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Case fatality rate and risk factors for Nipah virus encephalitis: A systematic review and meta-analysis

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ABSTRACT

Background: A wide range of Nipah virus (NiV) encephalitis case fatality rates (CFR) have been reported. Data on the involvement of several potential risk factors in Nipah virus transmission remain controversial. We performed a systematic review and meta-analysis to estimate the pooled CFR of NiV encephalitis and to assess the risk factors for NiV infection.

Methods: Articles published up to the 27thof November 2018 in MedLine, Embase and Web of knowledge databases were considered for this study. We included cross-sectional, cohort, and case-control studies that have reported NiV CFR and/or risk factors. Data were pooled with random-effects model. This review was registered in the PROSPERO, CRD42018116242.

Findings: This global review included 22 citations (25 studies) including 2156, 1682, and 474 suspected, probable, and confirmed cases of NiV encephalitis, respectively. We determined a pooled CFR for NiV encephalitis at 61.0% (95% CI, 45.7–75.4; I^2 = 96.8%). Climbing trees (OR = 1.4; 95% CI; 1.0–1.9), male gender (OR = 1.5; 95% CI; 1.1–2.0), travel outside their own sub-district (OR = 2.0; 95% CI; 1.4–2.9), and exposure to date palm sap (DPS) (OR = 5.7; 95% CI; 3.8–8.6) or pigs (OR = 7.6; 95% CI; 1.2–45.4) were significantly associated with NiV infection.

Conclusion: Findings from this study suggest that NiV Encephalitis is associated with a high CFR and that male gender, travel outside their sub-district, climbing trees, and exposure to pigs and DPS are associated with an increased risk of NiV encephalitis.

1. Introduction

Nipah Virus (NiV) encephalitis is an emerging infectious disease endemic to Southeast Asia and Western Pacific and a concern for a global pandemic [1,2]. The emergence of NiV has led to a high morbidity and mortality [2,3]. Mortality rates of up to 95% have been recorded during NiV outbreaks. In addition, the NiV is recognized as a class C biological weapon that includes emerging pathogens that can be used in the context of bioterrorism [4]. NiV is a zoonotic pathogen included in the family of Paramyxoviridae and the genus of Henipavirus [2,5]. NiV is made of approximately 18 kb RNA genome, single-stranded and non-segmented. The clinical presentation of NiV-infected patients ranges from asymptomatic infections to cough with respiratory distress and encephalitis or meningitis [2,6–8]. Most survivors of NiV encephalitis develop long-term neurological complications [9]. NiV has been found in several parts of the world outside of Asia among bats and several domestic animals including pigs, goats, sheep, cats, horses and dogs [10]. Serological evidence of the presence of NiV in humans has also been reported outside of Asia [11]. Studies have shown controversial data on the involvement of human-to-human transmission, tree climbing, exposure to fruit, bats, pigs, other sick and/or dead animals or date palm sap in the transmission of NiV [12,13]. There is

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currently no effective vaccine or antiviral against NiV. Management of cases is mainly based on palliative measures such as aciclovir, antibiotics, antipyretics and additive ventilation [8,9]. Preventive measures such as washing hands, wearing gloves and face masks have been shown to break the NiV transmission [14]. Data on the case fatality rate (CFR) of NiV encephalitis and multiple ways how this virus spread including in animals, plants, bats, and humans have not yet been synthesized. We performed a systematic review and meta-analysis to estimate the pooled CFR of NiV encephalitis and to assess the risk factors associated to NiV infection.

2. Methods

2.1. Study design

This systematic review and meta-analysis was reported according to the PRISMA checklist for systematic review and meta-analysis (Supplementary Table 1) [15].

2.2. Search strategy

Articles published up to 27th November 2018 in the MedLine, Embase and Web of knowledge databases were considered for this review. Key terms of the search strategy that cover the fields of Nipah virus and encephalitis are presented in Supplementary Table 2. References of included articles and relevant reviews were checked to complete the electronic search. We planned inclusion of relevant studies published during manuscript writing.

2.3. Inclusion and exclusion criteria

We included cross-sectional, cohort, and case-control studies that have reported NiV outbreaks and/or risk factors for NiV transmission. We considered articles in all languages published in peer-reviewed journals. We excluded case reports and reviews. Two authors (SK and AFM) independently selected studies based on titles and abstracts on Rayyan website [16].

2.4. Case definition

In this study the authors defined a suspected case of NiV encephalitis as a person with encephalitis associated to a NiV outbreak with clinical features such as altered mental status, headache, fever or seizure. We considered a probable case as aperson suspected of NiV encephalitis who died before samples could be taken or who had negative serology to NiV when taken within 10 days of disease onset. A laboratory-confirmed case was defined as a person suspected of NiV encephalitis that showed positive results for NiV antibodies (IgM or IgG), viral antigen or RNA. To assess risk factors for NiV infection, participants meeting either the confirmed or probable case definition in original studies were included in this study as a case and the comparator was healthy patients.

2.5. Data extraction

We extracted the following information from references: study title, author name, publication year, exclusion reason, study design, country, cities, outbreak period, field investigation period, description of proxy respondents, description of control patients, viral diagnostic method, sample type, target detected, ethnicity, age, sex, incubation period, date of index case identification, delay between the onset of illness and death, number of deaths, number of enrolled patients, number of probable cases, number of confirmed cases, cluster observation, treatment administered, and risks factors of NiV infection. Potential risk factors were grouped into the following categories: exposure to any animal, exposure to pigs, exposure to bats, exposure to plants, exposure to fruits, exposure to date palm sap, and socio-demographic risk factors (Supplementary Table 3). We initially investigated 296 potential risk factors described in the studies included and considered only risk factors that were reported in three or more studies. Two authors (SK and FBNS) extracted the data independently and the disagreements were resolved by discussion among themselves.

2.6. Evaluation of the methodological quality of the studies

To evaluate the methodological quality of the studies in this systematic review, we used an adapted version of the Newcastle-Ottawa scale (NOS) for non-randomized studies [17] and the Hoy et al. assessment scale (–10, 4–6, and 0–3) for cross sectional studies(Supplementary Table 4) [18]. This evaluation of the methodological quality was carried out by two authors (SK and FBNS). Disagreements between the investigators during the evaluation of the quality of the included studies were resolved by discussion.

2.7. Data analysis

The overall CFR and odds ratio of potential risk factors for transmission were estimated according to random-effect meta-analysis [19]. The variance of the proportions was stabilized by a Freeman-Tukey double arcsine transformation. Heterogeneity between studies was estimated by the Cochran Q test and quantified with the I^2 statistic [20]. The subgroup analysis was carried out by country. For prevalence estimation, a sensitivity analysis was conducted with exclusion of low and moderate quality studies and case control studies. Publication bias was estimated using the Egger test and visual inspection of the funnel plots [21]. The synthesis of the data was carried out using the R version 3.5.1 [22]. The values of $p < 0.05$ were considered statistically significantly different. This review has been declared in the PROSPERO database under CRD42018116242.

Role of the funding source

There was no funding source for this study. All authors had access to all data and the corresponding author had the final responsibility to submit for publication.

3. Results

The literature search process is presented in Fig. 1. A total of 929 citations were obtained by the electronic and manual search. The reasons for exclusion are presented in Supplementary Table 5. The global review included 22 citations (25 studies) including 2156, 1682, and 474NiV encephalitis suspected, probable, and confirmed cases, respectively [23–44].

Table 1 presents overall characteristics of the included studies. The age of people studied ranged from 6 months to 85 years. In 88% of studies where gender was indicated, with the exception of two [31,33], the majority of people studied were male (ranging from 56 to 100%). All outbreaks were reported from1999 to 2016 in 5 countries in two WHO regions, Southeast Asia (Bangladesh and India) and Western Pacific (Malaysia, Singapore, and Philippines) (Supplementary Fig. 1), yet a majority were in Bangladesh (15/25). Nipah virus infection was frequently detected through the IgM (14/25) and IgG (11/25) in serum samples (22/25) and cerebrospinal fluid (13/25) using enzyme immunoassays (16/25) and ELISA (11/25). For patients who died or were seriously ill and could not respond to questions, proxy respondents such as family members or friends were interviewed. In some studies, multiple proxy respondents were interviewed for the same case and in other studies guardians were included in interviews with children ≤ 13 years of age [29,33,36]. To reduce bias in data collection one study also used proxy respondents for matched controls of deceased patients [38]. The majority of the studies included several healthy community-based

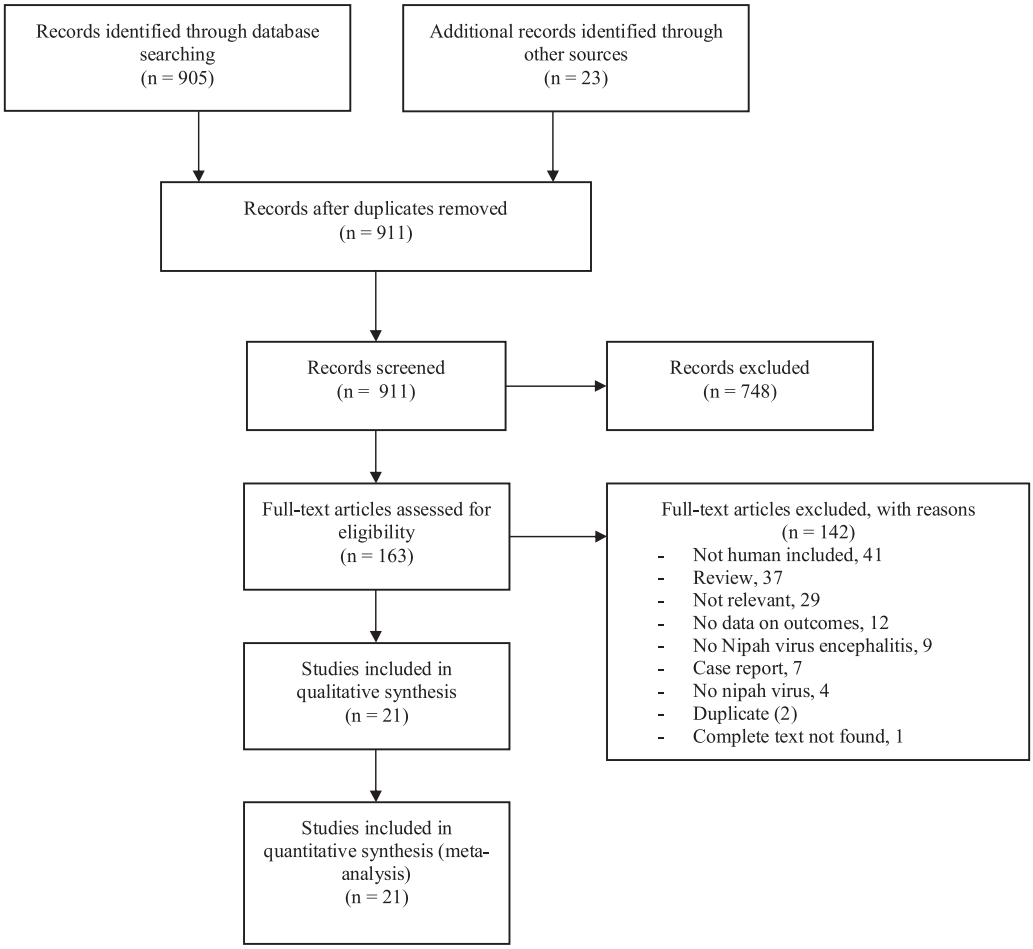

Fig. 1. Study selection.

controls randomly selected and matched in age, gender, and geographic location. Five citations (6 studies) verified the absence of NiV infection in controls by virological detection assays [23,26,36,38,40]. In contrast to other studies that found no evidence of NiV encephalitis in controls, Parashar et al. and Chew et al. detected IgM and/or IgG in controls and reclassified them as cases [26,40]. The risk of bias in 15 (60.0%) studies was low and moderate in the remaining 10 (40.0%). A general overview of all studies is presented in the Supplementary Table 6.

A total of 20 studies involving 1961 patients determined that the pooled CFR for NiV encephalitis was 61.0% (95% CI, 45.7–75.4; I^2 = 96.8%) (Fig. 2). This CFR could vary within a predicted range of 2.1–100%. In sensitivity analysis, no significant changes were observed in CFR with only low risk of bias 67.4% (95% CI, 52.8–80.6; I^2 = 89.1%) and only cross sectional studies 47.3% (95% CI, 30.4–64.6; I^2 = 96.6%). In 24 studies, the prevalence of confirmed and probable cases of NiV encephalitis was 39.5% (95% CI, 23.8–56.3%; I^2 = 97.8%) and 60.4% (95% CI, 43.6–76.1%; I^2 = 97.8%) respectively (Supplementary Figs. 2 and 3).

NiV infection was significantly associated with exposure to pigs in 8 studies involving 373 cases and 698 controls (OR = 7.6; 95% CI; 1.2–45.4). Exposure to live pigs (OR = 11.7; 95% CI; 1.1–122.7) showed association with NiV infection while owning or working on a pig farm was not associated (OR = 4.3; 95% CI; 0.2–76.4). In 25 studies that involved overall 420 cases and 1718 controls, exposure to healthy, sick or dead animals (cows, goats, dogs, cats, ducks, and chickens) were not associated with NiV infection. According to NiV infection, a total of 348 cases exposed to bats showed no statistically significant difference compared to 1447 controls (OR = 1.8; 95% CI; 0.7–4.6). However, in a subgroup analysis, observation of bats in the night next to the house was significantly associated with NiV infection (OR = 2.9; 95% CI; 1.1–7.9). In 8 studies, NiV infected patients (260) were significantly more susceptible to have climbed trees than healthy controls (999) (OR = 1.4; 95% CI; 1.0–1.9). Unexpectedly, the combined probability of fruit consumption was higher in controls compared to cases (OR = 0.7; 95% CI; 0.6 to 0.9). This higher tendency to consume fruit in controls was confirmed in a subgroup analysis with plum/boroi (OR = 0.6; 95% CI; 0.4 to 0.8) and guavas (OR = 0.6; 95% CI; 0.4 to 0.8) while there was no difference with bananas and papayas. Exposure to date palm sap was significantly associated with NiV infection in 14 studies including 273 cases and 1157 controls (OR = 5.7; 95% CI; 3.8–8.6). This association was confirmed in a subgroup analysis for harvested date palm sap (OR = 4.2; 95% CI; 1.7–10.3), the consumption of date palm sap (OR = 7.4; 95% CI; 4.2–13.0) and the presence of a person in the house harvesting the date palm sap (OR = 4.5; 95% CI; 2.1–9.9). Sociodemographic factors such as male gender (OR = 4.5; 95% CI; 2.1–9.9) and travel history (OR = 2.0; 95% CI; 1.4–2.9) were significantly associated with NiV infection (Table 2). Supplementary Figs. 4–11 present the risks of NiV infection following exposure to pigs, other animals, sick or dead animals, bats, plants, fruits, date palm sap and socio-demographic factors.

Considerable heterogeneity was detected in all prevalence meta-analysis (Supplementary Table 7). No heterogeneity was observed in the majority of risk factors meta-analysis (Table 2). The Egger test revealed a publication bias for prevalence calculations (CFR, prevalence of probable and confirmed cases) and some NiV infection risk factors. Asymmetry was observed in the funnel diagrams for only exposure to fruits (Supplementary Figs. 12–20).

Table 1
General characteristics of included studies.

Characteristics		N = 25	%
%Male. range		25-100	
Age (years). Median, IQR		32	[22.5-38]
Outbreak period range		1999-2014	
Year of publication. range		1999-2016	
Study design	Case control	14	56
	Cross-sectional	11	44
Timing of data collection	Prospective	23	92
	Retrospective	2	8
Study bias	Low risk	15	60
	Moderate risk	10	40
Countries	Bangladesh	15	60
	India	2	8
	Malaysia	5	20
	Singapore	2	8
	Philippines	1	4
Detection assays	EIA	16	64
	ELISA	11	44
	Culture	6	24
	RT-PCR	7	28
	IHC	1	4
	Seroneutralisation	2	8
Sample type	Serum	22	88
	CSF	13	52
	Urine	5	20
	Throat swab	4	16
	Brain tissue/aspirate	2	8
	Tracheale secretions	1	4
	Nasal secretions	1	4
	Saliva	1	4
	Clot	1	4
	Lung tissue/aspirate	1	4
	Liver tissue/aspirate	1	4
	Rectal swab	1	4
	Lung tissues	1	4
	Kidney tissues	1	4
	Not reported/Unclear	1	4
Target detected	IgM	14	56
	IgG	11	44
	RNA	5	20
	Viral antigen	3	12
	Not reported/Unclear	7	28

4. Discussion

This systematic review meta-analysis suggests that the NiV encephalitis is associated with high risk of death. Outbreaks were recorded only in the "Nipah virus belt" in Southeast Asia and especially in Bangladesh. The findings of this systematic review further supported the involvement of exposure to pigs or date palm sap and parameters such as tree climbing, male gender and travel outside his sub-district in the transmission of NiV infection. The results of this meta-analysis showed no association between NiV infection and exposure to bats, live, sick or dead animals and fruits.

Prior study revealed the infection of pigs with NiV in several tissues [10]. Thus in this synthesis, direct contact with pigs, such as feeding, assistance in birth, hunting, cleaning, contact with fluids or secretions, and drug administration, were strongly associated with infection while being a worker or farm owner was not associated. Relative contribution of these specific pig farm activities was not evaluated during this study given the limited number of studies that reported. This is an aspect that should be taken into account in future studies. Contrary to the involvement of pigs in the transmission of NiV in Malaysia and Singapore, pigs were not identified in the outbreaks in Bangladesh where the majority of the population consists of Muslims who do not eat meat of pigs.

Apart from pigs, several other animals have been suspected to be involved in the NiV transmission. Indeed, NiV antibodies have been reported in dogs, cats and many other animals [10]. This systematic review shows that apart from pigs, there were no association between other living, sick or dead animals (cows, goats, dogs, cats, ducks or chickens) and the transmission of NiV.

Frugivorous bats of the genus *Pteropus* are considered as the main reservoir of NiV [45–47]. However, this study reveals that there is no association between exposure to bats and transmission of NiV. In the subgroup analysis, however, observation of bats near the house at night was associated with an increased risk of NiV infection. It has been shown that bats can excrete the virus in urine and saliva [46,48,49]. Studies have also reported evidence of the presence of NiV in partially consumed fruits [50]. Thus the introduction of NiV into the community could be via accidental contact between secretions of bats or any material contaminated by bats and ultimately to humans.

The results of this review suggest that patients who climbed trees and those exposed to date palm sap had a higher odds of being infected with NiV. Tree climbing is common among young boys who harvest fruits or adults who harvest date palm sap. Additionally, harvested fruits may be partially eaten. Fruit bats have been known to drink from date palm sap collection bowls and feed on the fruits at night [51]. It is therefore likely that date palm sap and fruit contaminated by the secretions/excretions of fruit bats are the source of contamination. Indeed, it has been shown that this virus can survive for several days in the urine of the flying fox and the fruit juice [50]. Since date palm sap has an alcohol concentration of about 4%, this virus can also survive in such conditions [52].

Male gender and participants who traveled outside their sub-district in this study were significantly at risk of NiV infection. This increased risk of NiV transmission could be attributed to exposure to different vehicles (date palm sap, partially consumed fruits, contact with infected patients, etc.) of NiV transmission in the visited area.

The probability of fruit consumption was significantly higher among the controls in this study. Although this hypothesis is speculative, this protective effect against NiV infection could be attributed to the antiviral action of ascorbic acid of fruit vitamin C [53].

Like all other systematic reviews, this study is affected by the limitations of included primary studies that are important to address. NiV encephalitis is characterized by high mortality and multiple community awareness campaigns and several study participants would have prior knowledge of the potential factors for Nipah virus transmission that may guide their response to the questionnaires. The use of proxy respondents in the majority of included studies may have led to inaccurate responses. This limitation is amplified by the use of proxy interviews with a case-control ratio largely in favor of cases since these are the cases that would die and were more likely to be subject to proxy interview. The consideration of probable cases of NiV encephalitis in the analysis may have compromised the findings of this study. Although all the controls in the studies were declared to be healthy, the lack of verification of the absence of NiV infection in controls in some studies may have led to misclassification of some cases as control especially as cases of asymptomatic infections with NiV have been reported and reclassifications of controls in cases have been recorded. Responses may also have been affected by recall because some questions related to activities that took place several years ago. Human-to-human propagation could also be an important mode of transmission of NiV. However, due to the low number of studies which investigated human to human transmission of NiV, we were not able to evaluate this aspect in this study. Future studies should focus on specific mechanisms, viral doses, the stage of severity of infection required for effective human-to-human transmission of NiV, and the survival time of NiV on inert surfaces.

It seems unlikely, however, that the above-mentioned limitations had impact on the conclusions of this study for several reasons. First, in the majority of the studies the cases were matched to the controls on several criteria including age, sex, and geographical location. Secondly, multiple respondents and medical records verification were considered in proxy respondent interviews. We also conducted a sensitivity

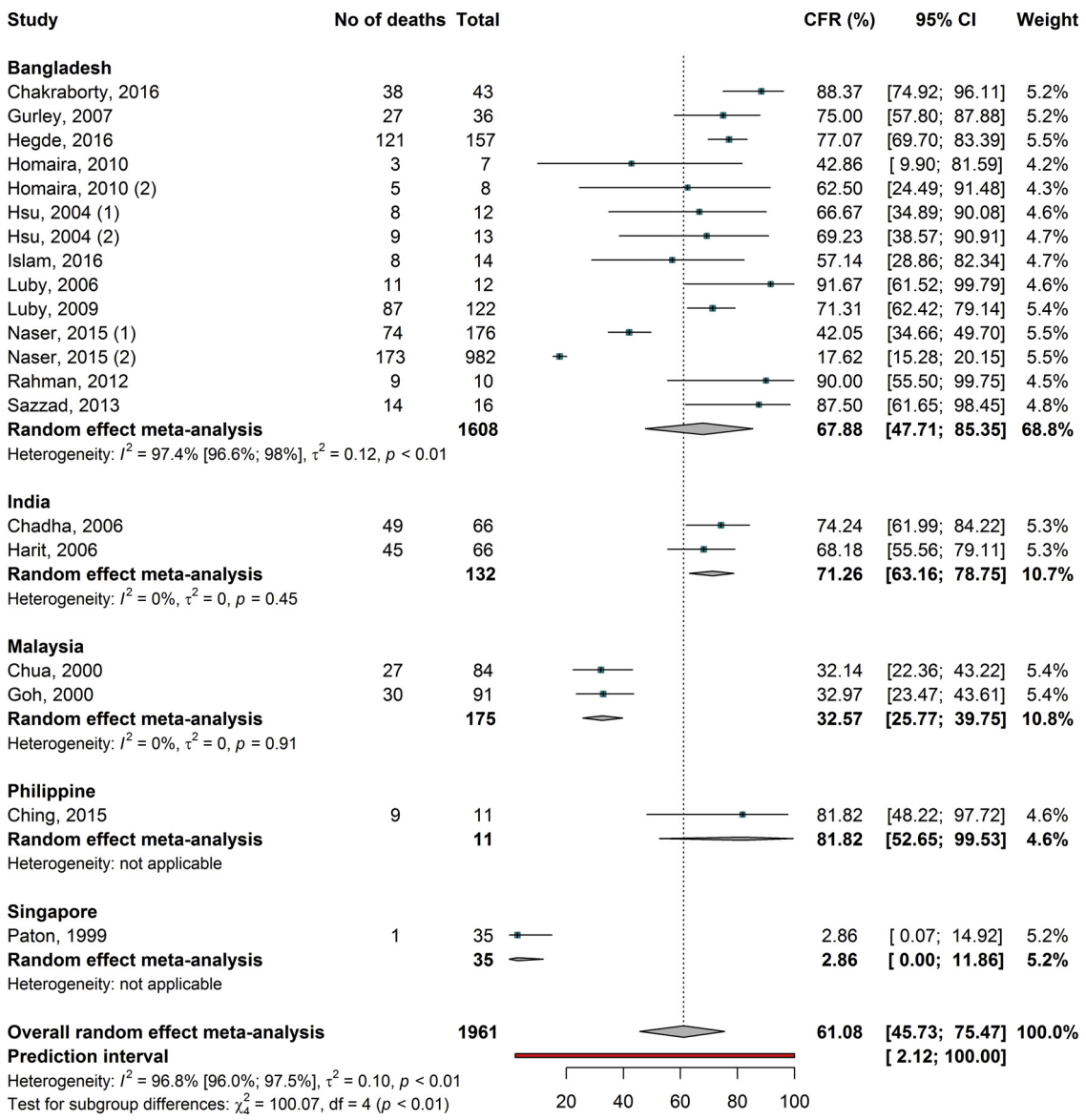

Fig. 2. Case fatality rate of Nipah virus encephalitis outbreaks among people in Asia.

analysis considering only low risk of bias studies and study design that showed no difference in prevalence finding. The strengths of this meta-analysis also include a comprehensive search strategy with no language restriction, the participation of two independent investigators at all stages of the process, and the use of rigorous and robust statistical methods. Finally, to the best of our knowledge, this study is the first systematic review and meta-analysis of studies on CFR and risk factors for NiV infection.

This study shows that NiV encephalitis is associated with considerable CFR. This synthesis also provides evidence in support that direct contact with pigs; climbing trees; exposure to date palm sap; and sociodemographic risks including male gender and traveling outside own sub-district are the main risk factors of NiV transmission. Basic measures such as hand washing with soap should be the absolute rule and especially during epidemics. Employees and owners of pig farms should limit direct contact with pigs during the epidemic period to prevent new infections. Interventions that aimed at reducing the access of fruit bats to the device for the production of date palm sap are important ways in preventing NiV associated infections.

Further research is needed to better understand factors required for transmission of NiV from bats to multiple intermediate vehicles, specific pathways of NiV transmission from intermediate vehicles to humans, and a clarification of the means of man-to-man transmission.

Conflict of interest

The authors declare that they have no competing interests.

Data sharing and data accessibility

All data generated or analyzed during this study are included in this published article and its supplementary information files.

Authors' contributions

Conception: SK, RN. Design: SK, RN. Literature search: JJB, SK. Selection of studies: SK, AFM. Full texts search: SK, FBNS. Data extraction: SK, FBNS. Data synthesis and analysis: SK, JJB, CKN. Data interpretation: SK, JJB, CKN. Manuscript drafting: SK. Manuscript editing and revision: SK, JJB, AFM, FBNS, CKN, SASM, SE, RN. Manuscript final version approval: SK, JJB, AFM, FBNS, CKN, SASM, SE, RN. Guarantor of the review: SK, RN.

Table 2
Risk factors of Nipah virus infection.

	OR (95%CI)	95% Prediction interval	N Studies	H (95%CI)	I^2 (95%CI)	P heterogeneity	P Egger test	P-value subgroup difference
Exposure to pigs	7.6 [1.2-45.4]	[0.0- > 1000]	8	2.8 [2.1-3.8]	87.6 [77.7-93.1]	< 0.001	0.901	0.597
- Contact with pigs	11.7 [1.1-122.7]	[0.0- > 1000]	5	2.0 [1.3-3.2]	76.4 [42.4-90.3]	0.002	0.502	
- Pig farm owner/worker	4.3 [0.2-74.4]	[0.0- > 1000]	3	3.9 [2.5-6.1]	93.7 [84.8-97.3]	< 0.001	0.858	
Exposure to animals	1.1 [0.8-1.5]	[0.7-1.8]	25	1.0 [1.0-1.2]	5.1 [0.0-36.3]	0.390	0.196	0.751
- Contact with living cows	0.9 [0.5-1.5]	[0.3-2.1]	7	1.0 [1.0-1.9]	8.0 [0.0-73.1]	0.367	0.228	
- Contact with living goats	0.9 [0.5-1.5]	[0.4-2.1]	5	1.0 [1.0-1.2]	0.0 [0.0-31.3]	0.876	0.263	
- Contact with living dogs	1.7 [0.6-4.7]	[0.2-15.0]	4	1.0 [1.0-1.7]	0.0 [0.0-66.6]	0.711	0.073	
- Contact with living cats	1.4 [0.2-8.0]	[0.0- > 1000]	4	1.8 [1.1-3.1]	72.1 [20.8-90.2]	0.013	0.722	
- Contact with living ducks	1.4 [0.7-3.1]	[0.0-189.5]	3	1.0 [1.0-2.0]	0.0 [0.0-75.8]	0.650	0.768	
- Contact with living chickens	1.3 [0.5-3.4]	NA	3	1.0	0.0	0.384	NA	
Exposure to sick or dead animals	1.3 [0.9-1.7]	[0.8-1.9]	23	1.0 [1.0-1.2]	5.0 [0.0-36.6]	0.393	0.730	0.949
- Contact with a sick animal	1.0 [0.4-2.8]	[0.0- > 1000]	3	1.4 [1.0-2.6]	50.4 [0.0-85.6]	0.133	0.739	
- Contact with sick cow	1.4 [0.2-9.7]	[0.0- > 1000]	4	1.5 [1.0-2.6]	56.7 [0.0-85.7]	0.074	0.253	
- Contact with sick chicken	1.1 [4.0-2.7]	[0.1-8.4]	4	1.0 [1.0-2.5]	0.0 [0.0-84.3]	0.403	0.948	
- Contact with sick goat	1.7 [0.7-4.5]	[0.0-741.1]	3	1.0 [1.0-1.3]	0.0 [0.0-43.4]	0.832	0.283	
- Ate meat of a sick animal	1.2 [0.8-2.0]	[0.6-2.5]	6	1.0 [1.0-1.0]	0.0 [0.0-0.0]	0.990	0.073	
- Touched or observed a dead animal	1.8 [0.6-5.2]	[0.0- > 1000]	3	1.2 [1.0-2.3]	40.1 [0-81.6]	0.188	0.026	
Exposure to bats	1.8 [0.7-4.6]	[0.1-27.6]	6	1.7 [1.1-2.7]	67.8 [23.8-86.4]	0.008	0.578	0.015
- Contact with living bats	0.4 [0.1-1.4]	NA	3	1.0	0.0	0.762	NA	
- Report of seeing a bat at night near home	2.9 [1.1-7.9]	[0.0-156.1]	4	1.7 [1.0-3.0]	67.5 [5.5-88.9]	0.026	0.763	
Climbed a tree	1.4 [1.0-1.9]	[0.9-2.1]	8	1.0 [1.0-1.4]	0.0 [0.0-52.8]	0.682	0.723	NA
Exposure to fruits	0.7 [0.6-0.9]	[0.5-1.1]	16	1.0 [1.0-1.3]	10.9 [0.0-48.1]	0.329	0.071	0.058
- Eaten plum/Boroi	0.6 [0.4-0.8]	[0.0-4.4]	3	1.0 [1.0-1.3]	0.0 [0.0-48.5]	0.817	0.593	
- Eaten bananas	1.2 [0.6-2.4]	[0.1-8.9]	4	1.1 [1.0-2.8]	18.5 [0.0-87.5]	0.297	0.417	
- Eaten papayas	1.1 [0.6-1.9]	[0.3-3.7]	4	1.0 [1.0-2.5]	0.0 [0.0-84.0]	0.411	0.040	
- Eaten guavas	0.6 [0.4-0.8]	[0.3-1.0]	5	1.0 [1.0-1.6]	0.0 [0.0-61.0]	0.711	0.372	
Exposure to DPS	5.7 [3.8-8.6]	[3.6-9.0]	14	1.0 [1.0-1.3]	0.0 [0.0-40.8]	0.703	0.727	0.458
- Sap harvester	4.2 [1.7-10.3]	[1.0-18.0]	5	1.0 [1.0-2.0]	0.0 [0.0-76.4]	0.474	0.994	
- Drank raw DPS	7.4 [4.2-13.0]	[3.3-16.4]	6	1.0 [1.0-1.8]	0.0 [0.0-69.5]	0.527	0.999	
- Anyone in household harvested DPS	4.5 [2.1-9.9]	[0.0-693.8]	3	1.0 [1.0-1.7]	0.0 [0.0-68.0]	0.722	0.073	
Sociodemographic risks	1.7 [1.3-2.2]	[1.3-2.2]	14	1.0 [1.0-1.2]	0.0 [0.0-33.1]	0.792	0.240	0.183
- Male	1.5 [1.1-2.0]	[1.0-2.2]	10	1.0 [1.0-1.2]	0.0 [0.0-32.0]	0.836	0.606	
- Visited any area outside own sub-district	2.0 [1.4-2.9]	[0.9-4.5]	4	1.0 [1.0-2.0]	0.0 [0.0-76.8]	0.576	0.021	

CI: confidence interval; OR: Odds ratio; DPS: date palm sap NA: not applicable.

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Ethical approval

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Appendix A. Supplementary data

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