



Burden of Infectious Diseases in North East India: A Mini-Review

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Abstract

North East India, with its unique geographical and cultural characteristics, bears a significant burden of infectious diseases. This mini review provides an overview of the prevalent infectious diseases in the region, highlighting the highest disease burden and the most endemic diseases. Malaria emerges as a major public health concern, with frequent outbreaks and substantial morbidity and mortality. Dengue fever, tuberculosis, Japanese encephalitis, Chikungunya, rickettsia diseases, waterborne enteric infections, hepatitis, and HIV/AIDS are also prevalent in the region. Challenges such as rugged terrain, limited transportation infrastructure, limited healthcare infrastructure, inadequate diagnostics, socio-economic factors and sharing of international border with four neighboring countries etc hinder disease control efforts. Strengthening vector control, improving diagnostics, expanding healthcare access, and raising community awareness are crucial strategies for reducing the burden of infectious diseases. Surveillance and research efforts are needed to enhance understanding and control of these diseases. Febrile illness like Scrub typhus stands out as the most endemic disease in the hilly regions, characterized by high prevalence, associated morbidity and mortality, and a lack of knowledge about its epidemiology and impact. Active surveillance is crucial to better understand the burden and distribution of the disease and address the challenges in the region.

Keywords: Infectious Disease; Northeast India; Burden

Abbreviations: Pf: *Plasmodium falciparum*; Pv: *Plasmodium vivax*; IMCP: Integrated Malaria Control Program; LLINs: Long-lasting Insecticidal Nets; RDTs: Rapid Diagnostic Kits; API: Annual Parasite Incidence ; NVBDCP: National Center for Vector Borne Disease Control; DENV: Dengue; TB: Tuberculosis; JE: Japanese Encephalitis; JEV: Japanese Encephalitis Virus; CFR: Case Fatality Rate; NE: North-East; HBV: Hepatitis B Virus; HCV: Hepatitis C Virus; MoHFW: Ministry of Health and Family Welfare; CHIKV: Chikungunya Virus; ICMR: Indian Council of Medical Research; HIV: Human Immunodeficiency Virus; AIDS: Acute Immunodeficiency Syndrome; DR: Drug-resistant; CDC: Centers for Disease Control and Prevention; MDR: Multi Drug Resistant; IDU: Injecting Drug Use; WNV: West Nile Virus; AES: Acute Encephalitis Syndrome; MERA India: Malaria Elimination Research Alliance India; MESA: Malaria Eradication Scientific Alliance; PTB: Pulmonary Tuberculosis; EPTB:

Extra-pulmonary Tuberculosis; CI: Confidence Interval; AES: Acute Encephalitis Syndrome; IoT: Internet of things; NACP: National AIDS and STD (Sexually transmitted diseases) Control Program; AI: Artificial Intelligence; AR: Augmented Reality; VR: Virtual Reality; QC: Quantum Computing.

Introduction

NE India, comprising the seven sister states (Assam, Meghalaya, Arunachal Pradesh, Nagaland, Manipur, Mizoram and Tripura) and the Himalayan state of Sikkim, is a diverse region characterized by unique geographical, cultural, and environmental factors [1,2]. This region is prone to various infectious diseases due to its climatic conditions, dense forests, and limited healthcare access in certain areas [3]. The NE region shares international borders with neighboring countries like Bhutan, China, Myanmar and

Bangladesh [4]. This geographical proximity with south east Asian countries, coupled with increased cross-border movements, contributes to the challenges in preventing and controlling infectious diseases [5]. The region's rugged terrains, dense forests, and remote areas further complicate healthcare delivery and surveillance efforts, making it susceptible to transmission of infections and outbreaks [6]. NE India is affected by a range of endemic infectious diseases, which impose a substantial burden on public health [7]. The region exhibits a high prevalence of communicable diseases, including malaria, DENV, Scrub typhus and JE all transmitted through vectors [7]. Water-borne illnesses, such as typhoid, cholera, and diarrheal diseases, are prevalent due to inadequate sanitation facilities, lack of awareness and limited access to safe drinking water [8,9]. Moreover, a significantly diminished sensitivity pattern of antitubercular drugs is seen in Meghalaya [10]. HIV/AIDS and respiratory infections are also significant health concerns within the region [11-14].

The challenges in addressing infectious diseases in NE India are multifaceted. Limited healthcare infrastructure, non-availability of point of care diagnostics, inadequate healthcare access in remote areas, and scarcity of trained healthcare professionals hinder the effective management and control of these diseases. Socio-economic factors, including poverty, illiteracy, and lack of awareness, further contributes to the vulnerability of the population [15]. To

address the complex landscape of infectious diseases in NE India, it is crucial to have a comprehensive understanding of the epidemiology, aetiology and impact of these diseases in the region. This mini review aims to provide an overview of the prevalent infectious diseases in NE India, their public health implications, and the challenges associated with their prevention and control. Additionally, the review will highlight the ongoing efforts and strategies implemented to mitigate the burden of infectious diseases in the region.

Malaria

Malaria is a potentially life-threatening disease caused by the Plasmodium parasite. It is transmitted to humans through the bites of infected female Anopheles mosquitoes [16]. Globally malaria poses a significant threat primarily to children and has exerted considerable evolutionary pressure on the human genome, making it one of the most impactful factors in recent evolutionary history [17]. Malaria remains a significant public health concern in NE India (Figure 1). Frequent outbreaks of Pf, the main parasite species, result in substantial morbidity and mortality in the region [18]. In a cross-sectional mass survey (n=8,233) to screen malaria and anemia prevalence in two high and low endemic districts of NE India, it was reported that 79.6% malaria prevalence in East Garo Hills of Meghalaya and 20.4% in Udalguri district of Assam respectively [19].

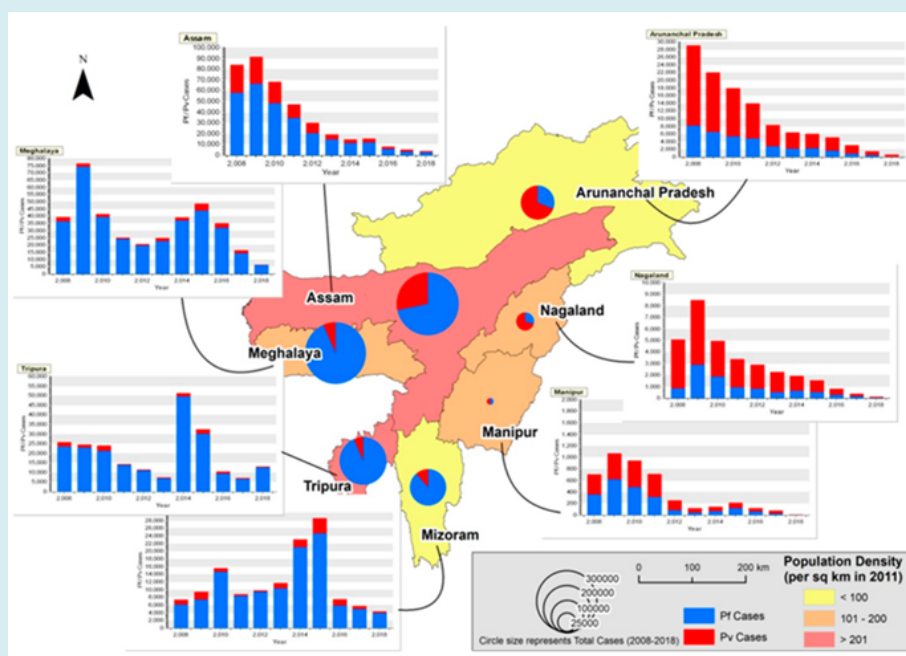


Figure 1: From 2008 to 2018, the spatio-temporal distribution of Pf and Pv cases in NE India was analyzed. Background color denoted state population density based on the 2011 census. Pie-charts illustrated reported Pf and Pv cases, with Pv data derived by subtracting Pf cases from total malaria cases due to NVBDCP data limitations [20].

States such as Assam, Arunachal Pradesh, and Tripura bear a disproportionate burden of malaria cases due to factors like forested areas, favourable climate, and inadequate vector control measures [21]. The IMCP launched in 2005 aimed to combat malaria in NE India. A study in Udalguri, Assam, assessed the IMCP's impact, which included LLIN distribution, bi-valent rapid diagnostic kits, and malaria awareness programs. The results showed a significant decline in API with 37% reduction after LLINs in 2009 and a further 64% reduction after RDTs. Udalguri major malarial parasites were Pf (29%) and Pv (71%) [22].

During 2019, Dr. Balram Bhargava, the Director General of the Indian Council of Medical Research (ICMR), launched a significant initiative called "MERA India" on the occasion of 'World Malaria Day'. With an objective to bring together government agencies, research institutions for conducting research and implement evidence-based strategies. Aim of MERA-India is to unite researchers and national programs working on malaria, with alliance focus on reducing malaria cases and achieving eventual eradication. It promotes multicenter studies to provide comprehensive "pan-India data" for malaria elimination efforts [23]. On the other hand MESA is an international initiative aimed at accelerating the development of tools and strategies for malaria eradication worldwide. It was launched by a consortium of global organizations and institutions in 2012. It is an initiative aimed to combat malaria. MESA brings together researchers, scientists, and experts from around the globe to collaborate on research projects and initiatives related to malaria eradication. The alliance's primary focus is on supporting research efforts to develop new tools and intervention such as vector control methods, and diagnostics, which can effectively combat malaria [24,25]. India engages in malaria control and elimination through the NVBDCP employing strategies such as vector control and surveillance, treatment, and research partnerships [26].

Efforts to control malaria have been hampered by difficult terrain, inadequate healthcare infrastructure, and a lack of community awareness. However, initiatives such as insecticide-treated bed nets, indoor spraying, and effective anti-malarial drug distribution have shown promising results in reducing malaria burden [27]. Efforts should focus on strengthening vector control programs, enhancing access to early diagnosis and treatment, and promoting community awareness to reduce the impact of malaria.

Dengue

Dengue fever is a common mosquito-borne illness caused by different serotypes of DENV: DENV-1, DENV-2, DENV-3, DENV-4, and the newly discovered DENV-5 [28,29]. DENV is classified under the Flaviviridae family and possesses a

single-stranded, positive-sense RNA as its genetic material [30,31]. Dengue fever is another major concern in the region [32]. A detailed entomological survey conducted from 2004 to 2005 across seven states in the NE region of India indicated a significant presence of diverse mosquito species, particularly *Aedes* and related species. It was observed that the well-known dengue vectors, namely *Aedes aegypti* (Stegomyia) and *Aedes albopictus* (Stegomyia), which are container-breeding mosquitoes, were found in all seven states examined. These findings highlight the widespread presence of these *Aedes* mosquito species in the region [33].

The first reported case of dengue fever in NE India was reported from Pasighat, Arunachal Pradesh, in 2012, with DENV-3 as the predominant serotype, along with DENV-1 and DENV-2 and during 2014, all four DENV serotypes were detected in the region [34]. The DENV outbreaks were attributed to enhanced breeding sites, vector presence, and elevated temperatures associated with El Nino episodes, moreover, mean extrinsic incubation period for mosquitoes shortens at higher temperatures. (34) The overall seroprevalence of DENV in the NE region was observed to be 5.0% [35]. During 2016-17 Guwahati Medical College and Hospital screened over 21,000 suspected sera samples for DENV (NS1 and IgM antibody) from 17 districts of Assam and 9543 (45.4%) tested positive for DENV and typing showed three serotypes (DENV1, DENV2 and DENV3) and three genotype (V, IV, III) [36]. Inadequate sanitation and water storage practices, lack of awareness, delayed diagnosis, and limited access to appropriate medical care compounds the challenge of dengue control [37]. A comprehensive multi-functional environmental management measures were implemented in Pasighat, which resulted in a significant reduction in reported DENV cases [38]. Similar integrated vector management strategies, public education campaigns, and improved diagnostic facilities are essential for combating dengue in this region.

Tuberculosis

TB is an infectious disease caused by the bacterium *Mycobacterium tuberculosis*. It belongs to the *Mycobacteriaceae* family of bacteria [39,40]. NE India has a relatively high burden of TB due to poverty, malnutrition, HIV prevalence and high prevalence of MDR TB [41,42]. A significant number of TB patients (53.17%) had comorbidities, primarily diabetes mellitus (26.58%) and hypertension (17.34%). Comorbid conditions were more common in PTB cases than in EPTB cases [43]. The NE India had a prevalence of smear and/or culture positive PTB of 233 cases per lakh (95% CI: 134-331), the prevalence for other regions [44].

Various studies have identified certain factors associated with the higher prevalence of TB in specific populations.

These factors include lower socio-economic status, lower levels of education, unemployment, inadequate housing conditions, alcohol consumption, proximity to individuals with TB, travel history, lack of BCG vaccination, air borne transmission, participation in mass gatherings, and suboptimal weight status [45]. The region's hilly terrain and remote communities pose challenges in delivering healthcare services, including TB diagnostics and treatment. Strengthening healthcare infrastructure, expanding access to quality diagnostic facilities, and ensuring timely initiation of treatment are crucial to tackling TB in this region.

Japanese Encephalitis

JE is a mosquito-borne (*Culex tritaeniorhynchus*) viral disease that primarily affects children which is caused by the JEV, belongs to the Flavivirus family and is primarily transmitted by Culex mosquitoes [46,47]. The genome of JEV composed of a single-stranded, positive-sense RNA

[48]. WNV closely related to JEV is also reported from JEV endemic regions [49].

Since 1976, JE has been sporadically occurring in outbreaks or epidemics in Assam, primarily due to favorable climatic conditions, the presence of numerous potential mosquito vectors, amplifying hosts, agricultural practices, and socio-cultural behaviors of the local population that contribute to the spread of the disease in the state [50]. More than one-third of the national burden of JE in India comes from the state of Assam alone [51]. In Assam, there has been a significant shift in the prevalence of JE cases by age, unlike other JE-endemic states in India. The number of cases among individuals above 15 years old has increased significantly compared to those below 15 years old. Assam is facing a surge in JE and AES cases, with the disease spreading from upper Assam to all other districts in the state and seasonality of JE is shown in Figure 2 [7].

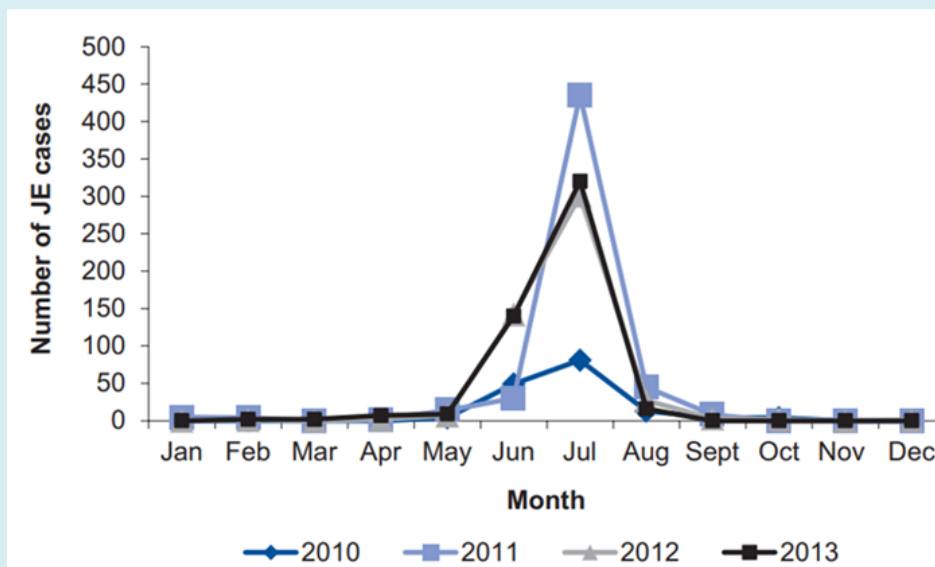


Figure 2: Seasonality of Japanese encephalitis (JE) cases from 2010 to 2013, data from the State Health Directorate of Assam [7].

Incidence of adult JE cases reduced from 10.5 to 5.7 per 100,000 following vaccinations in two districts (Sivasagar and Dibrugarh) of Assam [51]. During 2011 to 2020 reported 1081 AES and 588 JE cases, with 333 and 180 deaths, (CFR 30.61%) respectively from Sivasagar, Assam. And it was also reported that AES/JE cases peaked in June and July and were more common among elderly and males [52]. Routine JE vaccination covered over 50% of the 9-18 months age group. Although AES/JE cases are declining, intensified surveillance and increased immunization coverage are needed [52]. The preventive method available for JE is JE vaccine; early detection and prompt medical intervention are important for

effective JE cases. Vaccination programs against the disease have shown effectiveness; primary comprehensive measures such as mosquito control, improving living conditions of vulnerable populations, and health education remain the most effective methods to prevent the disease [53,54].

Waterborne and Enteric Infections

Waterborne and Enteric Infections are caused by various pathogenic microorganisms such as bacteria, viruses, protozoa, and parasites [55]. Inadequate hygiene, sanitation, and polluted water contribute to 6.3% of worldwide fatalities

and 9.1% of the overall global burden of disease [56]. Diarrhea is a prominent water-borne disease that is endemic in numerous regions across the world, posing a significant health threat to global populations [57,58]. Rugged terrains, dense forests, and remote areas of NE India offers a diverse range of disease environments, with a predominant presence of communicable diseases (35.68%). Among these, diarrhoea stands out as a water-borne disease that significantly impacts the local society. The prevalence of RV associated diarrhoea among children below 5 years of age in India is 36.3% and prevalence in Nagaland and Assam is 40.3% and 38.4% respectively [59]. Other enteric pathogens like norovirus, adenovirus, campylobacter, sapovirus, astrovirus are also endemic in the region [60,61].

Sikkimese people's use untreated spring water poses a significant threat to public health due to the potential presence of waterborne pathogens [62]. In 2017 and 2018, Sikkim reported alarming cases of 41,816 and 41,449 acute diarrheal diseases, as well as 104 and 158 cases of enteric fever, respectively. A study also revealed severe fecal contamination in Sikkim's spring water, demanding immediate attention [63,64]. The main factors contributing to diarrhoea include Inadequate environmental sanitation, Absence of access to safe drinking water, seasonal flood, contaminated food, and transmission through fomites, flies, and cockroaches. However, the local population, deeply connected to nature, possesses valuable ethno biological knowledge about the plants in their surroundings. This knowledge enables them to effectively prevent and treat various disease complications [65]. Since, waterborne diseases have been a significant public health concern in Northeast India, particularly in areas with limited access to safe drinking water and proper sanitation facilities. Efforts have been made to monitor water quality and improve sanitation infrastructure [66].

Hepatitis

Hepatitis is a condition characterized by inflammation of the liver. It is caused by different hepatitis viruses, categorized as types A, B, C, D, and E, as well as non-infectious factors. Hepatitis can lead to a range of health complications, including potentially life-threatening outcomes [67,68]. Hepatitis B and C infections are a significant health concern in NE India [69]. Earlier studies have reported the prevalence of HBV and HCV in the region and risk factors for transmission, the recent surge in trade, trafficking, and the illicit use of drugs has had a significant impact on the epidemiology of HBV, particularly in the NE regions of India [70]. Among the South-East Asian nations, India falls under the category of intermediate prevalence for hepatitis B (2 to 5%) [71]. In the NE region of India, specifically in Tripura, the community-

level prevalence of hepatitis B is 3.6% (95% CI 3.14-4.06) [71]. Among Idu Mishmi tribe of Arunachal Pradesh, Hepatitis B virus infection is hyperendemic [72]. High incidence of hepatitis in the region is may be due to IDUs, as 15.9% of the tested injection drug users were found to have contracted HBV infection [73]. The estimated prevalence of Hepatitis B in NE India shows variation, ranging from approximately 2% in states like Assam to as high as 7-8% in Arunachal Pradesh and specific regions of Tripura. The increasing number of IDUs is a contributing factor to the rise in Hepatitis B prevalence and incidence, making it one of the highest in the country [74]. In a study it was reported, 9.9% prevalence of HBV infection among individuals with different liver diseases, blood donors, and healthcare workers in Northeast India and among the infected cases, 49.5% were HBV DNA positive [75].

MoHFWIndia has implemented several significant initiatives to combat Hepatitis infections, including HBV Immunization programs, Viral Hepatitis Surveillance. Surveillance systems are in place to monitor and track cases of viral hepatitis, Injection Safety and Infection Control, Biomedical Waste Management, Research, Awareness Programs. These comprehensive efforts in India working towards preventing new hepatitis infections, improving healthcare practices, and enhancing public awareness to mitigate the impact of hepatitis on individuals and communities [76]. However, further community-based studies should be made to develop more effective measures to combat and control hepatitis in the region.

Chikungunya Virus

CHIKV, an alphavirus classified within the *Togaviridae* family, is a small, spherical enveloped virus with a diameter ranging from 60 to 70 nm. The virus carries a genome comprising a single-stranded RNA molecule of positive polarity [77]. During 2011, the initial documentation of CHIKV infection among hospitalized individuals in Assam came to light [78]. CHIKV has been identified as a prevalent disease in the regions of Assam, Arunachal Pradesh, and Meghalaya [79]. The seroprevalence CHIKV in the NE region is recorded to be (0.3% [95% CI 0.1-0.8]) [80]. During 2014-17 1,510 CHIKV/DENV suspected cases from Assam, Arunachal Pradesh and Meghalaya were screened for CHIKV IgM antibody and 179 samples (11.83%) tested positive and the age group between 16 and 30 years showed the highest incidence [79]. In another study, CHIKV transmission was found to be lower in NE and eastern region (sero-prevalence < 5%) than rest of India [80,81].

CHIKV is generally a self-limiting infection however the rising morbidity caused by CHIKV infection has significant

impacts on the social and economic well-being of individuals [82,83]. Therefore, it is essential to implement community empowerment initiatives to effectively control the mosquito population through various mosquito control measures and personal protection methods. These proactive measures are necessary to address and mitigate the potential outbreak of this disease in the future [79].

Scrub Typhus

Scrub typhus is a bacterial infection caused by *Orientia tsutsugamushi*. It belongs to the family *Rickettsiaceae*. The genetic material of *Orientia tsutsugamushi* is composed of single-stranded DNA [84]. Several Scrub typhus outbreaks were reported from North, South, and Eastern India [85,86]. Scrub typhus is endemic in several states of NE India, reported from Assam, Nagaland, Arunachal Pradesh, and Mizoram [84,85,87]. During 2018 to 2022, Mizoram witnessed a total of 22,914 rickettsial cases, out of which 19,651 (85.76%) individuals tested positive for scrub typhus over all incidence rate of rickettsial disease in Mizoram was 3.34 [87]. In another sero-surveillance study in seven districts of Arunachal Pradesh showed prevalence of scrub typhus was 25.9% to 72.5% (Figure 3) [88]. The presence of extensive scrub vegetations, occupational (farming) exposure, *Jhum*

farming practices, and favourable environmental conditions collectively create a favourable environment for the spread of rickettsial infections [86]. During 2019 district hospital Lawngtlai reported Two (2) unfortunate death from Cheural village, Mizoram and multiple cases having scrub typhus like illness, after investigation of 242 cases, 80 (33.05%) cases found to be scrub typhus positive [89]. The investigation also revealed farmers particularly involved in forest farming under the working age groups (20-60 years) were most affected [89]. Moreover, Leptospirosis a zoonotic disease with multisystemic involvement is caused by the pathogenic strains of *Leptospira interrogans* is also reported from parts of NE region [90].

In less-explored areas of NE India, such as Arunachal Pradesh, Mizoram and other NE states there is a lack of knowledge about the epidemiology and impact of rickettsial diseases. Hence, it could be a significant factor contributing to undiagnosed cases of fever. It is crucial to conduct active surveillance to gain a better understanding of the true extent, epidemiological characteristics, and distribution of the disease's vectors and burden. This will help address the challenges posed by this re-emerging neglected tropical disease.

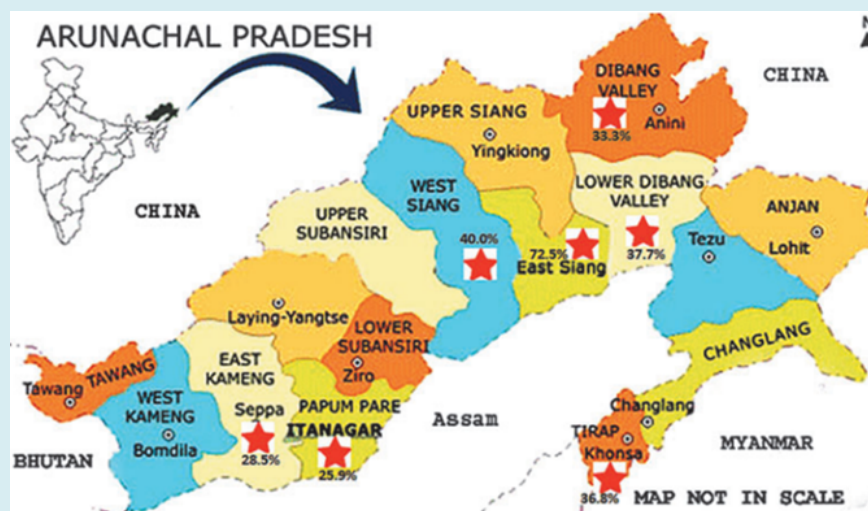


Figure 3: Map of Arunachal Pradesh, indicating the districts under study along with their respective prevalence rates represented in percentages. The study districts are marked with a red star symbol. For visual representation, color images can be accessed online at www.liebertpub.com/vbz [89].

Improving the estimation of scrub typhus burden in India can contribute to the development and implementation of more effective control and management strategies. Enhanced public awareness campaigns, implementation of robust vector control, strengthening healthcare infrastructure will help in combating this neglected tropical disease in NE India.

Human Immunodeficiency Virus

HIV is a virus that targets and compromises the immune system, leading to its weakening and impairment. It belongs to the *Retroviridae* family and has two single-stranded RNA as its genetic material [91]. HIV remains a significant

global public health concern, with numerous new infections annually and a staggering death toll of nearly 40.1 million lives so far [92]. The NE states of India, including Mizoram, Nagaland, and Manipur, exhibit the highest rates of adult HIV prevalence, with percentages standing at 2.70%, 1.36%, and 1.05% respectively [93]. The primary factor contributing to the HIV pandemic in this international border region is the utilization of illicit 'heroin' sourced from the 'South Asia Golden Triangle' [94]. The HIV pandemic in the border region presents distinctive complexities not encountered in other parts of the country. These complexities stem from the emergence of recombinant HIV forms and DR HIV-1 strains. IDU and intricate patterns of cross-border movement have contributed significantly to the challenges associated with the HIV/AIDS pandemic in the region [95]. Gaining a deeper understanding of the causes, challenges, and current situation of HIV/AIDS is crucial for improving patient investigation and treatment. Additionally, comprehensive studies exploring factors such as the impact of emerging genetic variants on antiretroviral treatment response and the effects of co-infections with different viruses should be conducted at all international borders. These efforts are necessary to curb the spread and limit the expansion of more complex forms of the virus [94].

Mizoram, has the second-highest AIDS mortality rate in the country, standing at 23.34 per 100,000 population [96]. In terms of AIDS-related deaths, there were 58.96 thousand deaths in 2019, which represents a 66% decline since 2010 [97]. Manipur had the highest AIDS mortality rate, followed by Mizoram and Nagaland, with estimates of 36.86, 28.34, and 26.20 AIDS-related deaths per 100,000 population, respectively [98]. The Government of India has implemented key interventions to achieve UN Sustainable Development Goal 3.3 of ending the HIV/AIDS epidemic by 2030. These include enacting the HIV & AIDS Prevention and Control Act, 2017, and implementing the National AIDS and STD Control Program (NACP) since 1992 [99].

NACO has been playing a crucial role in addressing the HIV/AIDS epidemic in NE India. The organization collaborates closely with state governments, NGOs, and various stakeholders to implement comprehensive prevention, testing and treatment programs in the region. NACO's efforts encompass raising awareness about HIV/AIDS, advocating for behavioural change, facilitating accessible testing and counselling services, and delivering antiretroviral treatment to individuals requiring it. Moreover, NACO strives to combat the stigma and discrimination associated with HIV/AIDS in the NE states of India [100,101]. The CDC has initiated Project Sunshine to implement strategies aimed at enhancing prevention, testing, and treatment options for individuals residing in NE states with the highest prevalence of HIV, namely Manipur, Mizoram, and Nagaland [102].

Conclusion

Infectious diseases continue to pose significant health challenges in NE India, primarily due to its unique geographic, socio-economic factors and sharing international border with four countries. Addressing these challenges requires a multi-faceted approach, including improved healthcare infrastructure, strengthened surveillance systems, enhanced vector control measures, community engagement, cross border smuggling and public awareness campaigns and further community-based studies. The region's high burden of tuberculosis highlights the need for strengthening healthcare infrastructure, expanding access to quality diagnostics and treatment, and addressing socio-economic factors that contribute to its prevalence. Japanese encephalitis and waterborne infections require a focus on vaccination programs, mosquito control, and improving sanitation and access to safe drinking water. The prevalence of hepatitis, CHIKV, and scrub typhus emphasizes the importance of surveillance, research, and public awareness campaigns. Collaborative initiatives, such as MERA India and MESA, play a crucial role in malaria control and elimination. To mitigate the burden of infectious diseases in NE India, a comprehensive understanding of the epidemiology, aetiology, and impact of these diseases is necessary.

Further, aid of latest technologies like metaverse may be considered to combat the burden of infectious disease in the region. Metaverse is a combined effort of technologies including AI, AR, VR, IoT, QC and robotics system [103]. The metaverse can enable remote consultations and medical examinations, bridging the gap between patients in remote areas and healthcare providers. With the incorporation of IoT sensors and Artificial Intelligence driven data analytics, real-time disease surveillance and monitoring become possible, enhancing healthcare response and management. Moreover, AR and VR technologies offer valuable tools to train healthcare workers effectively, covering infectious disease prevention, treatment protocols, and emergency procedures. The metaverse also fosters virtual collaboration among healthcare professionals, researchers, and organizations, expediting the development of vaccines, treatments, and medical interventions to combat infectious diseases. Additionally, the utilization of quantum computing allows complex simulations and predictive models, enabling better forecasting of disease outbreaks and evaluation of intervention strategies tailored to the North East region's healthcare needs. It will empower medical practitioners with precision and efficiency while Telemedicine reduces treatment delays. Additionally, the Metaverse may improve patient data security. Despite being in its early stages, it has the potential to transform Indian medical infrastructures, fostering progress and innovation. Collaboration among stakeholders can lead to improved health outcomes in

Northeast India.

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References

- Tripathi SK, Roy A, Kushwaha D, Lalnunmawia F, Lalnundanga, et al. (2016) Perspectives of Forest Biodiversity Conservation in Northeast India. *J Biodivers Biopros Dev* 3(2): 157.
- Hazarika M (2013) Prehistoric cultural affinities between Southeast Asia, East Asia and Northeast India: an exploration, *Unearthing Southeast Asia's Past*. National University of Singapore Press, Singapore, 1: 16-25.
- Dikshit KR, Dikshit JK (2014) *North-East India: Land, People and Economy*. Springer Science & Business Media.
- CUTS & FICCI (2017) *Harnessing the Potential for Cross-border Trade between North East India and its Neighbouring Countries*. Consumer Unity & Trust Society, Federation of Indian Chambers of Commerce and Industry.
- Baker RE, Mahmud AS, Miller IF, Rajeev M, Rasambainarivo F, et al. (2022) Infectious disease in an era of global change. *Nat Rev Microbiol* 20(4): 193-205.
- Press Information Bureau (2022) *Strengthening Healthcare in North East India*. (Ministry of Development of North Eastern Region) & (Ministry of Health and Family Welfare).
- Dev V, Sharma VP, Barman K (2015) Mosquito-borne diseases in Assam, north-east India: current status and key challenges. *WHO South East Asia J Public Health* 4(1): 20-29.
- CDC (2020) *Disease Threats and Global WASH Killers: Cholera, Typhoid, and Other Waterborne Infections*. Global Water, Sanitation and Hygiene (WASH). Centers for disease control and prevention.
- WHO (2022) *Drinking-water*. World Health Organization.
- Banik A, Das NS, Lyngdoh VW, Phukan AC, Dutta V (2018) Prevalence and first-line drug sensitivity trends of *Mycobacterium tuberculosis* at a tertiary center in North-East India. *The Egyptian Journal of Chest Diseases and Tuberculosis* 67(1): 32-37.
- Biswas D, Dutta M, Sarmah K, Yadav K, Buragohain M, et al. (2019) Genetic Characterisation of Influenza A(H1N1) pdm09 Viruses Circulating in Assam, Northeast India during 2009–2015. *Indian J Med Microbiol* 37(1): 42-49.
- Singh S, Crofts N (1993) HIV infection among injecting drug users in north-east Malaysia, 1992. *AIDS Care* 5(3): 273-281.
- Sarkar S, Mookerjee P, Roy A, Naik TN, Singh JK, et al. (1991) Descriptive epidemiology of intravenous heroin users—A new risk group for transmission of HIV in India. *J Infect* 23(2): 201-207.
- United Nations (1993) UNODC - Bulletin on Narcotics.
- Lyngdoh LM (2015) Inter-State Variations in Rural Healthcare Infrastructure in North-East India. *The NEHU Journal* 13(2): 31-48.
- WHO (2023) *Malaria*. World Health Organization.
- Kwiatkowski DP (2005) How Malaria Has Affected the Human Genome and What Human Genetics Can Teach Us about Malaria. *Am J Hum Genet* 77(2): 171-192.
- Mutheneni SR, Upadhyayula SM, Kadiri MR, Nishing K (2014) Malaria Prevalence in Arunachal Pradesh-A Northeastern State of India. *Am J Trop Med Hyg* 91(6): 1088-1093.
- Shankar H, Singh MP, Hussain SSA, Phookan S, Singh K, et al. (2022) Epidemiology of malaria and anemia in high and low malaria-endemic North-Eastern districts of India. *Front Public Health* 10: 940898.
- Sarma DK, Mohapatra PK, Bhattacharyya DR, Chellappan S, Karuppusamy B, et al. (2019) Malaria in North-East India: Importance and Implications in the Era of Elimination. *Microorganisms* 7(12): 673.
- Sharma J, Dutta P, Khan SA (2016) Epidemiological study of malaria cases in North East region of India. *Indian J Med Microbiol* 34(2): 261-262.
- Ahmed RA, Kumar A, Swargiary A, Suri HS, Shankar H, et al. (2023) Impact assessment of Intensified Malaria Control Project in transitioning a high malaria-endemic district to a low-endemic district: an epidemiological aspect. *Pathog Glob Health* 117(5): 493-504.
- ICMR (2020) *MERA India*. Indian council for medical research.
- MESA (2012) *Project – ISGLOBAL*. Malaria Eradication Scientific Alliance.
- Alonso P, Binka F, Brown G, Chitnis C, Milman J, et al. (2012) MESA - Malaria Eradication Scientific Alliance. *Int J Infect Dis* Volume 16(Suppl 1): E361.

26. (2015) National vector borne disease control programme. Government of India Ministry of health & family welfare.
27. Dev V, Bhattacharyya PC, Talukdar R (2003) Transmission of malaria and its control in the northeastern region of India. *J Assoc Physicians India* 51: 1073-1076.
28. Mustafa MS, Rasotgi V, Jain S, Gupta V (2015) Discovery of fifth serotype of dengue virus (DENV-5): A new public health dilemma in dengue control. *Med J Armed Forces India* 71(1): 67-70.
29. Holmes EC (1998) Molecular epidemiology and evolution of emerging infectious diseases. *Br Med Bull* 54(3): 533-543.
30. Guzman MG, Halstead SB, Artsob H, Buchy P, Farrar J, et al. (2010) Dengue: A continuing global threat. *Nat Rev Microbiol* 8(12 Suppl): S7-S16.
31. Nanaware N, Banerjee A, Bagchi SM, Bagchi P, Mukherjee A (2021) Dengue Virus Infection: A Tale of Viral Exploitations and Host Responses. *Viruses* 13(10): 1967.
32. Bhattacharya PK, Gautom D, Nath N, Sarma A, Saikia H (2017) Clinical profile of dengue in a hitherto non-endemic region—A hospital based study from northeast India. *India J Med specialities* 8(3): 124-130.
33. Dutta P, Mahanta J (2006) Potential Vectors of Dengue and the Profile of Dengue in the North-Eastern Region of India: An Epidemiological Perspective. *WHO Dengue Bull* 30: 234-242.
34. Khan SA, Dutta P, Topno R, Soni M, Mahanta J (2014) Dengue outbreak in a hilly state of Arunachal Pradesh in Northeast India. *ScientificWorldJournal* 2014: 584093.
35. Murhekar MV, Kamaraj P, Kumar MS, Khan SA, Allam RR, et al. (2019) Burden of dengue infection in India, 2017: a cross-sectional population based serosurvey. *Lancet Glob Health* 7(8): e1065-e1073.
36. Sharma A, Rajbongshi G, Alam ST, Rabha D, Chamuah K, et al. (2020) Molecular typing of dengue viruses circulating in Assam, India during 2016-2017. *J Vector Borne Dis* 57(3): 249-258.
37. Jansen CC, Beebe NW (2010) The dengue vector *Aedes aegypti*: what comes next. *Microbes Infect* 12(4): 272-279.
38. Apum B, Jakharia A, Borkakoty B, Das PK, Biswas D, et al. (2018) Comprehensive Environmental Management Measures Controlled Dengue Virus (DENV) in an Endemic Region. *J Assoc Physicians India* 66(10): 98-99.
39. WHO (2018) Tuberculosis. World Health Organization.
40. Martínez AG, Duran MJO, Bautista JFG, Márquez JAR, Aliaga L, et al. (2022) *Mycobacterium* infections. 1st(Edn.), *Encyclopedia of Infection and Immunity*, pp: 703-718.
41. Singh LS, Mazumder PB, Sharma GD (2014) Analysis of mutational pattern in multidrug resistant tuberculosis (MDR TB) in a geographically isolated northeastern region of India. *IOSR Journal of Pharmacy and Biological Sciences* 9(1): 4-10.
42. Kayina TKP, Tarao MS, Nula P (2019) Tuberculosis in North-East India: patient profile and treatment outcome of patient attending RNTCP. *Int J Community Med Public Health* 6(7): 2856.
43. Bhattacharya P, Talukdar K, Barman B, Jamil MD, Phukan P, et al. (2020) Clinical Spectrum and Medical Comorbidities in Tuberculosis: A Hospital-Based Study in Northeast India. *Cureus* 12(9): e10580.
44. Thomas BE, Thiruvengadam K, Vedhachalam C, Srividya A, Rao VG, et al. (2021) Prevalence of pulmonary tuberculosis among the tribal populations in India. *PLoS One* 16(6): e0251519.
45. Sailo CV, Kumar NS (2023) Tuberculosis (TB) status in Mizoram-A research perspective. *Bione* 25.
46. Reuben R, Gajanana A (1997) Japanese encephalitis in India. *Indian J Pediatr* 64(2): 243-251.
47. Mulvey P, Duong V, Boyer S, Burgess G, Williams DT, et al. (2021) The Ecology and Evolution of Japanese Encephalitis Virus. *Pathogens* 10(12): 1534.
48. Woo JH, Jeong YE, Jo JE, Shim SM, Ryou J, et al. (2020) Genetic Characterization of Japanese Encephalitis Virus Genotype 5 Isolated from Patient, South Korea, 2015. *Emerg Infect Dis* 26(5): 1002-1006.
49. Khan SA, Dutta P, Khan AM, Chowdhury P, Borah J, et al. (2011) West Nile virus infection, Assam, India. *Emerg Infect Dis* 17(5): 947-948.
50. Phukan AC, Borah PK, Mahanta J (2004) Japanese encephalitis in Assam, northeast India. *Southeast Asian J Trop Med Public Health* 35(3): 618-622.
51. Khan SA, Choudhury P, Kakati S, Doley R, Barman MP, et al. (2021) Effectiveness of a single dose of Japanese encephalitis vaccine among adults, Assam, India, 2012-2018. *Vaccine* 39(35): 4973-4978.
52. Ahmed RA, Swargiary A, Shankar H, Singh K, Bordoloi R,

- et al. (2021) Epidemiological study of Acute Encephalitis Syndrome and Japanese Encephalitis burden in Sivasagar district of Assam, India. Research Square 1-17.
53. Tiwari S, Singh RK, Tiwari R, Dhole TN (2012) Japanese encephalitis: a review of the Indian perspective. *Braz J Infect Dis* 16(6): 564-573.
 54. Wang H, Liang G (2015) Epidemiology of Japanese encephalitis: past, present, and future prospects. *Ther Clin Risk Manag* 11: 435-448.
 55. WHO (2022) Drinking-water. World Health Organization.
 56. Pal M, Ayele Y, Hadush A, Panigrahi S, Jadhav JV (2018) Public Health Hazards Due to Unsafe Drinking Water. *Air & Water Borne Diseases* 7(1): 1.
 57. WHO (2017) Diarrhoeal disease. World Health Organization.
 58. Ali M, Nelson AR, Lopez AL, Sack DA (2015) Updated global burden of cholera in endemic countries. *PLoS Negl Trop Dis* 9(6): e0003832.
 59. Kumar CPG, Giri S, Sarkar MC, Gopalkrishna V, Chitambar SD, et al. (2020) Epidemiology of rotavirus diarrhea among children less than 5 years hospitalized with acute gastroenteritis prior to rotavirus vaccine introduction in India. *Vaccine* 38(51): 8154-8160.
 60. Borkakoty B, Jakharia A, Sarmah MD, Hazarika R, Baruah PJ, et al. (2020) Prevalence of campylobacter enteritis in children under 5 years hospitalised for diarrhoea in two cities of Northeast India. *Indian J Med Microbiol* 38(1): 32-36.
 61. Jakharia A, Borkakoty B, Biswas D, Yadav K, Mahanta J (2016) Seroprevalence of Scrub Typhus Infection in Arunachal Pradesh, India. *Vector Borne Zoonotic Dis* 16(10): 659-663.
 62. Tambe S, Kharel G, Subba S, Arrawatia ML (2013) Rural Water Security in the Sikkim Himalaya: Status, Initiatives and Future Strategy Impact. India Mountain Initiative, Summit in Kohima, Nagaland, India.
 63. Singh AK, Das S, Kumar S, Gajamer VR, Najar IN, et al. (2020) Distribution of Antibiotic-Resistant Enterobacteriaceae Pathogens in Potable Spring Water of Eastern Indian Himalayas: Emphasis on Virulence Gene and Antibiotic Resistance Genes in *Escherichia coli*. *Front Microbiol* 11: 581072.
 64. Singh AK, Das S, Singh S, Pradhan N, Gajamer VR, et al. (2019) Physicochemical parameters and alarming coliform count of the potable water of Eastern Himalayan state Sikkim: An indication of severe fecal contamination and immediate health risk. *Front Public Health* 7:174.
 65. Laloo D, Hemalatha S (2011) Ethnomedicinal plants used for diarrhea by tribals of Meghalaya, Northeast India. *Pharmacogn Rev* 5(10): 147-154.
 66. (2022) Clean water in villages of NER. Ministry of Development of North-East Region.
 67. WHO (2016) Hepatitis. World Health Organization.
 68. Cropley A, Weltman M (2017) The use of immunosuppression in autoimmune hepatitis: A current literature review. *Clin Mol Hepatol* 23(1): 22-26.
 69. Desikan P, Khan Z (2017) Prevalence of hepatitis B and hepatitis C virus co-infection in India: A systematic review and meta-analysis. *Indian J Med Microbiol* 35(3): 332-339.
 70. Datta S (2008) An overview of molecular epidemiology of hepatitis B virus (HBV) in India. *Virology* 475:156.
 71. Bhaumik P (2015) Epidemiology of Viral Hepatitis and Liver Diseases in India. *Euroasian J Hepatogastroenterol* 5(1): 34-36.
 72. Biswas D, Borkakoty BJ, Mahanta J, Jampa L, Deouri LC (2007) Hyperendemic foci of hepatitis B infection in Arunachal Pradesh, India. *J Assoc Physicians India* 55: 701-704.
 73. Datta S, Banerjee A, Chandra PK, Mahapatra PK, Chakrabarti S, et al. (2006) Drug trafficking routes and hepatitis B in injection drug users, Manipur, India. *Emerg Infect Dis* 12(12): 1954-1957.
 74. Bhuyan D (2018) Growing Menace of Hepatitis B Infection in North-East India. *Health World*.
 75. Kar P, Goswami B, Mahanta J, Bhimo T, Das AK, et al. (2022) Epidemiology, Genotyping, Mutational and Phylogenetic Analysis of Hepatitis B Virus Infection in North-east India. *J Clin Exp Hepatol* 12(1): 43-51.
 76. Bhat B (2018) Combating hepatitis through multipronged approach. *India Science, Technology & Innovation - ISTI Portal*.
 77. Caglioti C, Lalle E, Castilletti C, Carletti F, Capobianchi MR, et al. (2013) Chikungunya virus infection: an overview. *New Microbiol* 36(3): 211-227.
 78. Khan SA, Dutta P, Topno R, Borah J, Chowdhury P, et al. (2015) Chikungunya outbreak in Garo Hills, Meghalaya: An epidemiological perspective. *Indian J Med Res*

- 141(5): 591-597.
79. Dutta P, Khan SA, Phukan AC, Hazarika S, Hazarika NK, et al. (2019) Surveillance of Chikungunya virus activity in some North-eastern states of India. *Asian Pacific Journal of Tropical Medicine* 12(1): 19-25.
 80. Kumar MS, Kamaraj P, Khan SA, Allam RR, Barde PV, et al. (2021) Seroprevalence of chikungunya virus infection in India, 2017: a cross-sectional population-based serosurvey. *Lancet Microbe* 2(1): e41-e47.
 81. Murhekar MV, Kamaraj P, Kumar MS, Khan SA, Allam RR, et al. (2019) Burden of dengue infection in India, 2017: a cross-sectional population based serosurvey. *Lancet Glob Health* 7(8): e1065-e1073.
 82. Elsinga J, Grobusch MP, Tami A, Gerstenbluth I, Bailey A (2017) Health-related impact on quality of life and coping strategies for chikungunya: A qualitative study in Curaçao. *PLoS Negl Trop Dis* 11(10): e0005987.
 83. CDC (2022) Chikungunya virus. Centers for disease control and prevention.
 84. Luce-Fedrow A, Lehman ML, Kelly DJ, Mullins K, Maina AN, et al. (2018) A Review of Scrub Typhus (*Orientia tsutsugamushi* and Related Organisms): Then, Now, and Tomorrow. *Trop Med Infect Dis* 3(1): 8.
 85. Khan SA, Dutta P, Khan AM, Topno R, Borah J, et al. (2012) Re-emergence of scrub typhus in northeast India. *Int J Infect Dis* 16(12): e889-e890.
 86. Varghese GM, Abraham OC, Mathai D, Thomas K, Aaron R, et al. (2006) Scrub typhus among hospitalized patients with febrile illness in South India: magnitude and clinical predictors. *J Infect* 52(1): 56-60.
 87. Pautu LV, Lalmalsawma P, Rosangkima G, Sarma DK, Malvi Y, et al. (2023) Epidemiology of scrub typhus and other rickettsial infections (2018-22) in the hyper-endemic setting of Mizoram, North-East India. *BMJ Yale*.
 88. Jakharia A, Borkakoty B, Biswas D, Yadav K, Mahanta J (2016) Seroprevalence of Scrub Typhus Infection in Arunachal Pradesh, India. *Vector Borne Zoonotic Dis* 16(10): 659-663.
 89. Pautu L, Lalmalsawma P, Vanramliana, Rosangkima G, Malvi Y, et al. (2022) Scrub typhus disease outbreak at Cheural village, Lawngtlai district, Mizoram, North east India. *J Adv Sci Res* 13(9).
 90. Borkakoty B, Jakharia A, Biswas D, Mahanta J (2016) Co-infection of scrub typhus and leptospirosis in patients with pyrexia of unknown origin in Longding district of Arunachal Pradesh in 2013. *Indian J Med Microbiol* 34(1): 88-91.
 91. German Advisory Committee Blood (Arbeitskreis Blut), Subgroup 'Assessment of Pathogens Transmissible by Blood (2016) Human Immunodeficiency Virus (HIV). *Transfus Med Hemother* 43(3): 203-222.
 92. WHO (2023) HIV and AIDS. World Health Organization.
 93. National AIDS Control Organization (2021) India HIV Estimates 2021 Fact sheet. ICMR- National Institute of Medical Statistics.
 94. Sharma AL, Singh TR, Singh LS (2019) Understanding of HIV/AIDS in the international border area, Manipur: Northeast India. *Epidemiol Infect* 147: e113.
 95. UNODC (1993) Bulletin on Narcotics- 1993-Issue 1.
 96. India HIV (2017) India HIV Estimations 2017, Technical Report. National AIDS Control Organization & ICMR- National Institute of Medical Statistics Ministry of Health & Family Welfare.
 97. National AIDS Control Organization (1985) Surveillance. Ministry of Health & Family Welfare.
 98. IANS (2020) Spread of HIV/AIDS in Northeast India alarming: Report.
 99. The Indian Practitioner (2022) 24 lakh HIV positive people in India: 2022..
 100. Strategy Document National AIDS and STD Control Programme Phase-V (2021-2026) Anchoring the national response towards ending the AIDS epidemic. National AIDS Control Organization, Ministry of Health & Family Welfare.
 101. CDC Global Health (2023) CDC in India. Centers for disease control and prevention.
 102. Sharma S, Gopal V (2022) Metaverse in Indian Health Sector – A Regime Shift. *International journal of convergence in healthcare* 2(2): 38-42.

