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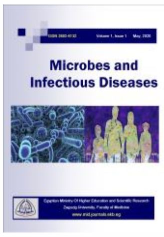

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Review article

Langya Virus - Recent insights into emerging Henipavirus

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ABSTRACT

Background: Zoonotic diseases and emerging infectious diseases pose a major global health burden and cause huge challenge to both human and animal health. The recent identification of Langya virus, a novel zoonotic pathogen originating from the Langya region of China raises concerns about emerging zoonotic diseases. This virus has been identified in febrile patients in eastern China, where shrews are suspected as the natural reservoir. The virus belongs to the *Paramyxoviridae* family. Langya virus has attracted significant attention, as it shares similarities with other henipaviruses such as Nipah and Hendra viruses, which are recognized for their high pathogenicity in animals and humans. Although it shares similarities with previously identified henipaviruses, the Langya virus remains poorly understood. The initial findings indicated that there is no human-to-human transmission. However, comprehensive research is essential to elucidate its clinical progression, transmission dynamics, and broader implications for public health. This identification of new virus underscores the importance of continued active surveillance among both human and animal population and preparedness to effectively manage emerging pathogens like Langya virus.

Introduction

The infectious diseases transmitted from vertebrate animals to humans are called zoonotic diseases (zoonoses) [1]. Most of the pathogens affecting humans are from animal origin particularly wildlife and it is often transmitted from animals to humans through zoonotic spill over events. Zoonotic diseases emergence through spill over events have increasingly become a major public health burden globally which accounts for 73% of emerging infectious diseases [2,3]. Among the microbial pathogens, viruses play a major role in human diseases, causing a wide range of illnesses from mild to severe infections. Zoonotic viruses are known to cause various outbreaks including zika, severe acute respiratory syndrome coronavirus (SARS-CoV), SARS-CoV-2, Middle East respiratory syndrome (MERS), Ebola, influenza, monkeypox, Marburg and many others in the past two decades claiming the lives of millions of people [4-6]. The drivers influencing the risk of spillover events are complex including, but not limited to climate change, habitat encroachment, animal husbandry and wildlife trade. Spillover events will increase the frequency of disease outbreaks unless underlying spillover drivers are addressed [3].

Coronavirus disease (COVID-19) pandemic has had a major impact on human health, lifestyle and global economy and many countries still have to recover [7]. After the COVID-19 and monkeypox outbreak [8,9], a new zoonotic virus outbreak has been reported in china causing febrile illness in humans. Langya virus belongs to the genus

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Henipavirus within the family *Paramyxoviridae* has recently been identified from a throat swab sample taken from a patient in Shandong and Henan provinces in Eastern China in August 2022 [10]. The virus was named after the town Langya in Shandong province. No cases have been reported outside China so far. Besides Langya virus, the *Henipavirus* genus includes Hendra virus, Nipah virus, Cedar virus, Ghanaian bat virus and Mojiang virus [11]. Of the identified henipavirus species, Hendra virus, Nipah virus and Langya virus are known to cause human disease. Phylogenetic analysis revealed that Langya virus is most closely related to Mojiang virus, a rat-borne virus identified in 2012 [10,12].

Henipaviruses significantly impact both human and animal health, posing significant threat for public health systems globally. They have long been considered a potential cause of future pandemics [13]. Langya virus is related to Hendra and Nipah viruses (bat-borne pathogens) which are known to cause fatal diseases in humans [14]. Hendra and Nipah virus was first identified in Australia and Malaysia, respectively in the mid- to late 1990s. Hendra virus has caused sporadic disease outbreaks in Australia and Nipah virus has caused few notable outbreaks in Asia including Malaysia, Bangladesh and India. Both these viruses are highly pathogenic transmitted from bats with a high case fatality rate of up to 75% [15,16]. Due to its high public health risk, World Health Organization (WHO) has categorized henipavirus as top priority pathogens that has the potential to cause severe future outbreaks [17,18].

Langya Virus

Similar like other henipaviruses, Langya virus contains a single-stranded negative-sense RNA genome of 18.4 kb encoding six structural proteins namely nucleocapsid, phosphoprotein, matrix protein, surface glycoprotein, fusion protein, and large viral RNA-dependent RNA polymerase [19]. The attachment glycoprotein (G) and fusion protein (F) is responsible for binding and virus entry into the host cell. These proteins are the target for neutralizing antibodies and hence it is suitable candidates for vaccine development [20,21]. The protein sequence comparison of Langya virus-G and Mojiang virus-G reveals 94% sequence similarity, while Langya virus-G shares only 64% similarity with Nipah virus-G. *In vitro* studies showed that the Langya virus-G didn't bind to the other reported henipavirus receptors ephrin B2 and ephrin B3 [22,23]. Langya virus may have different receptor (yet unknown) and host-cell recognition mechanism than Nipah and Hendra virus. Notably, polyclonal and monoclonal antibodies raised against Nipah and Hendra virus failed to cross-react with Langya virus suggesting that vaccines and therapeutics currently being developed against other henipaviruses cannot be used against Langya virus, whereas the antibodies raised against Mojiang virus reacts with Langya virus structural proteins suggesting the close evolutionary and antigenic relationships between these two viruses [24]. It is still unclear about the receptor tropism of Langya virus. Further investigation is necessary to provide additional evidence on the receptor engagement and other structural transitions occurring during the binding and virus entry [25].

Symptoms and Transmission

Henipaviruses are found in a wide range of animal hosts, including bats, shrews, cattle and rodents, across various regions such as Asia, Africa, Europe, and America [26]. Langya virus was detected in the shrews belonging to the species *Crocidura lasiura* and *Crocidura shantungensis* which might be the natural reservoir for the virus [27]. This is the first human-infecting henipavirus from shrew origin. Further, domestic animals such as goats and dogs were also found to be infected by Langya virus through serologic investigation. The virus might be transmitted directly from shrews or through another intermediate host [10,28]. In the past, shrews have been identified as reservoir of viruses such as rotavirus, hantavirus and mammarenavirus [29-31]. The transmission dynamics of shrew-associated viruses remain poorly understood [32]. Further studies are needed to determine the natural host and susceptible species.

Since 2018, 35 cases have been reported primarily among farmers and no mortality has been identified due to this virus [10]. The symptoms of the patients infected with Langya virus are generally mild including anorexia, cough, fatigue, fever, headache, myalgia, nausea and vomiting [10]. Although, few affected persons reported severe symptoms such as decrease in white blood cells (54 %), low platelet count (35 %), reduced liver (35 %) and kidney functions (8 %), Langya virus doesn't appear to cause serious disease [10]. The management of disease relies on supportive care based on the symptoms and management of complications by taking proper rest, keeping the body hydrated, taking counter-measure medications to reduce the symptoms of fever and pains. The antivirals such as ribavirin and chloroquine could potentially be effective against Langya virus, as both either in standalone or in combination showed antiviral activity against the henipaviruses with limited clinical benefits [33]. The virus is likely transmitted from animals to humans. As the findings are based on small number of cases, human-to-human transmission is unclear and has not been reported yet [34,35]. The diagnosis is based on laboratory testing of infected samples. As an emerging virus, unsurprisingly there are still no approved vaccines or therapeutic drugs available for treating henipavirus infection yet [36]. The henipavirus G and F glycoproteins are the major targets of virus-neutralizing antibodies and hence these could be potential candidates for developing vaccines [37]. A chimeric multi-epitope vaccine using immunoinformatics approach and peptide-based vaccine using reverse vaccinology approach was employed to develop vaccine against Langya virus. However, these studies need further laboratory investigations and experimental validations to elucidate its potential [38,39].

Prevention and Control Measures

After the COVID-19 pandemic, there is a concern about the possibility of any zoonotic viruses evolving into a more aggressive form and causing major epidemics or pandemics [40]. Presently, viruses like the Langya virus or other emerging henipavirus virus has the potential to develop the ability for sustained human-to-human transmission. Thus research into henipavirus should remain a priority for the researchers. Currently, limited information is available about Langya virus [41]. In the shadow of COVID-19 pandemic, other zoonotic outbreaks should not be neglected. Some practical recommendations for the prevention of zoonotic diseases include reducing the exposure to potentially infected animals, practicing good hygiene, strengthening surveillance and capacity building [42]. It is important to focus the research and development efforts on viral characterization, evolution, adaptation to their host and epidemiological investigation using one health approach by integrating human, animal, and environmental health strategies which can help to reduce the risks associated with the virus transmission [43]. Importantly, establishing the platform technologies for the rapid development of diagnostic reagents and vaccines are critical, as vaccination is the key to prevent the spread of viral infection. Further using appropriate animal models reflecting the disease progression and pathogenesis is crucial for vaccine development and testing [44]. The platform technologies currently used for developing vaccines against Nipah and Hendra virus could be adapted to develop vaccines for the Langya virus [45]. The adaptability of existing technologies can expedite the development of effective vaccines. However, it should be noted that the development of vaccine and therapeutic interventions are time consuming, as it requires extensive *in vitro* and *in vivo* studies as well as rigorous validation and approval. Hence, it is crucial to control the viral spread at the initial phase of virus outbreak through global collaboration and implementing realistic strategies such as early warning, creating awareness, strengthening the nation's healthcare system, border controls, containment strategies, data sharing, establishing regional centers for research, capacity building and related public health measures [46,47]. Early diagnosis and implementing established prevention methods could significantly reduce the disease burden associated with Langya virus.

In conclusion, the available data so far do not indicate any worrisome trends related to the virus. However, frequent testing of suspected animals and humans is essential to control the virus spread. How the Langya virus will evolve remains to be seen, but it is vital to remain vigilant by engaging in active research, devising appropriate control and preventive measures that could prevent the henipavirus outbreaks in the future [48].

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

I hereby provide consent for the publication of this manuscript.

Availability of data and material

The data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Competing interests

None. The author declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Author contributions

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Research involving human participants and / or animals

Not Applicable

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References

1. Rahman MT, Sobur MA. Zoonotic diseases: Etiology, impact, and control. 2020;8(9)doi:10.3390/microorganisms8091405
2. Tomori O, Oluwayelu DO. Domestic animals as potential reservoirs of zoonotic viral diseases. Annual review of animal biosciences. 2023;11:33-55. doi:10.1146/annurev-animal-062922-060125
3. Vora NM, Hannah L, Walzer C, Vale MM, Lieberman S, Emerson A, et al. Interventions to reduce risk for pathogen spillover and early disease spread to prevent outbreaks, epidemics, and pandemics. Emerging infectious diseases. 2023;29(3):1-9. doi:10.3201/eid2903.221079
4. Haruna UA, Muhammad AD, Lucero-Prisno DE, 3rd. Emerging viral zoonotic diseases: time to address the root causes. Bulletin of the National Research Centre. 2023;47(1):14. doi:10.1186/s42269-023-00993-3
5. Shanmugaraj B, Kothalam R, Mohamed Sheik TAA. A brief overview on the threat of zoonotic viruses. Microbes and Infectious Diseases. 2024:. doi:10.21608/mid.2024.294905.1975
6. Shanmugaraj B, Loganathan N, Chandra HM. Plant system as a versatile and robust platform for the development of vaccines against arboviral infections. Vacunas. 2024;25(4):492-501. doi:https://doi.org/10.1016/j.vacun.2024.06.005
7. Naseer S, Khalid S, Parveen S, Abbass K, Song H, Achim MV. COVID-19 outbreak: Impact on global economy. Review. Frontiers in Public Health. 2023;10: 1009393. doi:10.3389/fpubh.2022.1009393
8. Yee J, Unger L, Zadravecz F, Cariello P, Seibert A, Johnson MA, et al. Novel coronavirus 2019 (COVID-19): Emergence and implications for emergency care. Journal of the American College of Emergency Physicians Open. 2020;1(2):63-69. doi:https://doi.org/10.1002/emp2.12034
9. Shanmugaraj B, Khorattanakulchai N, Phoolcharoen W. Emergence of monkeypox: Another concern amidst COVID-19 crisis. Asian Pacific Journal of Tropical Medicine. 2022;15(5):193-195. doi:10.4103/1995-7645.346081
10. Zhang XA, Li H, Jiang FC, Zhu F, Zhang YF, Chen JJ, et al. A zoonotic henipavirus in febrile patients in China. 2022;387(5):470-472. doi:10.1056/NEJMc2202705
11. Weatherman S, Feldmann H, de Wit E. Transmission of henipaviruses. Current Opinion in Virology. 2018;28:7-11. doi:https://doi.org/10.1016/j.coviro.2017.09.004
12. Adesola RO, Miranda AV, Tran YSJ, Idris I. Langya virus outbreak: current challenges and lesson learned from previous henipavirus outbreaks in China, Australia, and Southeast

Asia. 2023;47(1):87. doi:10.1186/s42269-023-01064-3

13. Quarleri J, Galvan V, Delpino MV. Henipaviruses: an expanding global public health concern? GeroScience. 2022;44(5):2447-2459. doi:10.1007/s11357-022-00670-9
14. Qiu X, Wang F, Sha A. Infection and transmission of henipavirus in animals. Comparative Immunology, Microbiology and Infectious Diseases. 2024;109:102183. doi:https://doi.org/10.1016/j.cimid.2024.102183
15. Field H, Young P, Yob JM, Mills J, Hall L, Mackenzie J. The natural history of Hendra and Nipah viruses. Microbes and Infection. 2001;3(4):307-314. doi:https://doi.org/10.1016/S1286-4579(01)01384-3
16. Gazal S, Sharma N. Nipah and Hendra Viruses: deadly zoonotic paramyxoviruses with the potential to cause the next pandemic. 2022;11(12). doi:10.3390/pathogens11121419
17. Mehand MS, Millett P, Al-Shorbaji F, Roth C, Kieny MP, Murgue B. World health organization methodology to prioritize emerging infectious diseases in need of research and development. Emerging infectious diseases. 2018;24(9). doi:10.3201/eid2409.171427
18. WHO. Prioritizing diseases for research and development in emergency contexts. Accessed October 18, 2024. https://www.who.int/activities/prioritizing-diseases-for-research-and-development-in-emergency-contexts
19. Lawrence P, Escudero-Pérez B. Henipavirus immune evasion and pathogenesis mechanisms: lessons learnt from natural infection and animal models. Viruses. 2022;14(5): 936. doi:10.3390/v14050936
20. May AJ, Acharya P. Structural studies of henipavirus glycoproteins. Viruses. 2024;16(2): 195. doi:10.3390/v16020195
21. Loomis RJ, Stewart-Jones GBE, Tsybovsky Y, Caringal RT, Morabito KM, McLellan JS, et al. Structure-based design of Nipah virus vaccines: a generalizable approach to paramyxovirus immunogen development. Frontiers in Immunology. 2020;11:842. doi:10.3389/fimmu.2020.00842
22. Guo Y, Wu S, Li W, Yang H, Shi T, Ju B, et al. The cryo-EM structure of homotetrameric attachment glycoprotein from langya henipavirus. Nature Communications. 2024;15(1):812. doi:10.1038/s41467-024-45202-5
23. Xu K, Broder CC, Nikolov DB. Ephrin-B2 and ephrin-B3 as functional henipavirus receptors. Seminars in cell & developmental biology. 2012;23(1):116-23. doi:10.1016/j.semcdb.2011.12.005
24. Wang Z, McCallum M, Yan L. Structure and design of Langya virus glycoprotein antigens. 2024;121(16):e2314990121. doi:10.1073/pnas.2314990121
25. Wang C, Li M, Wang Y, Ding Q, Fan S, Lan J. Structural insights into the Langya virus attachment glycoprotein. Structure. 2024;32(8):1090-1098.e3. doi:https://doi.org/10.1016/j.str.2024.05.003
26. Meier K, Olejnik J, Hume AJ, Mühlberger E. A Comparative assessment of the pathogenic potential of newly discovered henipaviruses. Pathogens. 2024;13(7):587. doi: 10.3390/pathogens13070587.
27. Caruso S, Edwards SJ. Recently emerged novel henipa-like viruses: shining a spotlight

on the shrew. Viruses. 2023;15(12):2407. doi: 10.3390/v15122407.

28. Mallapaty S. New 'Langya' virus identified in China: what scientists know so far. Nature. 2022;608(7924):656-657. doi:10.1038/d41586-022-02175-z
29. Johne R, Tausch SH, Grützke J, Falkenhagen A, Patzina-Mehling C, Beer M, et al. Distantly related rotaviruses in common shrews, Germany, 2004-2014. Emerging infectious diseases. 2019;25(12):2310-2314. doi:10.3201/eid2512.191225
30. Wang B, Cai CL, Li B, Zhang W, Zhu Y, Chen WH, et al. Detection and characterization of three zoonotic viruses in wild rodents and shrews from Shenzhen city, China. 2017;32(4):290-297. doi:10.1007/s12250-017-3973-z
31. Falkenhagen A, Tausch SH, Labutin A, Grützke J, Heckel G, Ulrich RG, et al. Genetic and biological characteristics of species A rotaviruses detected in common shrews suggest a distinct evolutionary trajectory. 2022;8(1):veac004. doi:10.1093/ve/veac004
32. Zhang J-T, Hu Z-Y, Tang F, Liu YT, Tan WL, Ma XF, et al. Decoding the RNA viromes in shrew lungs along the eastern coast of China. npj Biofilms and Microbiomes. 2024;10(1):68. doi:10.1038/s41522-024-00543-3
33. Rockx B, Bossart KN, Feldmann F, Geisbert JB, Hickey AC, Brining D, et al. A novel model of lethal hendra virus infection in african green monkeys and the effectiveness of ribavirin treatment. Journal of Virology. 2010;84(19):9831-9839. doi:doi:10.1128/jvi.01163-10
34. Sanchez S, Ly H. Langya henipavirus: Is it a potential cause for public health concern? Virulence. 2023;14(1):2154188. doi:10.1080/21505594.2022.2154188
35. Uwishema O, Shariff S. Is the New Langya virus in China a threat to global health? A short communication. 2023;85(4):1348-1351. doi:10.1097/ms9.0000000000000322
36. Satterfield BA, Mire CE, Geisbert TW. Overview of experimental vaccines and antiviral therapeutics for henipavirus infection. Methods in molecular biology (Clifton, NJ). 2023;2682:1-22. doi:10.1007/978-1-0716-3283-3_1
37. Gómez Román R, Tornieporth N, Cherian NG, Shurtleff AC, L'Azou Jackson M, Yeskey D, et al. Medical countermeasures against henipaviruses: a review and public health perspective. The Lancet Infectious Diseases. 2022;22(1):e13-e27. doi:10.1016/S1473-3099(21)00400-X
38. Fahira A, Amin RS, Arshad U, Khan MI, Shah Syed AA, Alshammari A, et al. Chimeric vaccine design against the epidemic Langya Henipavirus using immunoinformatics and validation via immune simulation approaches. Heliyon. 2023;9(6):e17376. doi:https://doi.org/10.1016/j.heliyon.2023.e17376
39. Nazim H, Areej S, Muhammad Usama S, Ajaz A, Saif ul M, Qurban A. A reverse vaccinology approach towards a peptide-based vaccine against the newly emerged langya henipavirus. Journal of Biological Regulators and Homeostatic Agents. 2023;37(9):4773-4783. doi:10.23812/j.biol.regul.homeost.agents.20233709.465
40. Shokoufamanesh A, Raesi R. Scientific and practical solutions to deal with the possible pandemic of re-emerging langya virus

disease based on the lessons learned from the COVID-19 pandemic. The Open Public Health Journal. 2024;17doi:10.2174/0118749445326994240724053727

41. Taseen S, Abbas M, Nasir F, Wania Amjad S, Asghar MS. Tip of the iceberg: Emergence of Langya virus in the postpandemic world. Journal of Medical Virology. 2023;95(1):e28173. doi:https://doi.org/10.1002/jmv.28173
42. Kadir AKMS, Umar TP, Rabbi AA, Chowdhury MS, Shemanto MU. Preparedness of South Asian countries regarding Langya virus emergence: A view on the current situation. Health Care Science. 2023;2(3):194-197. doi:https://doi.org/10.1002/hcs2.42
43. Cunningham AA, Daszak P, Wood JLN. One Health, emerging infectious diseases and wildlife: two decades of progress? Philosophical Transactions of the Royal Society B: Biological Sciences. 2017;372(1725):20160167. doi:doi:10.1098/rstb.2016.0167
44. Pigeaud DD, Geisbert TW. Animal models for henipavirus research. Viruses. 2023;15(10):1980. doi:10.3390/v15101980
45. Amaya M, Broder CC. Vaccines to emerging viruses: Nipah and Hendra. Annual review of virology. 2020;7(1):447-473. doi:10.1146/annurev-virology-021920-113833
46. Thien DH, Tran HB, Uyen NNP, Thao HLP, Tam HTM, Quan NK, et al. A comprehensive review of Langya virus and framework for future zoonotic disease control. Reviews in Medical Virology. 2024;34(1):e2520. doi:https://doi.org/10.1002/rmv.2520
47. Struelens MJ, Ludden C, Werner G, Sintchenko V, Jokelainen P, Ip M. Real-time genomic surveillance for enhanced control of infectious diseases and antimicrobial resistance. Frontiers in Science. 2024;2: :1298248. doi:10.3389/fsci.2024.1298248
48. Bhusal A, Kumari N. Langya virus emergence: is the ongoing COVID pandemic and monkeypox re-emergence not enough? IJS Global Health. 2024;7(2):e0269. doi:10.1097/gh9.0000000000000269

Shanmugaraj B. Langya virus - Recent insights into emerging Henipavirus. Microbes Infect Dis 2025; 6(3): 984-990.