


BMJ Open Rabies in Southeast Asia: a systematic review of its incidence, risk factors and mortality

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ABSTRACT

Objective Rabies is a neglected zoonotic disease that can infect all mammals, including humans. We aimed to summarise the current knowledge of the incidence, risk factors and mortality of rabies in Southeast Asia.

Design Systematic review based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020.

Data sources Scopus, Web of Science and PubMed were searched from 1 January 2012 to 21 February 2023.

Eligibility criteria Original English language articles published between 2012 and 2023 were included.

Data extraction and synthesis Nine independent reviewers extracted data and assessed the risk of bias. The quality appraisal of included articles was carried out using the Mixed Methods Appraisal Tool.

Results A total of eight articles were included in this analysis. In Vietnam, the incidence of rabies ranged from 1.7 to 117.2 per 100 000 population. The cumulative incidence in Sarawak was estimated at 1.7 per 100 000 population. In Indonesia, 104 human rabies cases were reported from 2008 to 2010, while in Thailand, a total of 46 rabies cases were reported in Thailand from 2010 to 2015. In the Philippines, the incidence of rabies ranged from 0.1 to 0.3 per 100 000 population. An increased risk of rabies virus infection was associated with a high population density, illiteracy, seasonal patterns and dog butchers. The case fatality rate was 100%.

Conclusion This study included research from Southeast Asia, which may not represent rabies infection in other regions or continents. In addition, the role of publication bias should be acknowledged as grey literature was not included. The occurrence of rabies in Southeast Asia is due to the high number of unvaccinated stray and pet dogs, working hazards (dog butchers in Vietnam), the unavailability of the rabies vaccine in rural regions and misinformation about the significance of seeking treatment after dog bites.

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INTRODUCTION

Rabies is a neglected zoonotic disease caused by an RNA virus from the family *Rhabdoviridae*, genus *Lyssavirus*.¹ Once clinical symptoms appear, rabies is almost 100% fatal.² All mammals can be infected with the rabies

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This review only includes research from Southeast Asia, which may not represent rabies infection in other regions or continents.
- ⇒ We did not include grey literature or national guidelines, which could have been useful in this study.
- ⇒ The inclusion of studies that defined or diagnosed rabies based on clinical signs or laboratory tests increased the chances of identifying rabies cases in Southeast Asian countries.

virus, including humans. More than 99% of human rabies cases are transmitted via dogs.³ With the necessary evidence and tools in place for the control and elimination of rabies, canine rabies can be eliminated, as demonstrated in Western Europe, Canada, the USA, Japan, a few Latin American countries and many parts of Asia. However, rabies is still widespread, occurring in more than 80 countries, particularly low/middle-income countries in Africa and Asia.^{3,4} Furthermore, half of the global population lives in canine rabies-endemic areas and hence is at risk of contracting rabies.³

Globally, canine rabies is estimated to cause approximately 59 000 human deaths annually. In Asia, rabies is clearly a major problem: the number of human deaths due to rabies in Asia is higher than in any other region in the world. Most human rabies deaths occur in Asia (59.6%), followed by Africa (36.4%), while only less than 0.05% of human rabies deaths occur in the Americas. In addition, India alone accounts for 35% of global human rabies deaths, higher than any other country.⁴ In Asia, canine rabies is estimated to cause a loss of 2.2 million disability-adjusted life-years per year, while the annual cost of postexposure prophylaxis (PEP) is highest in Asia, estimated at up to US\$1.5 billion.⁵

In Southeast Asia, only Singapore has eradicated canine rabies through the

implementation of robust national rabies control programmes, while other countries in this subregion are not considered rabies-free.⁶ Malaysia was declared rabies-free by the World Organisation for Animal Health in July 2013, but several rabies outbreaks since 2015 have caused Malaysia to lose its rabies-free status.⁷ Even though Thailand and Vietnam have not been able to eliminate rabies, there has been a substantial reduction in human rabies deaths through the implementation of dog mass vaccination, intensified PEP in humans and awareness education.⁸

Rabies is 100% preventable through vaccination in animals and humans.⁹ The WHO has recommended pre-exposure prophylaxis for those with continual, frequent or increased risk of exposure to rabies virus (eg, veterinarians and animal handlers). If exposed to a rabid animal, the WHO recommends PEP, which consists of immediate wound management, immediate vaccination and the administration of rabies immunoglobulin for high-risk exposures.¹⁰ Nevertheless, dog vaccination is considered the most cost-effective strategy for preventing rabies in humans.²

Despite the availability of evidence and guidelines for the control and management of rabies, countries in Southeast Asia face some constraints in controlling rabies, including inadequate resources, lack of political commitment, lack of consensus on strategy, weak inter-sectoral coordination, insensitive surveillance systems, limited accessibility to modern rabies vaccines and supply problems, as well as a lack of public awareness and cooperation.⁸ However, the high estimated burden of rabies more than justifies the need to prioritise rabies control, particularly in Asian countries.

Information on rabies epidemiology is a prerequisite for the effective planning of rabies control programmes. Previous systematic reviews focused on rabies epidemiology in India,¹¹ Nepal¹ and Arab countries,¹² while literature synthesising data on rabies epidemiology in Southeast Asia is limited. Hence, this systematic review aims to provide an in-depth assessment of the incidence, risk factors and mortality of rabies in Southeast Asian countries, based on the published literature.

MATERIALS AND METHODS

This systematic review was registered with the PROSPERO database (CRD42022311654) and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.¹³ A meta-analysis was not carried out as the included studies differed in terms of methodology, settings, participants, interventions and outcomes, suggesting heterogeneity. An internal protocol was developed to document the criteria for conducting this systematic review, but this is not published.

Patient and public involvement

There was no patient and/or public involvement in this study (none).

Research question formulation

The review question was developed based on the CoCoPop (condition, context, population) and PEO (population, exposure, outcome) concepts.¹⁴ The population, intervention, comparison intervention, outcome measures framework is commonly used to develop focused clinical questions for quantitative reviews,¹⁵ while the CoCoPop and PEO concepts are suitable for reviews related to prevalence and aetiology.¹⁴ Based on the CoCoPop concept, the condition refers to the incidence of rabies, the context refers to Southeast Asia and the population is the general population. Based on the PEO concept, the population refers to the general population in Southeast Asia, the exposure refers to rabies and the outcome is the mortality caused by rabies. Hence, the main research questions are (1) What is the incidence of rabies among the general population in Southeast Asian countries? (2) What are the risk factors of rabies among the general population in Southeast Asian countries? and (3) What is the mortality rate of rabies among the general population in Southeast Asian countries?

Data source and search strategy

PubMed, Web of Science and Scopus were searched from 1 January 2012 to 21 February 2023. The keywords used to search for related articles are provided in [table 1](#).

Study selection

The inclusion criteria were (1) publications from 2012 to 2023, (2) original articles and (3) publications in the English language. The following types of studies were included in this review: (1) reports on the incidence and risk factors of rabies in Southeast Asia and (2) reports on the mortality rate of rabies in Southeast Asia. Non-original articles such as conference proceedings, perspectives, commentaries, opinions, reports, systematic reviews and meta-analyses were excluded. The publication period was limited to 2012–2023 so that the systematic review could be built on recent literature.

Data extraction and synthesis

Duplicates were deleted, and at least two reviewers rescreened the remaining papers. Before their inclusion in the review, articles were screened in three stages. Any article that did not meet the inclusion criteria based on title screening was eliminated in the first phase. The abstracts of the remaining papers were reviewed in the second phase, and any publications that did not fit the inclusion criteria were eliminated from the review. The full-text articles were examined attentively in the last phase to eliminate any papers that did not fulfil the inclusion criteria. Before the data extraction process, both reviewers needed to agree that the entire publication should be reviewed. Any disagreements were worked out through discussion. All data extraction was conducted independently using a standardised data extraction form that was organised using Microsoft Excel. Information collected in the form included (1) author, (2) publication

Table 1 Keywords search used in the screening process

Database	Search string
Scopus	<ol style="list-style-type: none"> TITLE-ABS-KEY(("rabies*" OR "rabies virus*" OR "dog bite*") AND ("Southeast Asia" OR "Brunei" OR "Myanmar" OR "Cambodia" OR "Timor-Leste" OR "Indonesia" OR "Laos" OR "Malaysia" OR "Philippines" OR "Singapore" OR "Thailand" OR "Vietnam") AND ("epidemiology" OR "outbreak" OR "case" OR "prevalence" OR "incidence" OR "causes" OR "risk factor")) TITLE-ABS-KEY(("Rabies*" OR "Rabies virus*" OR "dog bite*") AND ("Southeast Asia" OR "Brunei" OR "Myanmar" OR "Cambodia" OR "Timor-Leste" OR "Indonesia" OR "Laos" OR "Malaysia" OR "Philippines" OR "Singapore" OR "Thailand" OR "Vietnam") AND ("mortality*" OR "death*" OR "fatality*"))
Web of Science	<ol style="list-style-type: none"> ((ALL=("rabies*") OR ALL=("rabies virus*")) OR ALL=("dog bite*") AND (((((((((((ALL=("Southeast Asia")) OR ALL=("Brunei")) OR ALL=("Myanmar")) OR ALL=("Cambodia")) OR ALL=("Timor-Leste")) OR ALL=("Indonesia")) OR ALL=("Laos")) OR ALL=("Malaysia")) OR ALL=("Philippines")) OR ALL=("Singapore")) OR ALL=("Thailand")) OR ALL=("Vietnam")) AND (((((((((((ALL=("epidemiology")) OR ALL=("outbreak")) OR ALL=("case")) OR ALL=("prevalence")) OR ALL=("incidence")) OR ALL=("causes")) OR ALL=("risk factor")) ((ALL=("rabies*") OR ALL=("rabies virus*")) OR ALL=("dog bite*") AND (((((((((((ALL=("Southeast Asia")) OR ALL=("Brunei")) OR ALL=("Myanmar")) OR ALL=("Cambodia")) OR ALL=("Timor-Leste")) OR ALL=("Indonesia")) OR ALL=("Laos")) OR ALL=("Malaysia")) OR ALL=("Philippines")) OR ALL=("Singapore")) OR ALL=("Thailand")) OR ALL=("Vietnam")) AND ((ALL=("mortality*") OR ALL=("death*") OR ALL=("fatality*"))
PubMed	<ol style="list-style-type: none"> ((("rabies*") OR ("rabies virus*") OR ("dog bite*")) AND (((((((((((("Southeast Asia" OR ("Brunei")) OR ("Myanmar")) OR ("Cambodia")) OR ("Timor-Leste") OR ("Indonesia")) OR ("Laos")) OR ("Malaysia")) OR ("Philippines")) OR ("Singapore")) OR ("Thailand")) OR ("Vietnam")) AND (((((((((((("epidemiology") OR ("outbreak")) OR ("case")) OR ("prevalence")) OR ("incidence")) OR ("causes")) OR ("risk factor")) ((("rabies*") OR ("rabies virus*") OR ("dog bite*")) AND (((((((((((("Southeast Asia" OR ("Brunei")) OR ("Myanmar")) OR ("Cambodia")) OR ("Timor-Leste") OR ("Indonesia")) OR ("Laos")) OR ("Malaysia")) OR ("Philippines")) OR ("Singapore")) OR ("Thailand")) OR ("Vietnam")) AND (((("mortality*") OR ("death*") OR ("fatality*"))

year, (3) reference, (4) country, (5) study design, (6) statistical analysis and (7) results, which included incidence, risk factors and mortality. Due to the heterogeneity of the included studies, narrative synthesis was performed.

Quality assessment

Quality assessment was conducted by the authors on all eight studies using the Mixed Methods Appraisal Tool (MMAT).¹⁶ The MMAT is a critical appraisal tool that was developed to appraise studies included in systematic mixed study reviews. The quality of the methodology of five categories of studies (qualitative studies, randomised controlled trials, non-randomised studies, quantitative

descriptive studies and mixed methods studies) can be appraised using this tool. For each category, five criteria are used to assess the quality of the study. It is advised not to calculate an overall score from the rating of each criterion using the latest version of MMAT¹⁶. However, due to problems faced by researchers in reporting the MMAT results, a suggestion was provided for reporting an overall score (5*****/100% of the quality criteria met; 4*****/80% of the quality criteria met; 3*****/60% of the quality criteria met; 2***/40% of the quality criteria met; 1*/20% of the quality criteria met). The details of this assessment are reported in [table 2](#).

Table 2 The details of Mixed Methods Appraisal Tool assessment

Author	Type of study	Score	1.1	1.2	1.3	1.4	1.5
			Is the sampling strategy relevant to address the research question?	Is the sample representative of the target population?	Are the measurements appropriate?	Is the risk of non-response bias low?	Is the statistical analysis appropriate to answer the research question?
Nguyen <i>et al</i> ³¹	Quantitative	40%	Can't tell	Can't tell	Yes	Can't tell	Yes
Pham <i>et al</i> ³⁰	Quantitative	100%	Yes	Yes	Yes	Yes	Yes
Sim <i>et al</i> ²⁷	Quantitative	60%	Yes	Can't tell	Yes	Can't tell	Yes
Yurachai <i>et al</i> ³⁴	Quantitative	80%	Yes	Yes	Yes	Can't tell	Yes
Phung <i>et al</i> ²⁹	Quantitative	80%	Yes	Yes	Yes	Can't tell	Yes
Susilawati <i>et al</i> ³³	Quantitative	80%	Yes	Yes	Yes	Yes	No
Lee <i>et al</i> ³²	Quantitative	100%	Yes	Yes	Yes	Yes	Yes
Guzman <i>et al</i> ²⁸	Quantitative	80%	Yes	Yes	Yes	No	Yes

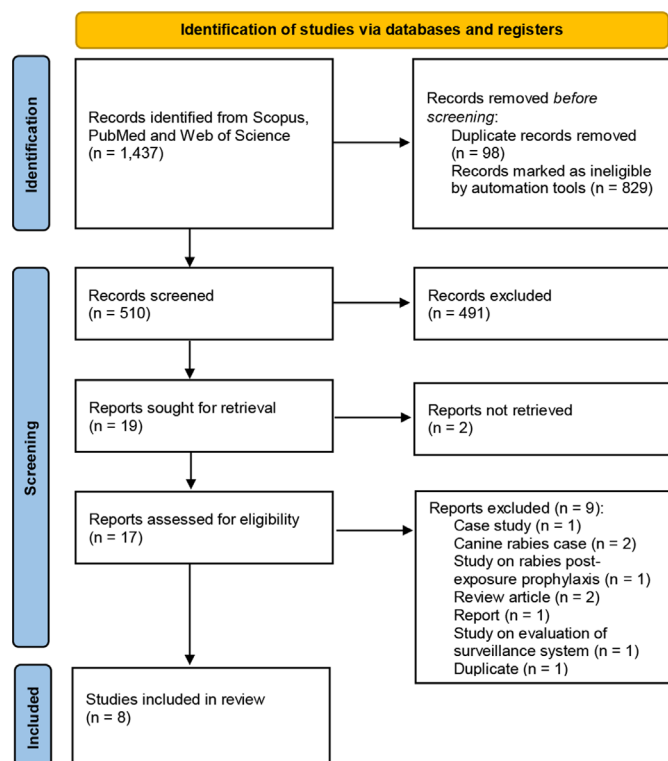


Figure 1 PRISMA 2020 flow diagram for new systematic reviews that included searches of databases. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

RESULTS

A total of 1437 records were identified from the 3 databases to evaluate the incidence, risk factors and mortality rate of rabies in Southeast Asia. Using automation tools, 829 records were excluded based on year, publication type and language. A total of 98 duplicate records were found and removed, leaving 510 records for title screening. The titles and abstracts were screened independently based on the review questions. A total of 491 articles were removed during the screening. For the remaining 19 articles, the full text was retrieved for assessment of eligibility. Disagreements were resolved through discussion to reach a consensus. Eleven articles were removed for the following reasons: they did not meet the objective (n=4),^{17–20} they were not primary/original research articles (n=4),^{21–24} the full article could not be retrieved (n=2)^{25 26} and they were duplicates (n=1),²⁷ leaving a total of eight articles for proceeding with the quality appraisal. The PRISMA flow chart is presented in [figure 1](#).

Quality appraisal

According to the MMAT evaluation criteria, 75% of the articles (n=6) met 75%–100% of the MMAT checklist, representing high quality. Of the articles, 12.5% (n=1) met 50%–75% of the evaluated criteria, representing moderate quality, while 12.5% of the articles (n=1) met less than 50% of the evaluated criteria, representing low quality.

Background of the eligible studies

A total of eight studies were included in this systematic review, of which four were conducted in Vietnam, and one each in Indonesia, Malaysia, Thailand and the Philippines (online supplemental table). The themes covered by all studies included incidence rates, case numbers and risk factors of rabies in Southeast Asia. Among the included studies, three studies particularly discussed rabies mortality.

Incidence and risk factors of rabies in Southeast Asian countries

Overall, the incidence of rabies ranged between 0.1 per 100 000 population in the Philippines²⁸ and 117.2 per 100 000 population in Vietnam.¹⁸ The average monthly number of rabies cases in Vietnam was 429 during the period from 2011 to 2015, with the incidence ranging from 1.7 to 117.2 per 100 000, with higher incidences observed in the Red River, South Central Coast (SCC) and Mekong River Delta (MRD) regions.²⁹ Specific to Southern Vietnam, a total of 94 human rabies cases were reported between 2009 and 2018, with an average of nine cases recorded annually, representing an incidence of 2.7 cases per 10 million population.³⁰ The highest number was reported in 2018 (5.5 cases per 10 million population). Most cases were among men and individuals aged 50 years and above.

Dog butchers in Vietnam were at high risk of rabies virus infection.³¹ The study found that 28.3% of butchers were at risk of rabies exposure due to the slaughtering of sick dogs and getting bites, scratches or knife cuts. Of 406 participants, 8.6% had sufficient levels of rabies neutralising antibody for protection and only 8.1% were vaccinated. In terms of location, rabies cases were limited to specific areas. Hotspots were identified in southern Vietnam, particularly in the MRD and SCC.³² Seasonal patterns were observed, with a strong peak in February/July and a minor peak in October/December in the MRD region. However, a strong peak was detected in the middle of each year in the SCC. Temperature, humidity and cumulative rainfall are positively associated with an increased incidence of rabies in Vietnam. In terms of socioeconomic factors, increases in population density, as well as the percentage of illiteracy, elevated the risk of rabies.²⁹

In Indonesia, 104 human rabies cases were reported in Bali from November 2008 to November 2010. Most of the cases were among men. Almost all (92%) cases had a history of a dog bite. Only 5.8% had their wounds treated and received an antirabies vaccine after the bite incident.³³ Even worse, rabies cases in Sibu, Sarawak, also did not seek medical attention following a dog bite.²⁷ The cumulative incidence in Sibu was estimated at 1.7 per 100 000 population. The incubation period varied from 17 days to 2 years.

A total of 46 confirmed and probable cases of human rabies were reported in Thailand from 2010 to 2015, of which 11 were reported in Eastern Thailand.³⁴ Even

though rabies can be prevented by vaccination, more than 90% of rabies death cases in Thailand did not receive or improperly stopped receiving PEP. In terms of suspected rabies exposures, 6204 exposures were reported from 8 provinces in Eastern Thailand, resulting in a crude exposure rate of 106 reported rabies exposures per 100 000 people. Dogs were the main source of exposure (77.8%), while children under the age of 15 and older persons over the age of 60 had the highest overall reported exposure rates (189.7 and 189.2/100 000, respectively).

In the Philippines, there were 575 rabies cases from 2006 to 2015, of which 70% were among men. Nearly 34% of the patients were aged 41–60 years. The incidence rate of human rabies per 100 000 population in 2007, 2010 and 2015 was 0.1305, 0.1356 and 0.1708 in the National Capital Region; 0.2890, 0.2965 and 0.1961 in Region III; and 0.1449, 0.1272 and 0.1041 in Region IV–A, respectively.²⁸

Rabies mortality in Southeast Asian countries

The case fatality rate was 100% as mentioned in 2 studies.^{27 33} Of the six deaths reported in Sibuyan, five patients succumbed to the illness within 2 weeks of symptom onset, with five out of the six cases reporting a dog bite history.²³ In Indonesia, Susilawati *et al*³³ reported 104 fatalities due to rabies, of which 96 cases had a history of dog bites.²² In the Philippines, 463 people died from rabies infection.²⁸

DISCUSSION

Incidence and risk factors of rabies in Southeast Asian countries

Rabies in Asia and Africa contributes to over 99% of the human rabies deaths that occur in the world today. The vast majority (60%) of these deaths occur in Asia.³⁵ Every year, an estimated 59 000 people die from rabies worldwide, with the majority (95%) of these deaths occurring in Africa and Asia due to a lack of PEP services for animal-bite patients and rabies surveillance personnel and facilities.³⁶ These statistics support the results of our study, which shows the reporting of a high number of rabies cases in Vietnam, Indonesia and Thailand, which are endemic for rabies.³⁷

Rabies is concentrated in Asia and Southeast Asia because it is frequently neglected when health and agriculture budgets are set, although the costs and economic benefits of implementing rabies prevention programmes have been successfully established in high-income countries.³⁸ The high number of rabies cases in Southeast Asia can also be attributed to the high number of unowned, free-roaming dogs that cannot be controlled without considerable effort and thus are not vaccinated.³⁹ Vaccination programmes for dogs can provide herd immunity and break the rabies transmission cycle in this reservoir species and have been successfully applied in several countries around the world.⁴⁰

Another cause of the high incidence of rabies in Southeast Asia is the working hazards of dog butchers, especially

in countries that have legalised dog consumption, such as Vietnam.⁴¹ The Centers for Disease Control and Prevention also reported the illegal trafficking of dogs for human consumption in Vietnam (https://www.cdc.gov/global-health/stories/rabies_southeast_asia.htm), which could possibly contribute to the high incidence of rabies in Vietnam. Professional dog butchers in northern Vietnam are at a high risk of rabies virus infection due to exposure during the slaughtering process from the handling of sick or dead dogs and getting bitten, scratched or cut with knives. A study reported that 91.9% of professional dog butchers in Vietnam were not vaccinated against rabies, which may be because of fear of the side effects of the rabies vaccine, inability to afford vaccination and incorrect knowledge of rabies prevention.³¹

The rabies incidence of 0.1 per 100 000 population in the Philippines is similar to that reported in China in 2016.⁴² The lower rabies incidence in the Philippines compared with other Southeast Asian countries may be due to the implementation of the Anti-Rabies Act of 2007 to prevent and control human rabies.⁴³ In addition, the consumption of dog meat was banned in 1998 with the implementation of the Animal Welfare Act, which may contribute to the lower incidence of rabies in the Philippines.⁴⁴

Men are more likely to contract rabies infection than women.¹⁹ Similar findings were reported in Iraq, where more than 89% of rabies cases were among men.⁴⁵ This can be attributed to the fact that most women are housewives, while men are engaged in outdoor activities.⁴⁶ Another study in Ethiopia also stated that men are more likely to perform nightly and outdoor activities, while women are more likely to remain indoors for cultural and religious reasons,⁴⁷ which could explain the increased incidence of rabies in men.

According to study by Yurachai *et al*,³⁴ rabies infection affects children more compared with other age groups.²⁴ This corresponds to a WHO report, stating that 40% of rabies victims are children ages 4–15 (<https://www.who.int/news-room/fact-sheets/detail/rabies>). Other studies in Yemen and Iran reported similar findings, with nearly 40% of the individuals exposed to rabies infection falling in this age group.^{45 48} Children in this age group are probably more likely to play with, annoy or approach biting animals, which contributes to the higher rate of bites in this age group.⁴⁵ In contrast, according to a study by Pham *et al*,³⁰ older people are more likely to become infected with rabies.¹⁹

In several studies included in this systematic review, the diagnosis of most rabies cases was based only on detailed history and clinical diagnosis.^{17 19 21} To diagnose rabies in humans, multiple samples such as saliva, serum, spinal fluid and skin biopsies of hair follicles from the nape of the neck are analysed. Viral isolation or reverse transcription-PCR can be used to analyse saliva. Serum and spinal fluid are tested for rabies virus antibodies. Skin biopsies can be used to detect rabies antigens in the cutaneous nerves at the base of the hair follicles (<https://www.cdc.gov>).

gov/rabies/diagnosis/animals-humans.html). In the future, low/middle-income countries need to standardise the diagnosis of rabies based on the laboratory tests mentioned above for the accuracy of the diagnosis and to enable comparison with other studies in developed countries.

Of the included studies, only one was conducted among butchers, who were at higher risk of contracting rabies.²⁰ Apart from butchers, individuals working as veterinarians, veterinary technicians, animal control workers and wildlife rehabilitators were also considered to have a higher risk of contracting rabies than the general population.⁴⁹ This calls for more studies incorporating individuals involved in occupations identified as high risk for rabies exposure and infection.

In this study, climate was postulated to be one of the risk factors for rabies infection. This was echoed by a study in China showing that the incidence of rabies increases with the ambient temperature. A warmer climate causes animals to be more active in their environment and to travel greater distances when tracking, which contributes to the spread of rabies. In addition, as temperatures rise, people tend to wear lighter clothing and expose more skin, which increases the likelihood of being bitten by a dog.⁵⁰ In South Korea, the seasonality of wildlife rabies was attributed to behaviours such as searching for food during the winter or early spring. Dogs may thus have more opportunities to come into contact with rabid animals during this period due to greater animal movement, which could contribute to seasonal patterns in the occurrence of rabies in humans.⁵¹

Rabies mortality in Southeast Asian countries

In this study, rabies had a high fatality rate, with 100% of the infected cases dying. This is supported by a review in Africa by Nyasulu *et al*, who reported that Algeria, Namibia, Eswatini (formerly Swaziland), Tunisia, Uganda, Zambia and Zimbabwe had high morbidity and mortality due to rabies, with 563 cases (33.9% deaths), 269 cases (94% deaths), 62 cases (88.7% deaths), 91 cases (90% deaths), 466 cases (40.9% deaths), 207 cases (32.8% deaths) and 114 cases (80.7% deaths), respectively.⁵² Because of the large population of stray dogs in this area, the chances of being bitten by a dog are high. Not only are the chances of being bitten high in these areas, but access to treatment in a timely and adequate manner is also very limited. Rabies vaccines may not be routinely available in rural areas where most exposures occur, and rabies immunoglobulins, which are required for category III bites, are always in short supply.⁵³

These factors significantly contribute to the high mortality rate, as the highly protective rabies vaccine is frequently unavailable in these poor areas. In addition, the public is often unconcerned and unaware of the need for early treatment after being bitten by dogs.⁵⁴ According to recent studies, many rabies victims contracted the disease owing to neglect, ignorance or a lack of primary health-care facilities.⁵⁵ Thus, health promotion and education

should be given to the public as knowledge regarding rabies is essential to reduce morbidity and mortality.⁵

In high-income countries such as the USA, the incidence of rabies and associated mortality is low. In the last decade, there have been only 25 cases of human rabies reported in the USA (2009–2018), with 23 deaths.⁶ The low number of cases of rabies infection is due to successful animal control and vaccination programmes, successful outreach programmes, public health capacity and laboratory diagnostics and the availability of modern rabies biologics.⁵⁶ Even though rabies is preventable, the exorbitant cost of vaccinations, combined with a lack of education and knowledge about the disease, limits PEP use.⁵⁵

Strengths and limitations

In this study, we only included research from Southeast Asia, which may not represent rabies infection in other regions or continents. We did not include grey literature or national guidelines, which could have been useful in this study. Nevertheless, the strength of this review lies in its inclusion of studies that defined or diagnosed rabies based on either clinical signs or laboratory testing. Given that rabies is often diagnosed clinically, especially in low/middle-income countries,⁵⁷ this process increased the chances of identifying rabies cases in Southeast Asian countries.

Recommendations

A successful rabies prevention and control programme requires integrating and strengthening intersectoral and transdisciplinary collaboration and cooperation among various societal components.⁵⁸ The Association of Southeast Asian Nations Rabies Elimination Strategy places great value on the organisational and One Health frameworks for rabies eradication. The single most significant way to deal with rabies concerns is to eliminate dog-mediated rabies. The requirement for PEP is considerably reduced when dog rabies is eradicated.⁵⁹ To benefit from the synergy and maximisation of shared resources, comprehensive rabies control programmes should involve the combination of human, financial and material resources with other disease programmes.³⁵

Mass canine vaccination campaigns will boost herd immunity and reduce the risk of human rabies exposure, but this will need strong governmental commitment and extensive social mobilisation. The veterinary authority's active engagement in animal rabies control at the national level is critical, and it is their social responsibility to prevent human rabies through well-planned dog rabies control programmes.³⁷ In 1983, the Pan American Health Organization initiated an elimination programme for human rabies transmitted by dogs that was mainly based on the mass immunisation of dogs; this has led to a 90% reduction in dog rabies in Chile and other Latin American countries.⁶⁰

Rabies control and elimination in low endemic rabies countries such as Malaysia and Singapore have been made possible by the strict enforcement of dog registration, vaccination and population management measures. Malaysia shares a border with Thailand, and the notion of

an immunological belt has been developed through dog licensing, required vaccination of dogs and the systematic extermination of unvaccinated dogs in a buffer zone to prevent rabies from entering the country.³⁷ Perhaps other middle and high endemic rabies countries could follow this rabies control strategy implemented by their South-east Asian neighbour.

Public information and education are important to increase awareness and enhance community participation and support in rabies prevention programmes. Dissemination of important information such as the high fatality rate of rabies, its epidemiology, its prevention and control, and the disease control programme, in general, is vital for programme implementation and responsible pet ownership. By recognising rabies' influence on people's daily lives and the fact that dogs can be a source of human infection, community and school-based rabies prevention initiatives will be easier to establish.⁶¹

The involvement of stakeholders is crucial, and by bringing together key stakeholders from the corporate and public sectors, health security and the need to form public-private partnerships, which are critical in rabies prevention programmes, can be addressed.⁶² National government agencies can maintain standardised approaches for rabies management and elimination and advocate on how to begin public-private cooperation to ensure long-term intervention. All stakeholders can benefit from such technical and administrative effort as they provide credibility and quality assurance to the prevention programme's effectiveness.³⁵ Various examples of public-private partnerships that aid in implementing public programmes, research and policy formation can be seen in Indonesia, India, Sri Lanka, the Philippines, Thailand and Vietnam.³

CONCLUSION

Rabies has often been neglected and not given priority in terms of funding for prevention programmes, resulting in the continued presence of rabies cases in Southeast Asia despite the endorsement of multiple programmes by the WHO. The high number of unvaccinated stray and pet dogs, working hazards (dog butchers in Vietnam), unavailability of the rabies vaccine in rural areas, as well as ignorance regarding the importance of seeking treatment after dog bites, are among the factors that contribute to rabies cases in Southeast Asia.

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