Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 456 - 465
Received 05 March 2021; Accepted 01 April 2021.

Nipah _ An Emerging Viral Zoonotic Disease: A Review

[1]Ozdan Akram Ghareeb , [2]Awni Ismail Sultan

[1]Department of Community Health Techniques, Kirkuk Technical Institute, Northern Technical University in Iraq.
[2]Department of Surgery, College of Medicine, Tikrit University in Iraq.
ozdanakram@ntu.edu.iq

Abstract

Nipah virus (Niv) is considered a high risk pathogen with zoonotic potential. Appearing zoonotic illnesses have possibly severe human health and economic effects. NiV can be a cause to different illnesses. For example, it can cause benign to serious encephalitis. It could also be a reason for fatal illnesses when infecting the humans' and animals' respiratory systems. Bats or domestic animals can transmit NiV to humans and can be transmitted among people. Here, we will review highlight some of the high-impact emerging Nipah disease, structure and zoonotic transmission of NiV, pathogenesis and clinical symptoms, then prevention and control. A preferable knowledge of the causes of spillover events, the strengthening follow-up systems to deter outbreaks is needed to reduce the NiV vulnerability .

Keywords : *Emerging , zoonotic disease , outbreaks*

Introduction

Of emerging infectious diseases treated to be developing, nearly 75% can be zoonotic [(1,2)], it is indicated that they could be naturally diffused between vertebrate animals and humans [(3,4)] . A developing zoonosis known as ‘a zoonosis' that is newly detected or freshly developed, or that has took place previously. However, it entails an increasing incidence or extension in the path range or in the geography of the host [(5)]. Current and reappearing zoonoses have arisen over the last three decades, in part because of humans' rising dependency on animals and their goods, as well as our intimate interaction with domestic animals. As a result, zoonoses should be regarded as the single most important risk factor for human health and well-being when it comes to contagious diseases. [(6,7)]. In 1998, in Malaysia, handlers of pigs have critically contracted an epidemic of acute encephalitis. From this incidence, NiV was discovered as a novel paramyxovirus [(8)]. In Malaysia and Singapore, NiV endangered the lives of 105 people and the skinning of over 1 million pigs between September 1998 and April 1999. [(9)]. After Kampung Sungai Nipah, this virus was given the name NiV where the first viral isolates were obtained[(10,11)]. In Bangladesh, in 2001 to 2005, it caused five consecutive outbreaks [(12)]. NiV is an emerging zoonotic, highly pathogenic because of its high

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 456 - 465
Received 05 March 2021; Accepted 01 April 2021.

fatality among people and the lack of adequate vaccination or medications. It is considered a high human risk select agent [13]. The cooperative worldwide efforts, like "One-Human-Environmental-Animal Health" is necessary to decrease the international vulnerability of zoonotic disease[14].

Nipah Virus

From an encephalitis patient, the University of Malayas virologists have extracted a virus from cerebrospinal fluid from people who were patients, in early March 1999 [15]. The newly discovered paramyxovirus was NiV belonging to a distinct genus known as Henipavirus in the Paramyxoviridae species (Order: Mononegavirales, subfamily Paramyxovirinae). In 1994, in Australia, the first genus associate appeared as Hendra virusin the Paramyxoviridae types and NiV was the second in the Henipavirus genus. It was discovered in Australia when there was an analysis on a fatal horse epidemic in 1994. HeV is the speciesl prototype of this virus.

In 2002, the International Committee for Virus Taxonomy (ICTV) acknowledged the developed novel Henipa virus genus. [16-17]. However, there is a slight difference between the Malaysian NiV strain (NiV-MY) and the Bangladeshi strain (NiV-BD). The NiV-MY strain was most likely to blame for the epidemic in the Philippines. These two strains are two main genetic lineages of NiVs and are possible causes for some human diseases. [18-20].

Henipaviruses have quite a non-segmented negative-stranded RNA genome. This genome consists of helical nucleocapsids. It is coated in an envelope creating viruses of difference particles such as spherical, filamentous and pleomorphic of (401900) nm. The gnomes of HeV and NiV are much bigger than most paramyxo viruses [21]. There are six genes in NiV that encode fusion protein, matrix protein, polymerase protein, glycoprotein, phosphoprotein and nucleocapsid. Like paramyxovirus, Niv does not have hemagglutinin and neuraminidase proteins. Unlike other paramyxoviruses, it has cytoplasmic inclusions closely related to endoplasmic reticulum. Niv is average larger than other paramyxoviruses [22-25] (Fig.1).

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 456 - 465
Received 05 March 2021; Accepted 01 April 2021.

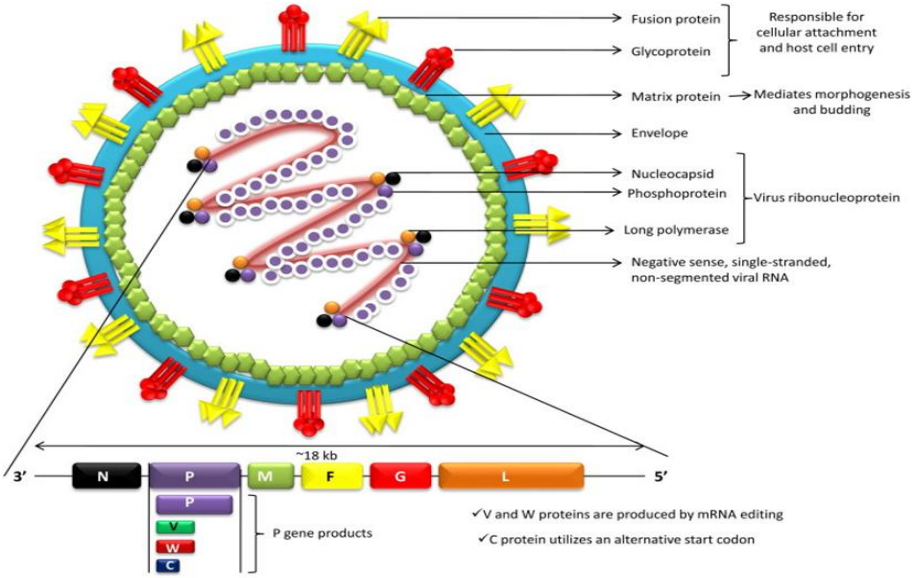

Fig. 1. Components of Nipah virus [26].

Reservoirs

The most natural reservoir for Nipah viruses are fruit bats called old-world fruit bats or Flying Foxes. They belong to *Pteropodidae* family. Bats carrying this virus were with Asymptomatic. There is some evidence the female bats, which are in the states of pregnancy and lactation, are more susceptible to infection [27-29]. Pigs play a midway role as hosts between bats and humans spreading this disease to other domesticated animals like horse, goats, sheep [not confirmed it is in controversial], cat and dogs. Niv infects different creatures such as guinea pigs, African green monkeys, ferrets and hamsters. It is highly contagious in pigs and cause different diseases such as encephalitic syndrome, barking pig syndrome and porcine in the respiratory and neurologic syndrome [30,31] .

Modes of Transmission

Zoonotic transmission of NiV happen primarily in two mechanisms-spillover. The first is from Flying Foxes via a temporary host. It can also transmit directly to huamns from bats. This transmission is mostly caused by close contact with cattle with NiV. It is also caused by contacting reservoir animals, and tainted food ingestions [32,33]. It was found that infected pigs were the main cause to infect humans when NiV out broke in Malaysia and Singapore, (92 percent) [34]. NiV infection in pigs and humans most likely happened via the respiratory system. [35]. Another way NiV is spread is by direct and extended contact with contaminated pig tissue [36]. During the Malaysian outbreaks, NiV was isolated from urinary and respiratory samples of contaminated individuals, indicating the risk of human transmission [37]. dna hsedalgnaB nI

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 456 - 465
Received 05 March 2021; Accepted 01 April 2021.

Indian outbreaks, there were evidences that NiV transmits among humans [38]. Figure 2 shows the cycle of how NiV transmits from natural reservoir such as bats to people.

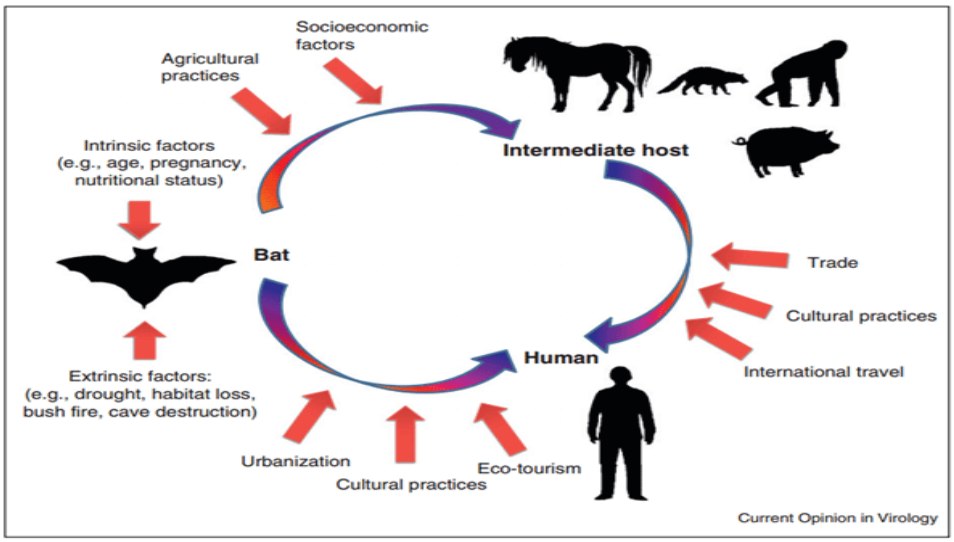

Fig. 2. Schematic representation of how NiV transmits.

Pathogenesis of the Disease

The virus reaches the host through the oro-nasal path and infects it. Replication stage in human can be performed in the bronchiole epithelial cells[39]. Significant inflammatory mediators emerge as soon as there is an infection in small airway epitheliumget [40]. At a later stage, the virus penetrates the lung endothelial cells and multiplies in them notianimessid suriv dipaR . metsys suovren lartnec eht sretne suriv eht ,sevren lainarc hguorhT .noticefni cimetsys gntiluser SNC)) and can be found in CSF samples [41,42]. During infection, two mechanisms are required in the virus enters CNS, one hematogenous and one anterograde by olfactory nerves . The central nervous system and respiratory system (62%) are also seriously impaired, while the cardiac, renal, and splenic systems are unaffected. In NiV-infected patients, multinucleated giant endothelial cells were found in the brain along with other organ biopsy samples [43,44]. In figure 3, a diagrammatic depiction of NiV pathogenesis was also provided.

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 456 - 465
Received 05 March 2021; Accepted 01 April 2021.

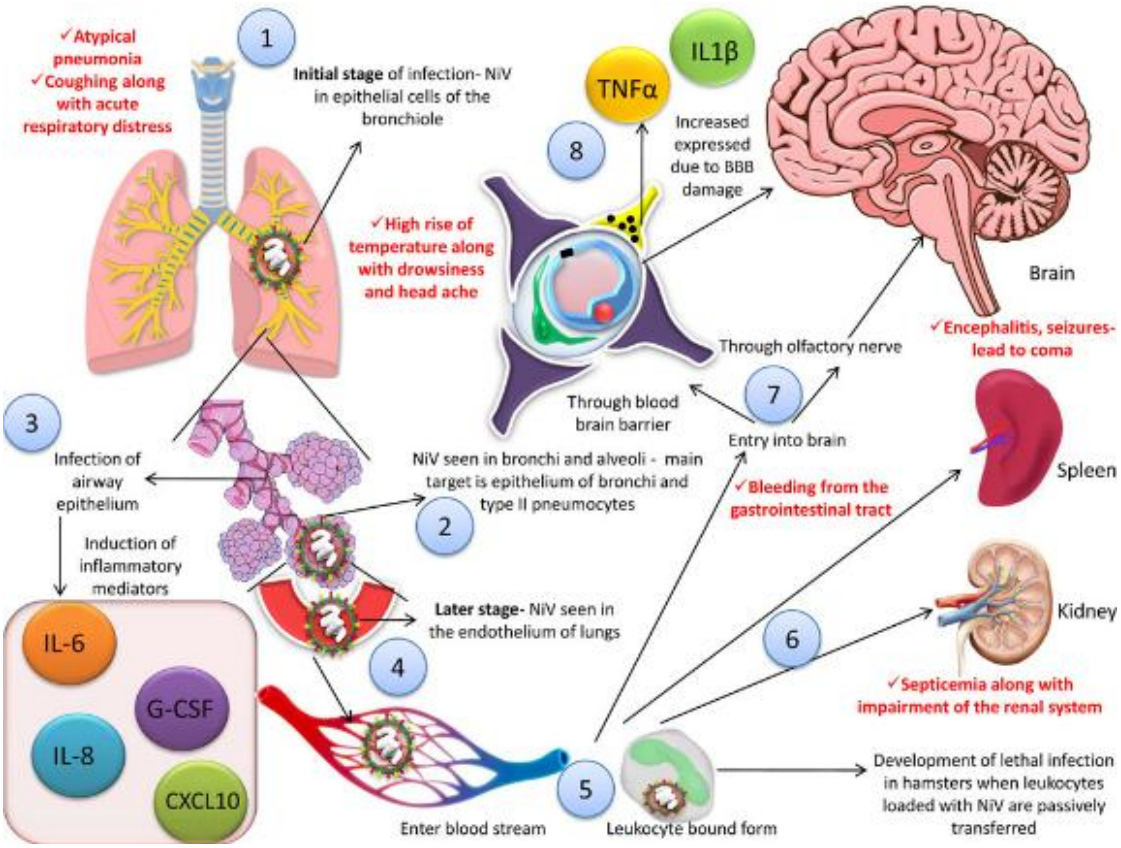

Fig. 3 . pathogenesis of NiV, the font in red color are symptoms in humans.

Clinical Signs and Symptoms

3–14 days after NiV exposure, Signs and symptoms of infection appear. In NiV infection in humans, neurological symptoms are the first and most frequent, while respiratory symptoms are the second most frequent. Besides the presence of drowsiness and headache, a rapid rise in temperature occurs, along with emotional distress and disorientation, as the patient finally collapses into a coma within one to two days. The critical complication of a NiV is encephalitis .

lanimodba fo sesac wef a tsuJ ,oslA .aenpsyd dna ,dloc ,hguoc edulcni smotpmys yrotaripseR ik ,aimectipeS .dedrocer erew notiaptisnoc dna ,stiirtsag ,aeohrraid ,niapdney dysfunction, and gastrointestinal bleeding are also potential complications [46]. In Malaysia, respiratory symptoms and chest irregularity were less common than the Bangladeshi epidemic [47].

Preventative and Control Measures

To reduce and prevent further spread of NiV, the infection must be controlled in animals (intermediate hosts). As for pigs and horses, they are vaccinated to prevent the spread of disease from one animal to another. Pig farms must be disinfected, preventing infected fruits

from being consumpted by other animals. Also, do not allow contact between pig farms and fruit bats and their secretions [48,49].

In humans, the infected persons should not have straight connection with the virus host (fruit bats and pigs) ,or their secretions .In addition, not to have direct contact with infected people . Educate and raise public awareness about avoidance of consumption of contaminated food (fruits or raw sap) by saliva or droplets of bats [50]. Maintain a good hygiene, follow the standard operating procedures such as frequent hand washing, sanitization with 70% ethanol , boil liquids before consuming them. Personal protective equipment, such as masks, goggles and gloves, must be used properly [51]. Bat viruses are dangerous to the health of humans and that of animals too[52,53]. For implementing a "One Health" policy, multidisciplinary teams (medical physicians, veterinarians, public health officials, scientists, phylogeneticists, and ecologists) must be established immediately. kaerbtuo erutuf erom tneverp ot stroffe nioj ot redro ni ([54].

Conclusion

Nipah virus is a zoonotic disease and it belongs to *Henipavirus* genus, *Paramyxoviridae* Family. It is the reason of several high rate-fatal illnesses in humans such encephalitis and other diseases in the respiratory system. It was first known in Malaysia. Some awareness programs must be conducted to prevent re-emerging the disease.

References

1- Taylor LH, Latham SM, Woolhouse ME. Risk factors for human disease emergence. Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences. 2001 Jul 29;356(1411):983-9.
2- Epstein JH, Field HE, Luby S, Pulliam JR, Daszak P. Nipah virus: impact, origins, and causes of emergence. Current infectious disease reports. 2006 Feb 1;8(1):59-65.
3- Al-Naqeeb SA, Abdullah HN, Khalaf MS. Molecular identification of Echinococcus granulosususing ISSR and RAPD markers. Journal of Pharmaceutical Sciences and Research. 2018 Dec 1;10(12):3313.mk
4- Khalaf MS, Rashid SA. Molecular Study of Enamoeba dispar and Entamoeba moshkovskii isolated from amoeboid dysentery in comparison with Entamoeba histolytica infections. Journal of Pharmaceutical Sciences and Research. 2018 Sep 1;10(9):2129-33.
5- World Health Organization. Report of the WHO/FAO/OIE joint consultation on emerging zoonotic diseases. World Health Organization; 2004.
6- World Health Organization. Combating emerging infectious diseases in the South-East Asia region. WHO Regional Office for South-East Asia; 2005.

7- Bidaisee S, Macpherson CN. Zoonoses and one health: a review of the literature. Journal of parasitology research. 2014 Oct;2014.
8- Wong KT, Shieh WJ, Kumar S, Norain K, Abdullah W, Guarner J, Goldsmith CS, Chua KB, Lam SK, Tan CT, Goh KJ. Nipah virus infection: pathology and pathogenesis of an emerging paramyxoviral zoonosis. The American journal of pathology. 2002 Dec 1;161(6):2153-67.
9- Chua KB, Goh KJ, Wong KT, Kamarulzaman A, Tan PS, Ksiazek TG, Zaki SR, Paul G, Lam SK, Tan CT. Fatal encephalitis due to Nipah virus among pig-farmers in Malaysia. The Lancet. 1999 Oct 9;354(9186):1257-9.
10- Lee KE, Umapathi T, Tan CB, Tjoei-Lian Tjia H, Chua TS, Oh HM, Fock KM, Kurup A, Das A, Tan AK, Lee WL. The neurological manifestations of Nipah virus encephalitis, a novel paramyxovirus. Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society. 1999 Sep;46(3):428-32.
11- Goh KJ, Tan CT, Chew NK, Tan PS, Kamarulzaman A, Sarji SA, Wong KT, Abdullah BJ, Chua KB, Lam SK. Clinical features of Nipah virus encephalitis among pig farmers in Malaysia. New England Journal of Medicine. 2000 Apr 27;342(17):1229-35.
12- Hsu VP, Hossain MJ, Parashar UD, Ali MM, Ksiazek TG, Kuzmin I, Niezgoda M, Rupprecht C, Bresee J, Breiman RF. Nipah virus encephalitis reemergence, Bangladesh. Emerging infectious diseases. 2004 Dec;10(12):2082.
13- Mukherjee P, Das S, Karam A, Chakraborty AK, Milton AA, Puro K, Sanjukta R, Ghatak S, Shakuntala I, Laha RG, Sen A. Nipah virus infection: An emerging zoonosis: A review. Indian Journal of Comparative Microbiology, Immunology and Infectious Diseases. 2018;39(2si):13-20.
14- GHAREEB OA , RAMADHAN SA. COVID 19-A Novel Zoonotic Disease: Origin, Prevention and Control.
15- Chua KB, Bellini WJ, Rota PA, Harcourt BH, Tamin A, Lam SK, Ksiazek TG, Rollin PE, Zaki SR, Shieh WJ, Goldsmith CS. Nipah virus: a recently emergent deadly paramyxovirus. Science. 2000 May 26;288(5470):1432-5.
16- Harcourt BH, Tamin A, Ksiazek TG, Rollin PE, Anderson LJ, Bellini WJ, Rota PA. Molecular characterization of Nipah virus, a newly emergent paramyxovirus. Virology. 2000 Jun 5;271(2):334-49.
17- Wang LF, Mackenzie JS, Broder CC. Henipaviruses, p 286–313. Fields virology, 6th ed. Lippincott Williams & Wilkins, Philadelphia, PA. 2013.
18- Wang LF, Yu M, Hansson E, Pritchard LI, Shiell B, Michalski WP, Eaton BT. The exceptionally large genome of hendra virus: support for creation of a new genus within the familyparamyxoviridae. Journal of virology. 2000 Nov 1;74(21):9972-9.
19- Ang BS, Lim TC, Wang L. Nipah virus infection. Journal of clinical microbiology. 2018 Jun 1;56(6).

20- Ang BS, Lim TC, Wang L. Nipah virus infection. Journal of clinical microbiology. 2018 Jun 1;56(6).
21- Harcourt BH, Tamin A, Halpin K, Ksiazek TG, Rollin PE, Bellini WJ, Rota PA. Molecular characterization of the polymerase gene and genomic termini of Nipah virus. Virology. 2001 Aug 15;287(1):192-201.
22- Harcourt BH, Lowe L, Tamin A, Liu X, Bankamp B, Bowden N, Rollin PE, Comer JA, Ksiazek TG, Hossain MJ, Gurley ES. Genetic characterization of Nipah virus, Bangladesh, 2004. Emerging infectious diseases. 2005 Oct;11(10):1594.
23- Lo MK, Peeples ME, Bellini WJ, Nichol ST, Rota PA, Spiropoulou CF. Distinct and overlapping roles of Nipah virus P gene products in modulating the human endothelial cell antiviral response. PLoS One. 2012 Oct 19;7(10):e47790.
24- Lo MK, Spengler JR, Krumpe LR, Welch SR, Chattopadhyay A, Harmon JR, Coleman-McCray JD, Scholte FE, Hotard AL, Fuqua JL, Rose JK. Griffithsin inhibits Nipah virus entry and fusion and can protect syrian golden Hamsters from lethal Nipah virus challenge. The Journal of infectious diseases. 2020 May 1;221(Supplement_4):S480-92.
25- Devaux P, Hodge G, McChesney MB, Cattaneo R. Attenuation of V-or C-defective measles viruses: infection control by the inflammatory and interferon responses of rhesus monkeys. Journal of virology. 2008 Jun 1;82(11):5359-67.
26- Singh RK, Dhama K, Chakraborty S, Tiwari R, Natesan S, Khandia R, Munjal A, Vora KS, Latheef SK, Karthik K, Singh Malik Y. Nipah virus: epidemiology, pathology, immunobiology and advances in diagnosis, vaccine designing and control strategies–a comprehensive review. Veterinary Quarterly. 2019 Jan 1;39(1):26-55.
27- Clayton BA, Middleton D, Arkinstall R, Frazer L, Wang LF, Marsh GA. The nature of exposure drives transmission of Nipah viruses from Malaysia and Bangladesh in ferrets. PLoS neglected tropical diseases. 2016 Jun 24;10(6):e0004775.
28- Yadav P, Sudeep A, Gokhale M, Pawar S, Shete A, Patil D, Kumar V, Lakra R, Sarkale P, Nichol S, Mourya D. Circulation of Nipah virus in Pteropus giganteus bats in northeast region of India, 2015. The Indian journal of medical research. 2018 Mar;147(3):318.
29- Ochani RK, Batra S, Shaikh A, Asad A. Nipah virus-the rising epidemic: a review. Infez Med. 2019 Jun 1;27:117-27.
30- Ang BS, Lim TC, Wang L. Nipah virus infection. Journal of clinical microbiology. 2018 Jun 1;56(6).
31- Pulliam JR, Epstein JH, Dushoff J, Rahman SA, Bunning M, Jamaluddin AA, Hyatt AD, Field HE, Dobson AP, Daszak P. Agricultural intensification, priming for persistence and the emergence of Nipah virus: a lethal bat-borne zoonosis. Journal of the Royal Society Interface. 2012 Jan 7;9(66):89-101.

32- Islam MS, Sazzad HM, Satter SM, Sultana S, Hossain MJ, Hasan M, Rahman M, Campbell S, Cannon DL, Ströher U, Daszak P. Nipah virus transmission from bats to humans associated with drinking traditional liquor made from date palm sap, Bangladesh, 2011–2014. Emerging infectious diseases. 2016 Apr;22(4):664.
33- Hegde ST, Sazzad HM, Hossain MJ, Alam MU, Kenah E, Daszak P, Rollin P, Rahman M, Luby SP, Gurley ES. Investigating rare risk factors for Nipah virus in Bangladesh: 2001–2012. Ecohealth. 2016 Dec;13(4):720-8.
34- Parashar UD, Sunn LM, Ong F, Mounts AW, Arif MT, Ksiazek TG, Kamaluddin MA, Mustafa AN, Kaur H, Ding LM, Othman G. Case-control study of risk factors for human infection with a new zoonotic paramyxovirus, Nipah virus, during a 1998–1999 outbreak of severe encephalitis in Malaysia. The Journal of infectious diseases. 2000 May 1;181(5):1755-9.
35- Hooper PT, Williamson MM. Hendra and Nipah virus infections. Veterinary Clinics of North America: Equine Practice. 2000 Dec 1;16(3):597-603.
36- Paton NI, Leo YS, Zaki SR, Auchus AP, Lee KE, Ling AE, Chew SK, Ang B, Rollin PE, Umapathi T, Sng I. Outbreak of Nipah-virus infection among abattoir workers in Singapore. The Lancet. 1999 Oct 9;354(9186):1253-6.
37- Chua KB, Lam SK, Goh KJ, Hooi PS, Ksiazek TG, Kamarulzaman A, Olson J, Tan CT. The presence of Nipah virus in respiratory secretions and urine of patients during an outbreak of Nipah virus encephalitis in Malaysia. Journal of Infection. 2001 Jan 1;42(1):40-3.
38- Gurley ES, Montgomery JM, Hossain MJ, Bell M, Azad AK, Islam MR, Molla MA, Carroll DS, Ksiazek TG, Rota PA, Lowe L. Person-to-person transmission of Nipah virus in a Bangladeshi community. Emerging infectious diseases. 2007 Jul;13(7):1031.
39- Chua KB, Lam SK, Goh KJ, Hooi PS, Ksiazek TG, Kamarulzaman A, Olson J, Tan CT. The presence of Nipah virus in respiratory secretions and urine of patients during an outbreak of Nipah virus encephalitis in Malaysia. Journal of Infection. 2001 Jan 1;42(1):40-3.
40- Escaffre O, Borisevich V, Rockx B. Pathogenesis of Hendra and Nipah virus infection in humans. The Journal of Infection in Developing Countries. 2013 Apr 17;7(04):308-11.
41- Wong SC, Ooi MH, Wong MN, Tio PH, Solomon T, Cardosa MJ. Late presentation of Nipah virus encephalitis and kinetics of the humoral immune response. Journal of Neurology, Neurosurgery & Psychiatry. 2001 Oct 1;71(4):552-4.
42- Weingartl H, Czub S, Copps J, Berhane Y, Middleton D, Marszal P, Gren J, Smith G, Ganske S, Manning L, Czub M. Invasion of the central nervous system in a porcine host by Nipah virus. Journal of virology. 2005 Jun 15;79(12):7528-34.
43- Wong KT, Shieh WJ, Kumar S, Norain K, Abdullah W, Guarner J, Goldsmith CS, Chua KB, Lam SK, Tan CT, Goh KJ. Nipah virus infection: pathology and pathogenesis of an

emerging paramyxoviral zoonosis. The American journal of pathology. 2002 Dec 1;161(6):2153-67.

44- Goh KJ, Tan CT, Chew NK, Tan PS, Kamarulzaman A, Sarji SA, Wong KT, Abdullah BJ, Chua KB, Lam SK. Clinical features of Nipah virus encephalitis among pig farmers in Malaysia. New England Journal of Medicine. 2000 Apr 27;342(17):1229-35.

45- World Health Organization. Nipah virus outbreak (s) in Bangladesh, January-April 2004= Flambée (s) d'infection à virus Nipah au Bangladesh, janvier-avril 2004. Weekly Epidemiological Record= Relevé épidémiologique hebdomadaire. 2004;79(17):168-71.

46- Giangaspero M. Nipah virus. Trop Med Surg. 2013 Jun 20;1(129):2.

47- Luby SP, Rahman M, Hossain MJ, Blum LS, Husain MM, Gurley E, Khan R, Ahmed BN, Rahman S, Nahar N, Kenah E. Foodborne transmission of Nipah virus, Bangladesh. Emerging infectious diseases. 2006 Dec;12(12):1888.

48- Tekola B, Myers L, Lubroth J, Plee L, Calistri P, Pinto J. International health threats and global early warning and response mechanisms. Revue scientifique et technique (International Office of Epizootics). 2017 Aug 1;36(2):657-70.

49- Satterfield BA. The future of preventing and treating Nipah virus infection.

50- Nahar N, Paul RC, Sultana R, Sumon SA, Banik KC, Abedin J, Asaduzzaman M, Garcia F, Zimicki S, Rahman M, Gurley ES. A controlled trial to reduce the risk of human Nipah virus exposure in Bangladesh. Ecohealth. 2017 Sep;14(3):501-17.

51- Donaldson H, Lucey D. Enhancing preparation for large Nipah outbreaks beyond Bangladesh: preventing a tragedy like Ebola in West Africa. International Journal of Infectious Diseases. 2018 Jul 1;72:69-72.

52- Brass VH, Astuto-Gribble L, Finley MR. Biosafety and biosecurity in veterinary laboratories. Rev Sci Tech. 2017 Aug 1;36(2):701-9.

53- Glennon EE, Restif O, Sbarbaro SR, Garnier R, Cunningham AA, Suu-Ire RD, Osei-Amponsah R, Wood JL, Peel AJ. Domesticated animals as hosts of henipaviruses and filoviruses: a systematic review. The Veterinary Journal. 2018 Mar 1;233:25-34.

54- Zumla A, Dar O, Kock R, Muturi M, Ntoumi F, Kaleebu P, Eusebio M, Mfinanga S, Bates M, Mwaba P, Ansumana R. Taking forward a 'One Health'approach for turning the tide against the Middle East respiratory syndrome coronavirus and other zoonotic pathogens with epidemic potential