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Correspondence

Langya virus, a newly identified Henipavirus in China - Zoonotic pathogen causing febrile illness in humans, and its health concerns: Current knowledge and counteracting strategies – Correspondence

Dear editor

Amid the global health threats of the ongoing COVID-19 pandemic, recent re-emergence of rising cases of monkeypox posing public health emergency of international concern, and the very recent re-emergence of Marburg virus disease in Ghana, another zoonotic disease as a febrile illness in humans, has most recently been reported from China in the first week of August 2022 that attracted global attention. The causative agent in this report was Langya virus (LayV), a new Henipavirus [1]. Mainly people of Shandong and Henan provinces of Eastern China have been affected, and 35 Langya virus infected patients with a recent history of animal exposure have been investigated from 2018 to 2022 [1,2]. Identification of the virus was done from a swab sample of a patient's throat by subjecting the sample to metagenomic analysis, and subsequently isolation of the virus as a phylogenetically distinct Henipavirus [1,3].

LayV belongs to the family *Paramyxoviridae* under the genus *Henipavirus*. This genus also contains the Hendra and Nipah virus which are responsible for causing fatal diseases in human. Both these viruses are zoonotic in nature and pose a constant threat to livestock animals and humans, but until now this is not the case with LayV [1,4,5]. Nipah and Hendra viruses are biosafety level-4 (BSL-4) pathogens. Thus, LayV should be considered to require BSL-4 facilities in current times till its real risk is known [6].

The LayV genome comprises of 18,402 nucleotides and its organization of genome shows similarity to that of other Henipaviruses [7]. LayV is most phylogenetically related to Mojiang Henipavirus, a rat-borne virus which was first identified in Southern China in 2012, and its potential cross-reaction with this virus need to be evaluated to improve serologic testing [1,8]. Researchers from Australia, South Korea and China have found many other Henipaviruses in bats, rats, and shrews. However, only Hendra, Nipah, and now LayV are known to infect humans.

The symptoms of LayV infection in people include high temperature, cough, fatigue, poor appetite and muscle pain [1]. Myalgia and nausea along with vomiting may be noticed in certain instances. Leucopenia and thrombocytopenia are evident. Fever is a common symptom in all the cases. Complications like pneumonia, impairment of kidney and liver functions may be noticed in a comparatively small proportion of individuals. However, reports are not yet available on the severity of these complications and the requirement of hospitalization. No deaths have yet been reported due to LayV infection. Healthcare authority is of the opinion that this viral infection is not serious and fatal, and there is no need for panic [1,9]. In the most recent LayV outbreak in China, majority of the 35 reported cases were either farmers or workers in factories, and LayV was potentially the pathogen in 26 patients (74% of the cases). The paired serum samples collected from 14 patients during the acute and convalescent phases of infection showed the immunoglobulin G (IgG) titers in the majority of samples (86%) collected during the convalescent phase were 4 times greater than the IgG titers in samples collected during the acute phase. Viremia has been observed in association with acute viral infection. The viral load was found to be higher in patients with pneumonia than those without pneumonia.

Transmission of the virus is likely to occur from animals to humans. The spread of infection is now monitored by the health authority of Taiwan and other health agencies [10]. Testings of 25 small wild animals were done by researchers for presence of the virus, and RNA of the virus was found mainly in shrews, suggesting that the natural reservoir of the virus to be shrews. Shrews have been found in the past to spread viruses like hantavirus and mammarenavirus [11]. Although determination of contagiousness of the virus and whether transmission of the virus can occur among humans have not yet been done by the Centre for Disease Control and Prevention (CDC), China warning has been given to people to pay attention to closely update on this virus [12].

A serosurvey of domestic animals detected seropositivity in goats (in 2% of the tested sera) and dogs (5% of the tested sera) [13]. When rodent and shrews samples were examined for LayV infection, viral RNA was found in three rodent and two shrews species, particularly in *Crocidura lasiura* shrews [14]. There was no evidence of an underlying epidemiological pattern among patients, thus lending credence to the theory of sporadic zoonotic transmissions, especially when many of the affected individuals were farmers [10].

The absence of close contacts being infected, clusters of cases were not found in the same family, and no common history of exposure all suggest the sporadic nature of LayV infection in the human population. However it is difficult to establish how exactly were individuals being exposed to LayV [15]. Contact tracing was done for nine patients who were in close contact with 15 family members, revealing no close contact transmission of LayV. Human-to-human transmission has not been proved. However, researchers are of the opinion that the sample size is not large enough to determine any possible transmission from human to human [1,13,16].

Approved treatments and vaccines are not available for henipaviruses. In animal studies researchers have tried various antivirals, and ribavirin may be a good therapeutic option. This drug has been found useful in infections caused by RNA viruses, particularly in viral infections that involve respiratory issues. Ribavirin when combined with the antimalarial drug chloroquine was found efficacious in treating Henra and Nipah viral infections, suggesting this drug combination can be used to control LayV infection, if required. At present no vaccine has

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been licensed against this viral infection [14].

The Taiwan Centers for Disease Control (CDC) has announced implementation of genome sequencing along with surveillance plans for LayV. Ongoing researches have been carried out to learn more about the transmission route of the virus and collaborative efforts have been ensured by the Taiwan CDC in association with the Council of Agriculture to carry out investigations on similar types of diseases in species that are native to Taiwan [13].

The recently available but limited data still fails to raise any worrisome concerns of global health panic or pandemic level spread of LayV [1,9]. However regular testing of animals and humans by researchers and diagnosticians is essential to timely identify the virus to keep the viral infection under control. There must be standard laboratories with facilities of nucleic acid testing to identify LayV for viral infection tracking in human. Further investigations need to be done to determine severity of LayV infection, the modes of transmission and to evaluate the extent of spread of the viral infection in China and the region as a whole. Warning has been given by infectious disease experts a long time back on the chances of zoonotic spillovers of viruses due to climate crisis and indiscriminate destruction of natural resources. In this regard, the LayV outbreak is a classic example. Efforts must be taken to conserve the nature and also the one health approach is urgently required to counter zoonotic infections. It is crucial to conduct active surveillance in a transparent and internationally collaborative manner to lessen the likelihood of an emerging virus becoming a global health concern. As the findings of the LayV infection are based on a relatively small number of incidences, whether human to human transmission of LayV infection can occur is still unclear. Further research and investigational studies are required to understand the microbiological and epidemiological features of the Langya virus infection [10].

Infection of human by LayV suggests how easily zoonotic viruses can be transmitted unnoticed from animals to humans, and indicates that animal viruses are frequently spilling in hidden ways into people around the globe as the 'tip of the iceberg' for undiscovered pathogens. LayV does not seem to spread easily among people, and it is not fatal. However, researchers are of the opinion that as shrews serve as a reservoir, they can transfer the virus between themselves and could infect people directly by chance or through an intermediate most. Further investigations are suggested to learn how this virus can in shrews and by what means humans could catch the LayV infection by spillover events.

The Langya virus has been identified very recently, much is yet to be learned [15]. Researches on LayV are required to strengthen surveillance and monitoring activities, to identify its hosts and animal species reservoir, and to adopt the one health concept to limit animal-human interface. Being a RNA virus that can mutate, its relatively low disease severity as revealed with limited cases/low sample size investigation, further in-depth studies and detailed epidemiological investigations are still need to carry out to determine its feasible dangers which could pose to human. However, we need to be ready in advance to adopt appropriate preventive measures and implement proactive control strategies to limit its possible spread to other regions and countries in order to lessen the chances as what happened recently with monkeypox outbreaks which suddenly raised quickly to a level of global health concern.

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Author contribution

Sandip Chakraborty: Conceptualization, Data Curation, Investigation, Writing - Original Draft, Writing - review & editing. Deepak Chandran: Validation, review & editing. Ranjan K. Mohapatra: Validation; reviewing. Md. Aminul Islam: Validation; reviewing. Mahmoud Alagawany: Validation; reviewing. Manojit Bhattacharya: Validation. Chiranjib Chakraborty: Validation; reviewing.Kuldeep Dhama: Validation; reviewing.

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