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Preventive strategies to innovate Japanese encephalitis control in eastern Uttar Pradesh: Accelerating towards zero incidence

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Japanese Encephalitis (JE) is a zoonotic mosquito-borne viral disease that primarily affects young children under the age of 15[1]. Annually, there are more than 50000 clinical cases and JE causes over 10000 fatalities globally[1]. In Japan, South Korea, China and Thailand, where it is now under control or almost entirely eradicated, the disease was initially noted to have a high incidence[1]. Later, it expanded to Nepal and India, becoming a serious public health issue in rural regions[1]. JE is a flavivirus-based neglected tropical disease that is spread by culicine mosquitoes of the *Culex* (*Cx.*) *tritaeniorhynchus* and *Cx. vishnui* species[2]. It causes severe neurological symptoms that can occasionally be fatal. Another morbid consequence of this viral illness is chronic neurologic sequelae in the form of long-term impairment[3]. Pigs are considered as amplifying hosts and play a significant part in the general epidemiology of the disease, whereas humans are a dead-end host. Only three of the five genotypes that are known to be present in the global population are found to be common in India[3]. While JE is endemic in many areas of India, including Bihar, Kolkata, Andhra Pradesh, Tamil Nadu, Uttar Pradesh, Assam, and other regions, the eastern section of Uttar Pradesh is the region that is most severely afflicted, and children under the age of 15 are the main victims[3].

The Government of India and the Uttar Pradesh State Government's multifaceted approach, which includes vector control measures, strengthened surveillance programmes, JE immunisation campaigns in children, behavioural change and community-based awareness programmes, may have helped to significantly reduce JE cases in the last 10 years, after which incidence decreased to 0.07 in 2019[4]. In spite of the numerous control efforts outlined above, sporadic JE cases frequently appear in the eastern Uttar Pradesh region. Improved targeting of interventions will result from changes to the current strategies, which will help the JE curve continue to shorten. The natural transmission cycle of JE virus includes JE

virus, mosquito vector, reservoir host pigs and birds and dead-end host human[3]. There is no human-to-human transmission of JE and current interventions are targeted to protect human from getting JE. Reservoir host and mosquito vectors play an important role in transmission of JE to newer areas. Increase in vector density is associated with agricultural practices in rural regions including paddy fields and irrigated crops[3]. In the current article, we are discussing the JE control strategies further needed to reduce the JE cases in eastern Uttar Pradesh to zero incidence by interrupting its natural cycle.

Robust surveillance system and vaccine strategy to control

JE: Every disease control programme needs a strong surveillance system to break the disease transmission cycle. Even though the JE vaccination programme was started and expanded before 2013, decision-makers still require information on disease surveillance and vaccine coverage in order to focus vaccinations based on age and region. JE is a paediatric disease and mainly affects school going children and vaccination is the mainstay to prevent the disease. Thus, a system should be established to check the vaccination status of the children on entry to school and educate the public on the benefit of vaccination. Further, a substantial proportion of adult cases in India seems to cause unrecognised burden of JE in adults, which warrants the establishment of adult vaccination policies[4,5]. Though strong

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motivation towards paediatric JE immunization has flattened the JE curve drastically, based on the burden of adult JE in eastern Uttar Pradesh, adult JE immunization may be prioritized which could take the JE cases to zero level. Importantly, JE surveillance data on vaccine efficacy, sustainability, and interchangeability will be critical to informing new vaccination policies in the JE endemic regions.

Understanding of viral pathogenesis and new therapeutic prospects: There is no specific treatment for JE other than best symptomatic treatment. Though several *in-vitro* and *in-vivo* studies provided substantial advances in understanding of JE pathogenesis and potential treatment targets, the potential treatment for JE is still lagging[6]. The immune system plays a paradoxical role in protection and susceptibility against JE, so a combination therapy is required which includes anti-inflammatory along with antiviral activities[6].

One Health approach to JE: One Health is defined as “A collaborative, multi-sectoral, and trans-disciplinary approach-working at local, regional, national, and global levels. It recognizes the interconnections between host, vector, and their environment”[7]. Strong integrated surveillance at human-animal-environmental interface is required to control JE epidemic under One Health umbrella. As natural cycle of JE involves pig as reservoir host and mosquito as vector, a collaborative approach is required to develop an understanding of transmission dynamics and policies to support health system.

Specific vector control strategies and reducing import of cross-border infection: Many districts of Eastern Uttar Pradesh share border with the Nepal which is also a JE endemic country. Cross border movements of amplifying hosts including migratory birds and pigs are a major contributor in cross border transmission of JEV[3]. Nepal is the main exporter of piglets in the north and north-east India[8]. During the recent years, pig farming has increased in Uttar Pradesh and contributes in gross domestic product (GDP) of the state. Mosquito vectors play a very crucial role in maintaining horizontal (animal-mosquito-human) and vertical (one generation to other generation of mosquito) transmission cycle of JEV in nature[9]. The average flight range of *Cx. tritaeniorhynchus* mosquitoes has been noticed between 2.0 km and 7.5 km and these infected mosquitoes may also travel through transport vehicles across the border. This mode of JEV transmission can be checked with the introduction of vaccination in piglets, making buffer zones across the border that never supports mosquito oviposition and use of integrated vector management strategies to manage JEV vector. Use of microbial larvicides, larvivorous fishes and management of paddy water through alternative wet and dry irrigation are also very important.

Community based communication and awareness programme:

Community engagement and participation in JE prevention must go hand in hand. The World Health Organization (WHO) refers to this ideology as "Health by the people," and it should be built on "of the people, for the people, and by the people" principles[10]. The JE immunization campaign may be successful if community involvement is used to address vaccine reluctance and low coverage. Any programmes and policies can be planned, organised, and managed by the community. Behavior change communication is a crucial communication approach that alters the way the community behaves in terms of health through a variety of methods. Any health programme or policy could benefit from an awareness campaign through behavior change communication that focuses on the community's specific needs and health issues.

Measuring progress and follow up of disease and disease interventions: Any initiative or programme is under surveillance when it is being monitored and evaluated. It keeps track of the program's development and evaluates the results. This also assists in changing programmes and regulations when necessary. Additionally, it highlights programme and policy implementation gaps and challenges. To gauge the efficacy of control techniques and determine the necessary adjustments, impact evaluation of actions performed to control JE must be implemented on a regular basis. The operational parameters for the Japanese Encephalitis/Acute Encephalitis Syndrome surveillance should include a monitoring and evaluation programme for JE interventions. Moreover, the severe neurological and mental repercussions that lead to dependency and a lifetime of socioeconomic stress on families can be lessened with adequate monitoring and assessment of the treated patients after discharge.

All of these can only be accomplished by bolstering the public health system and launching JEV prevention education programmes in localities with robust political and social commitments. This will assist in developing clear plans and prioritizing vaccination programmes, preventative measures, and readiness for potential outbreaks, vector control, case management, early treatment, and prompt referral of serious JE cases.

Conflict of interest statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Authors' contributions

NS conceptualized and wrote the first and revised draft of the manuscript. RB, BRM, UA and HD also have helped in preparing the manuscript. RK conceptualized, supervised and helped in editing of the manuscript. NS and RK conceptualized, reviewed and prepared the final version of the manuscript.

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