings underscore the necessity for targeted environmental management strategies within ecotourism areas to protect the health of both tourists and wildlife. Such strategies should encompass measures to enhance sanitation infrastructure, manage waste effectively, and protect water sources from contamination.

Effective management of ecotourism sites is paramount for minimizing the risk of pathogen transmission within these areas. Management authorities must strictly enforce regulations and address violations by tourists. For example, regulations prohibiting the feeding of macaques, approaching them at excessively close distances, or entering restricted areas should be strictly enforced through measures such as fines, warnings, or an increased presence of park rangers [31]. While strict enforcement of regulations, such as prohibiting feeding or close proximity to macaques, can contribute to risk mitigation, it is important to acknowledge that ecotourism environments generally present an increased likelihood of zoonotic pathogen transmission compared to settings with limited human-wildlife interactions. Studies conducted in pristine wilderness areas, where human contact with macaques is minimal, have reported lower prevalence rates of certain zoonotic pathogens [38]. However, the risk of pathogen transmission in other non-ecotourism environments, such as urban or rural areas where macaques may be present, varies considerably depending on the frequency and type of contact between humans and macaques.

Despite the growing awareness of the potential for zoonotic pathogen transmission in ecotourism settings characterized by direct human-macaque interactions, the volume of research conducted over the past two decades has remained comparatively limited. A total of seventeen articles met the eligibility criteria for inclusion in this review. This relative scarcity of research may be partially attributed to the inherent challenges associated with invasive sampling methods, such as blood collection from macaques. Acquiring blood samples require safe and effective trapping techniques and specialized expertise in animal handling, which often involve logistical challenges and potential stress for the

[DOI: 10.61186/JoMMID.12.4.243]

animals. Consequently, several studies have adopted non-invasive specimen collection methods as alternatives to blood sampling, including the analysis of fecal samples and carcasses [21, 25, 30, 33, 35-36]. Fecal samples offer a relatively straightforward and non-invasive approach for the detection of certain pathogens, although they may not be suitable for the detection of all zoonotic agents [21, 25-26, 29, 30, 33, 35]. Analysis of carcasses, while limited by the availability of deceased animals, can provide valuable insights into the cause of mortality and the presence of pathogens [36]. These alternative methods have demonstrated the feasibility of detecting zoonotic pathogens in ecotourism areas without the need for invasive blood collection.

While blood samples are frequently considered as the preferred sample type for many diagnostic assays and may yield more comprehensive or specific information regarding pathogen presence, their collection necessitates invasive procedures that can induce stress in animals. In addition to blood samples, other biological specimens, such as saliva, buccal fluid, urine, and oral swabs, can also be collected for pathogen detection [28, 41-43]. The adoption of these alternative sampling approaches is a critical consideration for several key reasons. Firstly, they minimize stress and discomfort for the animals, thereby promoting ethical research practices. Secondly, they often facilitate easier and more efficient sample collection, particularly in challenging field environments. Finally, non-invasive methods have the potential to be applied to a broader range of animal species and in diverse contexts, thus expanding the scope of zoonotic disease surveillance. Beyond individual animal diagnostics, assessing environmental conditions in ecotourism areas, such as water quality and sanitation practices, is essential for a comprehensive understanding and mitigation of broader zoonotic disease risks. This includes evaluating critical factors such as water quality, sanitation practices, and waste management protocols to identify potential sources of contamination and implement targeted interventions to reduce contamination risks [44]. By integrating non-invasive sampling methods with comprehensive environmental health assessments, researchers can achieve a more holistic understanding of zoonotic disease dynamics, facilitating the development of effective strategies to protect both animal and human health in ecotourism settings.

It is important to acknowledge the inherent limitations of this systematic review. A significant limitation is the relatively small number of studies that comprehensively examined ecological and behavioral factors, such as macaque population density, habitat fragmentation, and human activities like feeding and waste disposal, which influence pathogen transmission. Furthermore, small sample sizes and narrow geographical coverage in several individual studies may limit the generalizability of their findings to other regions and macaque species. Despite these limitations, the available studies provide a valuable preliminary assessment of the geographic distribution of risks associated with zoonotic pathogen transmission, as illustrated in Figure 4. The map highlights areas of elevated risk, particularly within Southeast Asia, where interactions between humans and macaques are most prevalent. Notably, countries such as Thailand, Indonesia, and Malaysia exhibit heightened transmission risks, primarily due to the high frequency of direct interactions observed in popular ecotourism sites. This underscores the critical need for targeted interventions, such as educational campaigns, vaccination programs, and improved sanitation infrastructure, in these high-risk regions to mitigate the risk of zoonotic disease transmission. Such measures could encompass educational campaigns to promote responsible tourist behavior, vaccination programs for both humans and macaques (where applicable and feasible), improved sanitation and waste management infrastructure, and stricter enforcement of regulations governing interactions between humans and macaques in ecotourism settings.

Our review clearly demonstrates the significant risk of zoonotic disease transmission associated with human-macaque interactions within ecotourism areas, underscoring the imperative for effective public health and wildlife management strategies. We recommend the implementation of strict regulations on human-macaque interactions, including explicit guidelines on feeding and direct physical contact. Authorities must consistently enforce these regulations to minimize the risk of close encounters that can facilitate pathogen transmission. Educating both the local community and tourists about zoonotic diseases and the regulations governing ecotourism areas represents a crucial strategy for mitigating transmission risks [25, 27, 30, 32, 33, 36]. Educational programs should emphasize the importance of maintaining a safe distance from macaques and avoiding practices such as feeding, which can significantly increase the risk of pathogen exposure. While we acknowledge that local traditions, such as feeding monkeys, may present challenges to the implementation of these recommendations, it is essential to explore and promote alternative forms of engagement with macaques that minimize health risks for both human and animal populations [17]. Structural changes, such as physical barriers, elevated walkways, or designated viewing platforms, can effectively prevent direct contact and minimize opportunities for pathogen transmission. Specific attention should be directed towards preventing close physical proximity, such as posing for photographs with macaques or directly placing food into their mouths. Furthermore, the potential consequences of these interactions, such as bites and scratches, should be addressed through the implementation of appropriate protocols for wound management and post-exposure prophylaxis. These protocols should be integrated into the overarching management plans for ecotourism areas to ensure prompt and effective responses to potential zoonotic exposures.

This systematic review provides strong evidence of the significant public health risks posed by zoonotic disease transmission from macaques to humans within ecotourism areas. While direct interactions, such as feeding and touching macaques, are primary drivers of zoonotic pathogen transmission, this review underscores the heterogeneity of pathogen prevalence across geographic regions and macaque species. The identification of viral, protozoan, and helminth pathogens in several high-risk locations, particularly in Southeast Asia, necessitates targeted public health interventions. Authorities must implement educational campaigns to inform both tourists and local communities about the risks associated with feeding and handling macaques, and the importance of maintaining a safe distance from these animals. Equally crucial is the meticulous adherence to hygiene measures, such as regular handwashing with soap and water after visiting ecotourism areas and avoiding contact with potentially contaminated surfaces, to minimize the risk of indirect transmission. These individual actions, when combined with integrated management approaches that address environmental sanitation, effective waste management, and the regulation of human-macaque interactions, are essential for effectively mitigating zoonotic disease risks in ecotourism settings.

Strict and enforceable regulations are essential for governing human-macaque interactions within ecotourism areas. These regulations should include clear policies that prohibit the feeding of macaques and restrict access to areas where close contact is highly probable. Effective enforcement of these regulations is paramount to minimize the risk of zoonotic disease transmission. Regular surveillance of ecotourism activities is also crucial to identify and prevent harmful behaviors that could elevate transmission risks. This surveillance can generate valuable data on the dynamics of human-macaque interactions, enabling timely interventions and the implementation of adaptive management strategies. Prioritizing research efforts aimed at elucidating the ecological and behavioral drivers of pathogen transmission across diverse environmental contexts is crucial for the development of targeted interventions. Future research should focus on gathering more comprehensive data regarding environmental contamination and other indirect exposure routes to develop holistic strategies that address both direct and indirect transmission risks. Expanding research to underrepresented regions and macaque species will further enhance our understanding of zoonotic risks, providing more effective guidance for public health interventions.

ACKNOWLEDGMENT

We extend our sincere gratitude to Mrs. Wulan Fauzana for her invaluable technical assistance in the preparation of this review article. This work was supported by the ZOOMAL project ('Evaluating zoonotic malaria and agricultural land use in Indonesia'; #LS-2019-116), Australian Centre for International Agricultural Research, Australian Government.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest associated with this manuscript.

REFERENCES

1. Bengis RG, Leighton FA, Fischer JR, Artois M, Mörner T, Tate CM. The role of wildlife in emerging and re-emerging zoonoses. Rev Sci Tech. 2004; 23 (2): 497-511.
2. Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, et al. Global trends in emerging infectious diseases. Nature. 2008; 451 (7181): 990-3.
3. Singh BB, Gajadhar AA. Role of India's wildlife in the emergence and re-emergence of zoonotic pathogens, risk factors and public health implications. Acta Trop. 2014; 138: 67-77.
4. Carrillo Bilbao GA, Navarro JC, Garigliany MM, Martin-Solano S, Minda E, Benítez-Ortiz W, et al. Molecular Identification of *Plasmodium falciparum* from Captive Non-Human Primates in the Western Amazon Ecuador. Pathogens. 2021; 10 (7): 791.
5. Gillespie TR, Nunn CL, Leendertz FH. Integrative approaches to the study of primate infectious disease: Implications for biodiversity conservation and global health. Am J Phys Anthropol. 2008; Suppl 47: 53-69.
6. Schillaci MA, Jones-Engel L, Engel GA, Paramastri Y, Iskandar E, Wilson B, et al. Prevalence of enzootic simian viruses among urban performance monkeys in Indonesia. Trop Med Int Health. 2005; 10 (12): 1305-14.
7. Pedersen AB, Davies TJ. Cross-species pathogen transmission and disease emergence in primates. EcoHealth. 2009; 6 (4): 496-508.
8. Silva-Ramos CR, Faccini-Martínez ÁA. Clinical, epidemiological, and laboratory features of *Rickettsia africae* infection, African tick-bite fever: A systematic review. Infez Med. 2021; 29 (3): 366-77.
9. Gautret P, Blanton J, Dacheux L, Ribadeau-Dumas F, Brouqui P, Parola P, et al. Rabies in nonhuman primates and potential for transmission to humans: A literature review and examination of selected French national data. PLoS Negl Trop Dis. 2014; 8 (5): e2863.
10. Muehlenbein MP, Wallis J. Understanding risks of disease transmission associated with primate-based tourism. In: Russon AE, Wallis J, editors. Primate Tourism: A Tool for Conservation? Cambridge: Cambridge University Press; 2014. Pp.278-291.
11. Sha JC, Gumert MD, Lee BP, Jones-Engel L, Chan S, Fuentes A. Macaque-human interactions and the societal perceptions of macaques in Singapore. Am J Primatol. 2009; 71 (10): 825-39.
12. Maréchal L, MacLarnon A, Majolo B, Semple S. Primates' behavioural responses to tourists: evidence for a trade-off

between potential risks and benefits. Sci Rep. 2016; 6: 32465.

13. Mardiah A, Rizaldi, Wilson N. Agresi Provokasi dan Non-Provokasi pada Monyet Ekor Panjang (*Macaca fascicularis*, Raffles 1821) Terhadap Pengunjung di Kawasan Gunung Meru. J Biol Univ Andalas. 2015; 258-63.
14. Ilham K, Rizaldi, Nurdin J, Tsuji Y. Effect of Provisioning on the Temporal Variation in the Activity Budget of Urban Long-Tailed Macaques (*Macaca fascicularis*) in West Sumatra, Indonesia. Folia Primatol (Basel). 2018; 89 (5): 347-56.
15. Carne C, Semple S, MacLarnon A, Majolo B, Maréchal L. Implications of Tourist-Macaque Interactions for Disease Transmission. EcoHealth. 2017 Dec; 14 (4): 704-17.
16. Engel G, Hungerford LL, Jones-Engel L, Travis D, Eberle R, Fuentes A, et al. Risk assessment: A model for predicting cross-species transmission of simian foamy virus from macaques (*M. fascicularis*) to humans at a monkey temple in Bali, Indonesia. Am J Primatol. 2006; 68 (9): 934-48.
17. Stenbak CR, Pinto-Santini DM, Murray SM, Linial ML. Simian Foamy Viruses: Infections in Human and Nonhuman Primate Hosts. In: Knauf S, Jones-Engel L, editors. Neglected Diseases in Monkeys. 2020. Cham: Springer.
18. The potential for zoonotic malaria transmission in five areas of Indonesia inhabited by non-human primates. Parasit Vectors. 2023 Aug; 16: 123. Available from: https://doi.org/10.1186/s13071-023-05845-7.
19. Yong Z, Jin-Hua L, Dong-Po X, Bing-Hua S, Yu-Rui X, Xi W, et al. Potential pathogen transmission risk in non-human primate ecotourism: A case study at Mt. Huangshan, China. Life Sci J. 2013; 10 (1): 2754.
20. Jones-Engel L, May CC, Engel GA, Steinkraus KA, Schillaci MA, Fuentes A, et al. Diverse contexts of zoonotic transmission of simian foamy viruses in Asia. Emerg Infect Dis. 2008; 14 (8): 1200-8.
21. Chavez GCS, Paller VG, Lorica RP, Dimalibot J. Zoonotic enteroparasites of *Macaca fascicularis* in Palawan, Philippines. J Parasit Dis. 2021; 10 (3): 123-30.
22. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. PLoS Med. 2021; 18 (3): e1003583.
23. Yadana S, Valitutto MT, Aung O, Hayek L-AC, Yu JH, Myat TW, et al. Assessing behavioral risk factors driving zoonotic spillover among high-risk populations in Myanmar. EcoHealth. 2023; 20 (1): 31-42.
24. Jones-Engel L, Steinkraus KA, Murray SM, Engel GA, Grant R, Aggimarangsee N, et al. Sensitive assays for simian foamy viruses reveal a high prevalence of infection in commensal, free-ranging Asian monkeys. J Virol. 2007; 81 (14): 7330-7.
25. Schurer JM, Ramirez V, Kyes P, Tanee T, Patarapadungkit N, Thamsenanupap P, et al. Long-Tailed Macaques (*Macaca fascicularis*) in Urban Landscapes: Gastrointestinal Parasitism and Barriers for Healthy Coexistence in Northeast Thailand. Am J Trop Med Hyg. 2019; 100 (2): 357–64.
26. Kosoltanapiwat N, Tongshoob J, Ampawong S, Reamtong O, Prasittichai L, Yindee M, et al. Simian adenoviruses: Molecular and serological survey in monkeys and humans in Thailand. One Health. 2022; 15: 100434.
27. Kaewchot S, Tangsudjai S, Sariya L, Mongkolphan C, Saechin A, Sariwongchan R, et al. Zoonotic pathogens survey in free-living long-tailed macaques in Thailand. Int J Vet Sci Med. 2022; 10 (1): 11-18.
28. Pumipuntu N, Tanee T, Kyes P, Thamsenanupap P, Karaket A, Kyes RC. Leptospira Seroprevalence in Free-Ranging Long-Tailed Macaques (*Macaca fascicularis*) at Kosumpee Forest Park, Maha Sarakham, Thailand. Infect Dis Rep. 2022; 15 (1): 16-23.
29. Li M, Zhao B, Li B, Wang Q, Niu L, Deng J, et al. Prevalence of gastrointestinal parasites in captive non-human primates of twenty-four zoological gardens in China. J Med Primatol. 2015; 44 (3): 168-73.
30. Chang AM, Chen CC, Huffman MA. *Entamoeba* Spp. in wild Formosan rock macaques (*Macaca cyclopis*) in an area with frequent human-macaque contact. J Wildl Dis. 2019; 55 (3): 608–18.
31. Zhu Y, Yang X, Tao R, Zhang Q. Implications for primate population management and the occupational safety of primate handlers: A natural, zoos and captive environment comparative study in China. Pak J Zool. 2024; 56 (1): 1–7.
32. Jones-Engel L, Engel GA, Schillaci MA, Rompis A, Putra A, Suaryana KG, et al. Primate-to-human retroviral transmission in Asia. Emerg Infect Dis. 2005; 11 (7): 1028-35.
33. Albani A, De Liberato C, Wahid I, Berrilli F, Riley EP, Cardeti G, et al. Preliminary assessment of gastrointestinal parasites in two wild groups of endangered Moor macaques (*Macaca maura*) from Sulawesi. Int J Primatol. 2019; 40: 671-86.
34. Jones-Engel L, Engel GA, Heidrich J, Chalise M, Poudel N, Viscidi R, et al. Temple monkeys and health implications of commensalism, Kathmandu, Nepal. Emerg Infect Dis. 2006; 12 (6): 900-6.
35. Adhikari A, Koju NP, Maharjan B, Khanal L, Upreti M, Kyes RC. Gastro-intestinal parasites of urban rhesus macaques (*Macaca mulatta*) in the Kathmandu Valley, Nepal. Int J Parasitol Parasites Wildl. 2023; 22: 175-83.
36. Lekko YM, Che-Amat A, Ooi PT, Omar S, Ramanoon SZ, Mazlan M, et al. *Mycobacterium tuberculosis* and avium complex investigation among Malaysian free-ranging wild boar and wild macaques at wildlife-livestock-human interface. Animals (Basel). 2021; 11 (11): 3252.
37. Nandi JS, Rathore SS, Mathur BR. Transmission of infectious viruses in the natural setting at human-animal interface. Curr Res Virol Sci. 2021; 2: 100008.
38. Ortiz-Cam L, Jones-Engel L, Mendoza P, Castillo-Neyra R. Association between seroprevalence of measles virus in monkeys and degree of human-monkey contact in Bangladesh. One Health. 2023; 17: 100571.
39. Fuentes A. Human culture and monkey behavior: assessing the contexts of potential pathogen transmission between macaques and humans. Am J Primatol. 2006; 68 (9): 880-96.
40. Fuentes A, Kalchik S, Gettler L, Kwiatt A, Konecki M, Jones-Engel L. Characterizing human-macaque interactions in Singapore. Am J Primatol. 2008; 70 (9): 879–83.

[DOI: 10.61186/JoMMID.12.4.243]

41. Simons ND, Lorenz JG, Sheeran LK, Li JH, Xia DP, Wagner RS. Noninvasive saliva collection for DNA analyses from free-ranging Tibetan macaques (*Macaca thibetana*). Am J Primatol. 2012; 74 (11): 1064-70.

42. Kawai S, Sato M, Kato-Hayashi N, Kishi H, Huffman MA, Maeno Y, et al. Detection of *Plasmodium knowlesi* DNA in the urine and faeces of a Japanese macaque (*Macaca fuscata*) over the course of an experimentally induced infection. Malar J. 2014; 13 (1): 1-9.

43. Evans TS, Barry PA, Gilardi KV, Goldstein T, Deere JD, Fike J, et al. Optimization of a novel non-invasive oral sampling technique for zoonotic pathogen surveillance in nonhuman primates. PLoS Negl Trop Dis. 2015; 9 (6): e0003813.

Cite this article:

Virdana S, Rizaldi, Maliza R. Potential Zoonotic Disease Transmission from Macaques to Human in Ecotourism Areas: A Systematic Review. J Med Microbiol Infect Dis, 2024; 12 (4): 243-258. DOI: 10.61186/JoMMID.12.4.243.