Research Articles

Dynamic Transmission of African Horse Sickness in Horse Populations during the First Epidemic in Thailand

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Abstract

Thailand faced the first outbreak of African horse sickness (AHS) in its history in 2020. The virus firstly attacked Nakhon Ratchasima province, where a large number of naïve horses lived. In this outbreak, over four hundred horses were infected and died within three months. This study applied DengueME application to simulate how the virus spread in the horse populations with the susceptible-infectious-removed (SIR) modeling framework in horses and susceptible-infectious (SI) in vectors. The basic reproduction number (R_0), herd immunity threshold, and vaccine coverage requirement were subsequently calculated. We estimated R_0 at 3.3. With the herd immunity threshold of 69.7%, we suggested vaccinating 86.1% of horse populations to prevent future outbreaks. Our model is applicable as a baseline to test interventions such as vector control and to monitor the dynamic transmission of AHS in horse populations.

Keywords: African horse sickness, dynamic transmission, herd immunity, mathematical model

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แบบจำลองพลวัตการแพร่กระจายของกาฬโรคแอฟริกาในม้าในการระบาดครั้งแรกในประเทศไทย

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บทคัดย่อ

ประเทศไทยได้เผชิญหน้ากับการระบาดของกาฬโรคแอฟริกาในม้าเป็นครั้งแรก ในปี พ.ศ. 2563 โดยมีรายงานการเริ่มระบาดที่จังหวัดนครราชสีมา ซึ่งเป็นจังหวัดที่มีม้าอาศัยอยู่เป็นจำนวนมาก ส่งผลให้มีม้าติดเชื้อและเสียชีวิตเป็นจำนวนมากกว่า 400 ตัว ภายในเวลา 3 เดือน ในการศึกษานี้ ผู้วิจัยได้ใช้แอพพลิเคชัน DengueME ในการจำลองสถานการณ์การแพร่ระบาดของเชื้อไวรัสผ่านแมลงพาหะด้วยแบบจำลอง susceptible-infectious-removed (SIR) ในม้า และ แบบจำลอง susceptible-infectious (SI) ในแมลงพาหะ หลังจากนั้น จึงคำนวณค่า basic reproduction number (R_0) ภูมิคุ้มกันระดับฝูง และความครอบคลุมวัคซีนที่จำเป็น ผลการคำนวณค่า R_0 ได้เท่ากับ 3.3 และค่า herd immunity threshold ได้เท่ากับ 69.7% และสัดส่วนของม้าที่ควรได้รับวัคซีนคือ 86.1% ของประชากร เพื่อป้องกันการระบาดในอนาคต แบบจำลองนี้สามารถใช้เป็นพื้นฐานในการทดสอบมาตรการอื่น เช่น การควบคุมแมลงพาหะ และใช้ในการติดตามพลวัตของการแพร่กระจายของกาฬโรคแอฟริกาในประชากรม้าได้

คำสำคัญ : กาฬโรคแอฟริกาในม้า พลวัตการแพร่ระบาด ภูมิคุ้มกันระดับฝูง แบบจำลองทางคณิตศาสตร์

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Introduction

African horse sickness (AHS) is a vector-borne viral disease caused by the African horse sickness virus (AHSV). The virus belongs to the genus *Orbivirus* of the family *Reoviridae* (Dennis et al., 2019). The *Orbivirus* is also well known as a cause of bluetongue disease and epizootic hemorrhagic disease. This virus is a vector-borne disease that can be spread by biting mosquitoes, biting midges or gnats (genus *Culicoides*), and gadflies (genus *Tabanus, Haematopota, Chrysops*). Especially, the *Culicoides imicola* and *Culicoides Bolitinos* are primary vectors for AHSV (Mellor and Hamblin 2004; Slama et al., 2017).

Nine distinct serotypes of the AHSV have been recognized to date. Equids, such as horses, donkeys, mules, and zebras, are the main hosts of the virus (Spickler 2015). Zebras are generally resistant, resulting in asymptomatic infection (Porphyre and Grewar 2019). Nonetheless, serious infections mostly occur in horses, mules, and donkeys leading to high morbidity and mortality rates of 34% and 50-95 %, respectively (Spickler 2015).

The AHSV was believed to first emerge in Yemen in 1327 (Hemida et al., 2017). In 1657, the virus was documented circulating in South Africa, with a major outbreak in 1854-1855 (Dennis et al., 2019). In 1960s, animal trades and movements acted as a trigger for AHSV to spread across the Middle East, Mediterranean, Arabia, and Asia (Pakistan and India). This serotype 9 outbreak of AHSV killed approximately 300,000 equids (McKenna 2015).

According to the World Organization for Animal Health (WOAH), Thailand has been recognized as an AHS non-endemic country until 2020. AHS was first reported on March 27, 2020, in Pak Chong district, Nakhon Ratchasima province (WOAH 2020). From 24th February 2020 to 20th April 2020, Nakhon Ratchasima was ranked first with 368 infected horses. Of which, 337 horses were fatal (case-fatality rate = 91.6%) (DLD 2020). The virus was later identified as AHSV serotype 1 (Kajaysri and Toompong 2020; King et al., 2020). As it was the very first outbreak in the country, all the horses were immunologically naïve and extremely susceptible, resulting in severe clinical signs and a high mortality rate (Castillo-Olivares 2021). All forms of the clinical manifestations (cardiac, respiratory, and mixed) were detected (Kajaysri and Toompong 2020).

During the outbreak, the disease control and eradication plan had launched. The outbreak response area was determined in three zones. The infected zone, protection zone, and risk zone were the area that had a radius from the infected farm of 20 km, 50 km, and 100 km, respectively. Mostly horses in the infected and protection zones were vaccinated as much as possible to create herd immunity. The disease surveillance was carried out by clinical surveillance, vector surveillance, and active surveillance. Horse transportation was restricted. The vector control was applied by hanging up the fine mosquito net and spraying the insecticide surrounding the stable to decrease the vector population and applying the insect repellent on the horses (DLD 2020; Ketusing 2020).

Mathematical modeling is an epidemiological tool used to describe the dynamic transmission of infectious diseases (Wiratsudakul et al., 2018). These models are basically built based on relevant epidemiology concepts (Huppert and Katriel 2013). The compartmental model has been widely used to simulate different infectious diseases due to its simplicity and ability to produce results in a timely fashion. Susceptible-Infectious-Recovered (SIR) is a compartmental model that was first proposed by Kermack and McKendrick (Doungmo Goufo et al., 2014). The model has been used for diseases that spread quickly with a short incubation period, such as Avian Influenza (Guan et al., 2007), COVID-19 (Cooper et al., 2020), and Chickenpox (Devi and Devachoudhury 2018). In the case of vector-borne diseases, additional compartments for the vectors are added to the classical SIR model (Wiratsudakul et al., 2018). The SIR-SI model is one of the widely used models for such diseases. The model has been used to describe the spread of Zika virus (Boreta et al., 2017), Dengue (Pandey et al., 2013), and Malaria (Putri et al., 2014). In the study of AHS, some mathematical models have already been developed (Lord et al., 1998; Backer and Nodelijk 2011). However, none was specifically tailored to the situations in Thailand.

This study, therefore, aimed to describe the dynamic transmission of AHSV in horse populations in Nakhon Ratchasima and further recommend the vaccine coverage requirement for the effective control of the disease in Thailand.

Materials and Methods

Data Retrieval

We retrieved the daily number of horses that were infected and died from the AHSV infections from the Thai Society of Equine Practitioners and the Department of Livestock Development, Thailand. The total number of horses was 1,835 horses from 117 horse farms in every district of Nakhon Ratchasima province, Thailand. This province contains 32 districts. Most horses were lived in Pak Chong district (1327/1835) and Muang district (390/1835). Most horses in Muang district were racehorses; meanwhile, Pak Chong district had many types of horses for several purposes i.e. competition, pleasure riding, western riding, showing, etc. Neither human nor animal ethical approval was required as only the secondary data was used; moreover, no humans and animals were involved in the study.

Estimation of vector population

Due to the data on the biting midges in Nakhon Ratchasima is not available, we then extrapolated the number of biting midges from a previous study. Thepparat et al., (2012) reported that the density of biting midges was 40.5 midges/km^2 in the area of Parai subdistrict, Arunyaprathet district, Sakaew province, Thailand. The size of Nakhon Ratchasima compared to Parai subdistrict is shown in Figure 1. The area of Nakhon Ratchasima was 12,495.13 km^2. Hence, the number of the biting midges in Nakhon Ratchasima was then estimated at 506,473 midges.

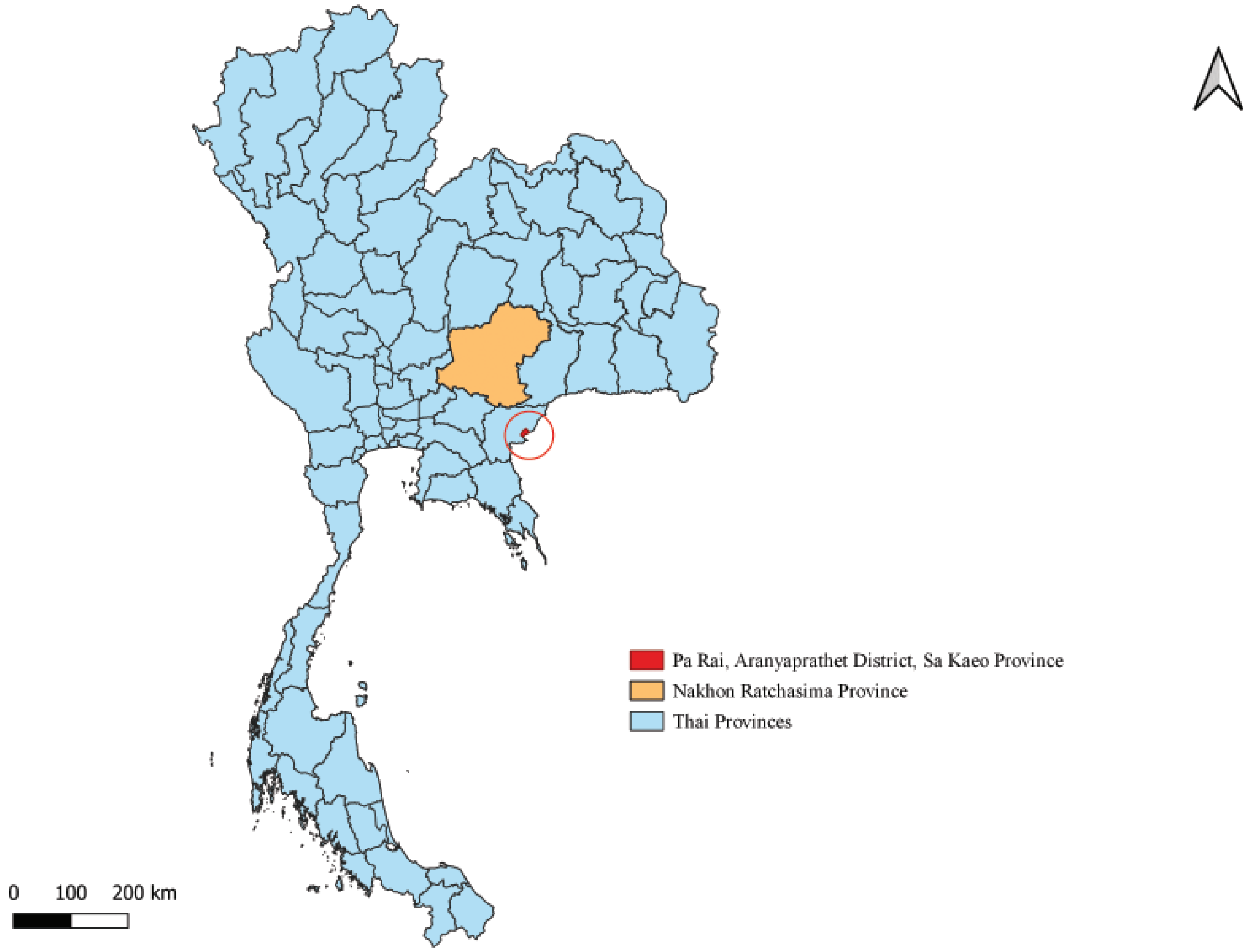

Figure 1. Geographical comparison between Parai subdistrict (red area) and Nakhon Ratchasima province (orange area) that the density of the biting midges was estimated.

Dynamic transmission of AHS in Nakhon Ratchasima province

An SIR-SI compartmental model was constructed to simulate how AHSV spread between horse and vector populations (Figure 2). The duration of the model was designed as 120 days. The dynamic transmission of the virus followed a set of differential equations shown in Eq 1. All parameters used in the equation were defined in Table 1. For the number of infected vectors during time t ($I_v(t)$) and the biting rates (α), we fitted the SIR-SI model with the given observed data until we got the values that reflected the field data. The software DengueMe (Federal University of Ouro Preto, Ouro Preto, Brazil, and National Institute for Space Research, São José dos Campos, Brazil) was used throughout the simulation.

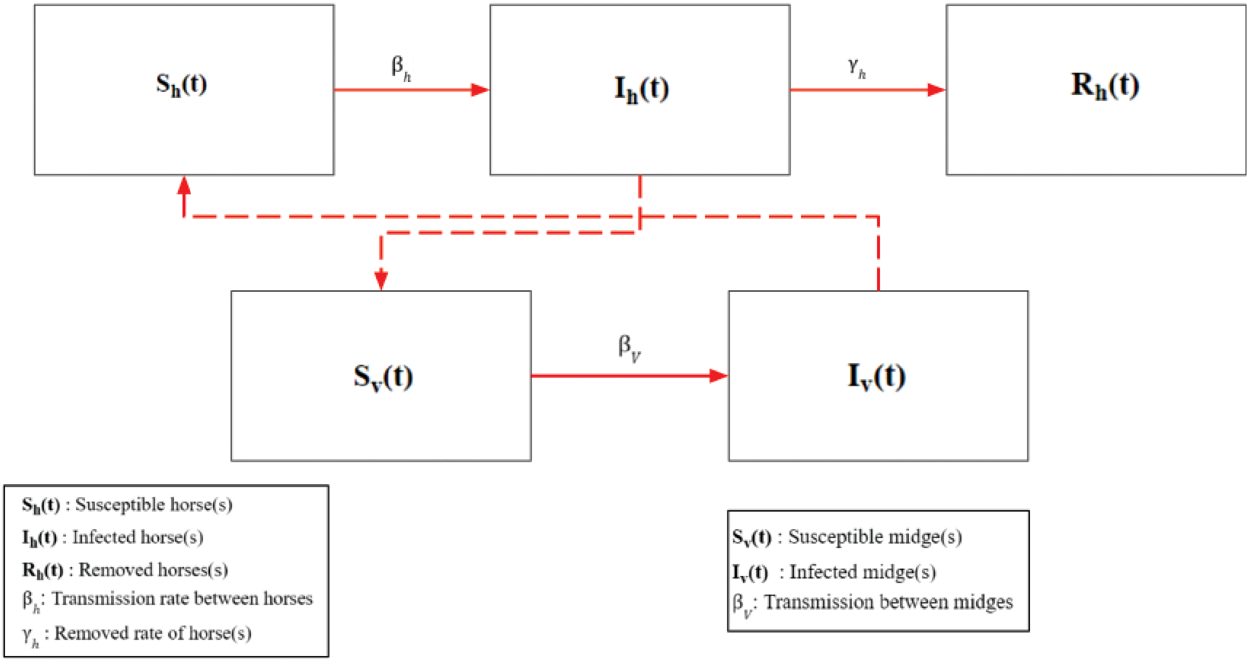

Figure 2. Conceptual framework of AHS model in Nakhon Ratchasima province.

Table 1. Model parameters for the AHS transmission model in Nakhon Ratchasima province.

Parameter	Definition	Values	References
S_h(t)	Numbers of susceptible hosts during time *t*	1,834 horses	Field data
I_h(t)	Numbers of infected hosts during time *t*	1 horse	Initial condition
R_h(t)	Numbers of removed hosts during time *t*	0 horse	Initial condition
S_v(t)	Numbers of susceptible vectors during time *t*	506,472 biting midges	Calculated from Thepparat et al., (2012)
I_v(t)	Numbers of infected vectors during time *t*	1 biting midges	Estimated from epidemic curve
α	The biting rates (Assumed constant and equal for all the hosts)	0.08 (1 vector/day)	Estimated from epidemic curve

Table 1. Model parameters for the AHS transmission model in Nakhon Ratchasima province. (Cont.)

Parameter	Definition	Values	References
β_h	Transmission probability from vectors to hosts	0.770	Backer & Nodelijk (2011)
β_v	Transmission probability from hosts to vectors	0.040	Backer & Nodelijk (2011)
γ_h	The rate at which the infected hosts are removed from the population	0.230	Backer & Nodelijk (2011)

Horses (Host) (Eq 1.)

$$S_h(t) = -\alpha\beta_h S_h(t) I_v(t)$$

$$I_h(t) = \alpha\beta_h S_h(t) I_v(t) - \gamma_h I_h(t)$$

$$R_h(t) = \gamma_h I_h(t)$$

Midges (Vector)

$$S_v(t) = -\alpha\beta_v I_h(t) S_v(t)$$

$$I_v(t) = \alpha\beta_v I_h(t) S_v(t)$$

, where the initial conditions were set for both host (horse) and vector (midges) parts as demonstrated in Table 1.

Estimation of the basic reproduction number

The transmission and recovery rates were used for calculating the basic reproduction number (R_0). The formula for calculating R_0 was described by Gubbins (2019) as shown in Eq 2.

$$R_0 = \sqrt{\frac{ba}{\gamma+\mu} \times \frac{\beta ma}{r_I}} \qquad \text{(Eq 2.)}$$

In addition, all parameters for calculating R_0 are noted in Table 2. Once the midge has its bloodmeal on the infected horses, a midge persists infected and contagious until the virus becomes inactivated or the vector dies out. In the mathematical term, it can be expressed as $1/(\gamma + \mu)$, a period in which the virus lasts on average days, where γ is the virus inactivation rate and μ is the mortality rate of midges. Concurrently, a midge can bite the susceptible hosts times per day (a is the reciprocal of the time interval between the blood meals), and proportion of these bites, noted as b (probability of transmission from midges to horses), is 0.770. To calculate a, we did the reciprocal of blood feeding interval of midges, 7.5, getting 1/7.5. This will result in newly infected horses. After horses are infected, the horses will continue to be contagious for its infectious phase, which typically lasts $1/r_I$ days. According to Backer & Nodelijk (2011), horses remain infectious for 4.4 days. During this time, the midges will bite the horses m x a times per day (m is the ratio of vector to hosts), 276 midges per 1 horse. Along with the proportion, β (probability of transmission from horse to midge) is responsible for the rise of newly infected midges.

Herd immunity threshold and vaccine coverage requirement

Herd immunity threshold was calculated from the R_0 (Herd immunity = $1\frac{1}{R_0}$) (Lahariya 2016). The efficacy of the AHS vaccine was up to 81% (Dennis et al., 2019). Vaccine coverage requirement was then calculated from a proportion of the herd immunity and the vaccine efficacy (Vc = $\frac{\text{Herd immunity (qc)}}{\text{vaccine efficacy (E)}}$) (MacIntyre et al., 2021).

Table 2. Model parameters for calculating R_0.

Parameter	Definition	Values	References
b	Probability of transmission from midge to horse	0.77	Backer & Nodelijk (2011)
a	Reciprocal of time interval between the blood meals	$\frac{1}{7.5}$	Backer & Nodelijk (2011)
$\gamma + \mu$	γ is the virus inactivation rate μ is the midge's mortality rate	16	Backer & Nodelijk (2011)
β	Probability of transmission from horse to midge	0.04	Backer & Nodelijk (2011)
m	Midge to horse ratio (N/H; N and H are the number of midges and horses, respectively)	276	Calculated from given field data
$\frac{1}{r_I}$	Average infection period dying hosts rate (days)	$\frac{1}{4.4}$	Backer & Nodelijk (2011)

Results

Observed AHS outbreaks in Nakhon Ratchasima province

The first group of infected horses was detected in Pak Chong district and then rapidly widespread to a nearby area. Overall, there were 56 farms in Nakhon Ratchasima confronted with the AHSV from 24th February 2020 to 20th April 2020. The number of sick and dead horses was 368 and 337 horses, respectively (DLD 2020). These cases were positively confirmed with RT-PCR (Bunpapong et al., 2021). The number of sick horses was used as baseline data to plot the epidemic curve, as shown in Figure 3.

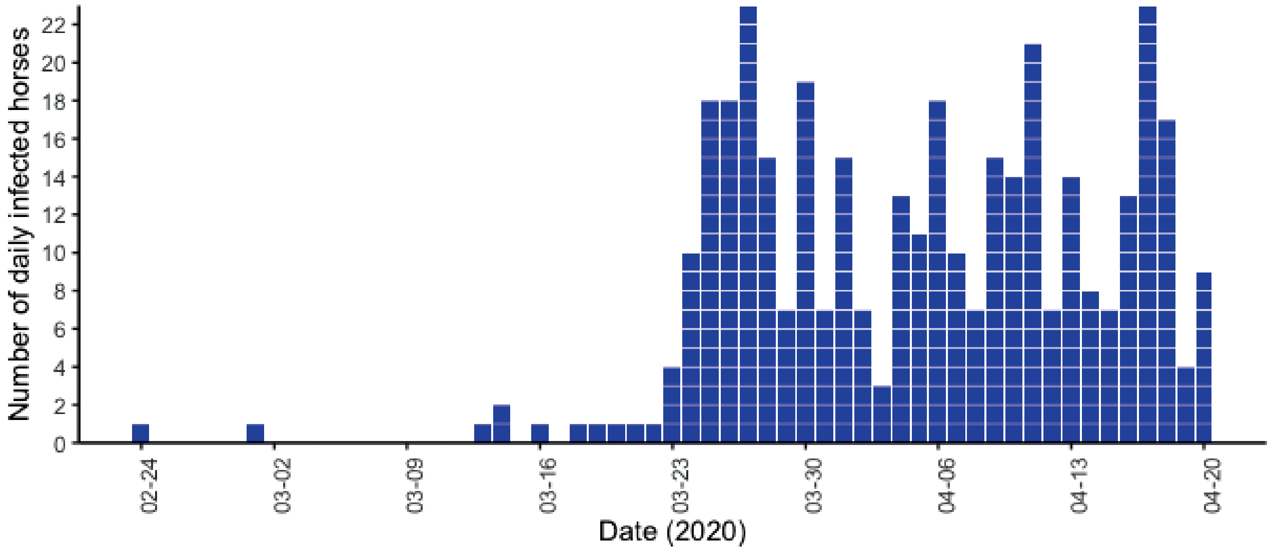

Figure 3. Epidemic curve of daily infected horses in Nakhon Ratchasima province during 24th February to 20th April 2020 (Data source: DLD 2020).

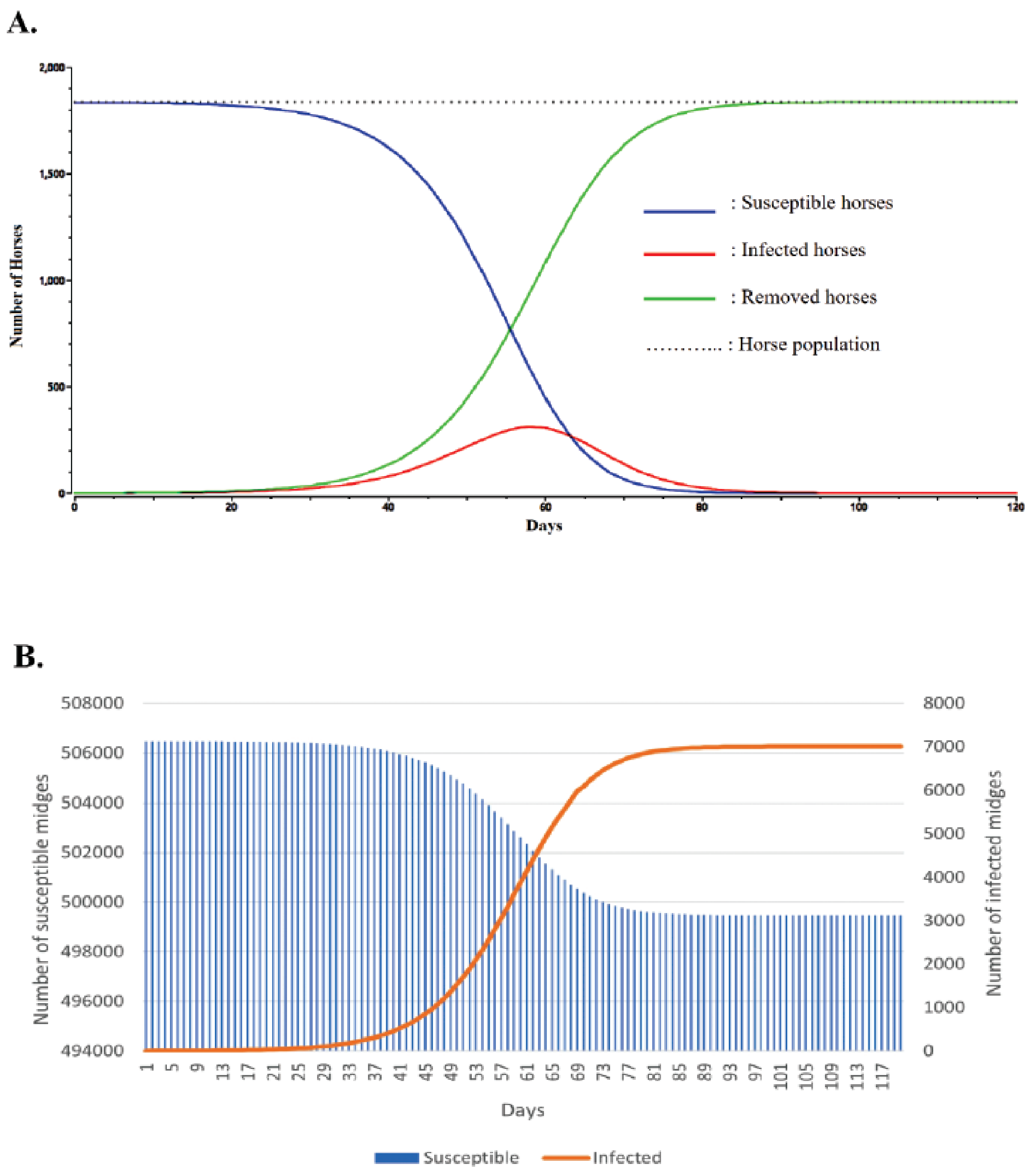

Figure 4. Dynamic transmission of AHSV in Nakhon Ratchasima province. A. Results in host populations B. Results in vector populations.

Dynamic transmission of AHSV in Nakhon Ratchasima province

In the host populations (Figure 4A), the number of infected horses peaked on day 59 and then gradually decreased later. The number of cases declined to zero on day 85. In the vector populations (Figure 4B), the number of susceptible midges was inversely proportional to the number of infected midges as there was a decline in the number of susceptible midges along the course of the outbreaks while the number of infected midges inclined. Throughout the studies, there was a significant change in the number of infected and susceptible midges. The number of infected midges started rising exponentially from 106 midges to 6,925 midges from day 28 until day 83. Later, the infectious rate of midges drops rapidly. Once, the infected midgesí population reached 6,999 midges on day 104, it remained nearly unchanged. On day 116, the number of infected midges reached its peak and threshold at 7,000, and there were no shifts afterward. On the other hand, the trend of susceptible midges went directly opposite to infected midges.

Values of basic reproduction number, herd immunity threshold, and vaccine coverage requirement

Based on our calculation, we estimated the values of basic reproduction number, herd immunity threshold, and vaccine coverage requirement at 3.3, 69.7%, and 86.1%, respectively.

Discussion

The present study used a mathematical model to demonstrate how the AHSV spread in horse populations in a province where the virus firstly emerged in Thailand. The field data were collected during the epidemic and used to estimate the disease transmission parameters. The herd immunity threshold and the vaccine coverage requirement were then suggested.

This study used the SIR-SI model for mathematical modeling. We omitted the E compartment as most infected horses in the actual outbreaks died relatively quickly, within a few days after showing clinical signs. Hence, such a short incubation period may be insufficient to transmit the disease from the asymptomatic infected horses to the susceptible ones.

Based on the epidemic curve (Figure 3), we found that the virus spread in the horse population like wildfire. Given that the AHS attacked Thailand for the first time, all affected horses were completely susceptible. Our model assumed that the population was homogeneous; however, there were many categories of horses in Nakhon Ratchasima province, which led to the heterogenicity of the population.

During the study period, the mortality rate of horses was observed at 91.6% (337/368). Our finding is in line with a previous study in the Western Cape province, South Africa when the AHSV type 1 was first notified in 2004 (Venter et al., 2006). In that outbreak, the mortality rate was recorded at more than 90% (Thompson et al., 2012). This is concrete evidence addressing the highly infectious characteristic of AHSV, especially in territories where the virus firstly hit.

As AHS is a vector-borne disease, the dynamic transmission greatly depends on how the virus spreads in both host and vector populations. Our model suggested that the number of infected horses peaked on day 59 (Figure 4A), and the number of infected midges was raised up to almost at the peak level on day 83 (Figure 4B). Our peak of the infected horses was delayed than a previous study conducted in South Africa. Their epidemic curve revealed that the peak number of infected horses was evident in the fourth week (Grewar et al., 2013). The soil moisture is an important factor for midges to develop their larva development, so the climate and weather are necessary factors affect to the number of midges (Diarra et al., 2018). The temperature during summer in Nakhon Ratchasima is between 21-37°C, whereas, in the Western Cape, South Africa, it is between 15-27°C. Hence, the hotter temperature in Nakhon Ratchasima might decrease the density of midges and delay the transmission rate of AHSV.

Once most of the horses are infected, other horses in the area are protected by herd immunity. A large new outbreak will not likely occur in the area. However, the travel distance of midges may vary from 40-700 km to the prevailing wind (Sellers et al., 1977). The epidemic can rapidly expand to surrounding areas where fully susceptible horses are raised. In Thailand, for example, the AHS occupied 18.18% of provinces (14/77) in the country within only 6 months (Yothakol 2019). Interestingly, the epidemic occurred in Nakhon Ratchasima, Prachuap Khirikhan, and Chonburi province, respectively, which has no adjoined border (DLD 2020). The intermittent distribution pattern of disease might come from the transportation of infected horses by illegal animal movement or feed/hay truck movement from the epidemic to non-epidemic area (Ketusing 2020). Moreover, the infected midges can also be hidden within the vehicle and then spread into the new area.

Early detection and prompt response to the outbreak are crucially important. In 1989, the outbreak of AHS in Southern Portugal was rapidly eradicated within 13 weeks with an effective vaccination policy, restriction of animal movement, and eradication campaign on infected horses (Portas et al., 1999). Besides, vector control programs should be urgently implemented in the non-outbreak areas once the virus is detected in the vicinity.

The basic reproduction number is an important epidemiological parameter indicating how fast a certain disease spreads (Lord et al., 1996). In this study, we estimated this value at 3.3. Our result aligns with a previous study in which the R0 was found at 2.6-8.0 (Backer and Nodelijk 2011). Indeed, the R0 of AHS was relatively high compared to other infectious diseases in horses, such as equine infectious anemia (R_0 = 0.18-1.9) (Schwartz and Smith 2014), equine influenza (R_0 = 2-5) (Satou and Nishiura 2006) and equine herpes virus type 1 (R0 = 2.94-10.25) (Meade 2012). AHS thus spread more rapidly. Therefore, the relevant control efforts must be rigorously implemented once the virus is detected.

Vaccination is an effective tool used to combat AHS. Selection of vaccine had to be matched with the serotype of the outbreak situation. In this very first AHS outbreak in Thailand, the polyvalent vaccine (serotypes 1, 3, and 4) was employed in which the vaccine efficiency was estimated at up to 81% (Dennis et al., 2019). That could provide the herd immunity threshold estimated to be around 69.7%. In a previous study, the protective herd immunity for AHS was estimated at 50% if 75% of the entire horses were vaccinated (Lord et al., 1997). These high herd immunity values reflect the high proportion of immunized horses. We recommended vaccinating at least 86.1% of the horse population. The eradication program in Portugal in 1999 vaccinated all horses in the country (Portas et al., 1999).

We used data from 2020, which was 2 years ago. The first vaccination campaign in 2020 was accomplished, in which 86.7% of total horses within Nakhon Ratchasima province (1,219 of 1,405) were vaccinated. This is agreed with our recommended number of vaccinations at least 86.1%. The latest case of AHS in Thailand was reported on 10th September 2020 in zebra and there was no further report of infected horses until September 2022 (Ketusing 2020). This implied that the national eradication plan, including disease surveillance, vaccination campaign, vector control, and movement control, was effective in controlling the epidemic and reducing the number of infected and dead horses.

In this study, we faced some potential limitations. First, the follow-up data collection from vaccinated and un-vaccinated horses in Thailand was insufficient to calculate the vaccine efficacy from an actual outbreak. We hence used the value estimated from a previous study (Dennis et al., 2019). In future studies, the number of sick animals should be recorded from both vaccinated and un-vaccinated horses after implementing a mass vaccination campaign. Such data is very useful for calculating vaccine efficiency from a particular outbreak. A future field study on estimating the number of midges is recommended to get the baseline data. Second, our model did not include the mortality rate of the vectors in each phase. Moreover, the transmission rate from midges to host did not describe all the biting rate, pathogen transmission efficiencies, daily survival rate of vectors, and duration of the extrinsic incubation period. Third, our model focused on only one province. Indeed, the virus had spread already to different provinces across Thailand. A nationwide study is suggested. Nevertheless, the modeling framework proposed here is extendable once more data is available.

Conclusion

Based on our model, we recommend vaccinating at least 86.1% of the horse population to prevent the upcoming AHS outbreaks. This model is applicable as a baseline to test interventions such as vector control and to monitor the dynamic transmission of AHS in the future.

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