

Minireview Article

Neglected Tropical Diseases Of Public Health Importance in India : Current Status And The Way Ahead

ABSTRACT

In global health, critical challenges have erupted from infectious diseases, including the emergence and re-emergence of old and new infectious diseases. This is directly attributed to rapid human development including massive changes in demographics, increasing population, and the deteriorating environment to name a few. Despite tremendous advances in the health of its poorest citizens, India bears a disproportionately high burden of neglected tropical diseases with over half of the 20 who classified neglected tropical diseases at endemic levels. In a global fight against these diseases, India occupies a unique place as a country that is both deeply affected by these devastating and deadly illnesses, but also holds solutions on how innovation might eliminate these ancient maladies. To obtain the high objective of improving health and reducing vulnerabilities, it is important that healthcare workers and professionals from other backgrounds bind together to broaden the perspective that are needed to address. There is a call for a comprehensive policy for neglected diseases research in India to foster drugs, diagnostics, and vaccine innovation, critical for evolving needs for elimination programmes.

Keywords: Neglected Tropical Diseases, NTDs, global health, Infectious diseases, endemic, disease burden, regulatory pathways, surveillance.

1. INTRODUCTION

Neglected Tropical Diseases (NTDs) are a multifarious group of communicable diseases that are common in tropical and subtropical conditions in 149 countries of the world (Table 1). The World Health Organization (WHO) states that these bunch of diseases affect more than one billion people and cost developing economies billions of dollars every year. Populations living in poverty, without adequate sanitation and in close contact with infectious vectors and domestic animals and livestock are those worst affected.

Table 1. List of Neglected Tropical diseases and their causal organisms by Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO):

S. No.	Name of the disease(NTD)	Causal Organism	Vector
1.	Buruli Ulcer	<i>Mycobacterium ulcerans</i>	
2.	Chicken Gunia	Chicken Gunia virus(CHIKV)	<i>Aedes aegypti</i> mosquito
3.	Chagas disease	<i>Trypanosome cruzi</i>	<i>Triatoma infestans</i> (kissing bug)

4.	Cysticercosis	Four stereotypes of virus (DENV)	<i>Aedes aegypti</i> and <i>Aedes albopictus</i> mosquitoes
5.	Dengue fever	Viruses of Flaviviridae family, Flavivirus genus	<i>Aedes aegypti</i> mosquito
6.	Dracunculiasis (Guinea worm disease)	<i>Dracunculus medinensis</i> worm	
7.	Echinococcosis	Larval stages of cestodes (Tapeworms) of genus <i>Echinococcus</i>	
8.	Facioliasis	<i>Fasciola hepatica</i> (liver fluke)	
9.	Food borne Trematodiasis	Trematode worms (flukes)	
10.	African Trypanosomiasis (sleeping sickness)	<i>Trypanosoma brucei gambiense</i> or <i>Trypanosoma brucei rhodesiense</i>	Tse – tse fly
11.	Leishmaniasis (kala-azar)	<i>Leishmania donovani</i>	<i>Phlebotomus argentipes</i> (sand fly)
12.	Leprosy	<i>Mycobacterium leprae</i>	
13.	Lymphatic filariasis	<i>Wuchereria bancrofti</i> (filarial worm), <i>Brugia malayi</i> and <i>Brugia timori</i>	
14.	Mycetoma	Filamentous bacteria (actinomycetoma) or fungi (eumycetoma) found in soil and water	
15.	Onchocerciasis (river blindness)	<i>Onchocerca volvulus</i> (nematode)	Black flies
16.	Rabies	RNA virus belonging to genus <i>Lyssavirus</i> transmitted by bite of rabid animals	
17.	Schistosomiasis	Trematode worms (blood flukes) of genus <i>Schistosoma</i> . Snails act as carrier.	
18.	Helmenthiasis	Intestinal nematodes- 1. <i>Ascaris lumbricoides</i> (round worm). 2. <i>Trichuris trichiura</i> (whip worm). 3. <i>Nectar americanus</i> and <i>Ancylostoma duodenale</i> (hook worm Sps.)	
19.	Yaws	<i>Trepanema pertense</i> (spirochete)	
20.	Trachoma	Bacteria <i>Chlamydia trachomatis</i>	

NTDs impact the lives of over 1 billion people in low – income and middle – income countries (WHO, 2012). Emerging infectious diseases and re-emerging infectious diseases can arise due to a multitude of factors and influences and must be addressed dynamically by diverse sectors of society; these include public health, medicine, environmental science, animal health, food safety, economics, and public policy stakeholders [1]

Today, India experiences the world's largest absolute burden of at least 11 major NTDs. Excluding NTDs that are spatially bound by their requirement for unique insect vectors or snail hosts (e.g. Schistosomiasis, Onchocerciasis, human African

Comment [11]: Author should get latest mortality and morbidity to predict the seriousness of NTDs.

Comment [12]: Rewrite the sentence with proper grammar.

Comment [13]: Reference mandatory.

Trypanosomiasis and Chagas disease), India leads the world in terms of total number of cases for each of the major NTDs as defined by the WHO [2]. Being the world's second most populous nation, India itself accounts for nearly 18% of the world's population. Therefore, we might expect the nation to harbor a significant NTD burden [3]. Based on most current available data of WHO in 2020, just over half of the population of India were affected by NTDs with respect to three diseases namely, elephantiasis, blinding trachoma, intestinal worms. With a population of 1.400 billion, India has the highest NTD burden in the world for these three diseases with around 752 million people requiring preventive chemotherapy (PC) for at least one NTD in 2020. In the year 2020, India had the highest burden in the world for elephantiasis with around 457 million people requiring PC. Further, in the same year India also had the highest burden for intestinal worms with around 436 million children requiring PC.

India also has the 5th largest economy in terms of total gross domestic product (GDP), and several diseases stand out for their disproportionate impact on India's health. For example, according to the Global Burden Disease study of 2016, India accounts for nearly one – half of the world's prevalent cases of visceral leishmaniasis and one – half of the global incident cases of dengue and visual impairment from trachoma. India also accounts for approximately one-third or more of the prevalent cases of leprosy, lymphatic filariasis (LF), cysticercosis, and incident cases of rabies. In addition, India also accounts for roughly one- quarter of the world's ascariasis and hookworm cases. Although no specific information about some other NTDs such as amoebiasis or giardiasis are provided, it is possible that India's high ranking extends beyond the diseases currently considered NTDs by WHO. Moreover, the high – disease – burden NTDs in India are not evenly - distributed, but instead focused in areas of urban and rural poverty.

It is imperative to state that though in recent years India has successfully eliminated certain infectious diseases such as guinea worm, trachoma, and yaws [4,5,6] yet, the neglected diseases such as leishmaniasis, filariasis, leprosy, snakebite, and soil transmitted helminthic infections still pose a challenge. There persist challenges in the implementation of new technologies and major research gaps. Covid 19 hugely impacted NTD programs across the globe. It halted disability saving surgeries such as sight – saving procedures for the chronic stages of trachoma. It halted mass treatment programs , reducing the number of treatments of levels not seen since 2012. It significantly reduced case detection for diseases like sleeping sickness, where quick accurate detection is paramount to successful treatment. It will have impacted countries reaching elimination, requiring a concerted effort to scale up programs to recover from these impacts. WHO analysis indicates that NTD programs have been among the health services most frequently affected by the pandemic. Furthermore, the economic shocks resulted in over a third of direct donor funding towards NTDs programs being removed with little or no warning. This meant millions of donated medicines risked expiry in warehouses across the world and has seriously impacted the ability of NTD programs to recover from the pandemic.

2. CURRENT SCENARIO

An all – inclusive policy to foster research and innovation in any drug discovery, diagnostics, and vaccine development in NTDs is lacking. The National Health Policy of 2017 which was set on an ambition to stimulate innovation to meet health needs and ensure that new drugs are affordable for those who need them the most [7], does not specially tackle neglected diseases.

Another such scheme of 2018 known by the name of “National Policy on Treatment of Rare Diseases”, includes infectious tropical diseases and identifies a need to support research on treatments of rare diseases. It has not yet prioritized diseases and areas of research funding or how innovation would be supported [8].

However , there has been development of a new treatment regimen for visceral leishmaniasis – liposomal amphotericin B (AmBisome). A single intravenous infusion of liposomal amphotericin B was found to be effective in treating visceral leishmaniasis [9] and is now recommended as first line treatment in the national programme in India[10]. But, with the reports of cases of resistance to miltefosine and liposomal amphotericin B, there is a need for new drug regimen to be developed periodically to overcome resistance. Though Indian labs have developed highly sensitive, specific and heat stable diagnostic probes such as rk39 and rkE16, their sensitivity is more variable in sample sets from East Africa and South America [11]. Still another diagnostic probe has been developed in India but has not yet been commercialized [12]. Financial support provided by the Japanese Global Health Innovative Technology Fund has played a vital role in vaccine program [13] against visceral leishmaniasis and vaccines are in different stages of development [14,15,16].

3. WAY AHEAD

There is a need for a well - established comprehensive scheme on neglected diseases that paves the way for greater funding and mechanisms to support research and innovation. A unified program on neglected diseases encompassing

research and elimination measures is likely to have a greater impact in prioritizing the matter in the health agenda and streamlining efforts towards disease elimination. Creating an enabling environment for research and innovation will be crucial if India is to achieve the target set in sustainable development goal to end epidemics of neglected tropical diseases by 2030 [19].

There is a need to earmark a proportion of public funds for neglected diseases research and innovation [20] and for translational research to support product development. It is also essential to develop mechanisms to facilitate priority regulatory pathways for innovations in neglected diseases. Further, by strengthening the existing integrated disease surveillance program, a comprehensive national survey database for neglected diseases can be created to monitor trends across the country.

The use of molecular diagnostics at point of care coupled with information technology is the future for robust surveillance. The emerging areas of genomics, transcriptomics and proteomics research can provide a better understanding of the modes of infection and treatment options. More drug and vaccine targets can be identified which would provide impetus to biotechnological research and industry. Innovation will also be facilitated by creating common repositories of biological samples and other materials accessible to researchers, industry and regulators.

4. CONCLUSION

An institutional mechanism to prioritize, coordinate and monitor research output, including on neglected diseases, is needed. This would allow policy makers, funders, researchers, and patient groups to identify areas of public investment and existing gaps and suggest improvements [21]. Partnerships involving major donor agencies, charitable organizations, NGOs, government leaders, pharma companies, and other stake holders are crucial in the fight against NTDs and enabling access to treatment for millions of people worldwide. Covid highlighted the importance of strengthening health systems, particularly at the community level. Concerted action is needed to strengthen health systems and resilience within the communities.

REFERENCES

1. World Health Organization. Neglected Tropical Diseases. <https://www.who.int/neglected%20diseases/diseases/en/> accessed May 4, 2020.
2. Mackey TK, Liang BA, Cuomo R, Hafen R, Brouwer KC, Lee DE. Emerging and re – emerging neglected tropical diseases: A review of key characteristics, risk factors, and the policy and innovation environment. *Clinical Microbial Reviews*. 2014; 27(4):249 – 279.
3. Hotez PJ, Damania A. India's Neglected Tropical Diseases. *PLOS Negl Trop Dis*.2018; 12 (3):e0006038 <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0006038>
4. Ministry of Health and Family Welfare. Chapter 5- Disease Control Programs. <https://main.mohfw.gov.in/sites/default/files/05Chapter.pdf>
5. Sharma R. India eradicate guinea worm disease. *BMJ*.2000;320:668. doi: <https://doi.org/10.1136/bmj.320.7236.668/b>
6. World Health Organization. India's triumph over yaws adds momentum to global eradication. 2016. <http://www.searo.who.int/mediacentre/releases/2016/1629/en>.
7. Open Government Data Platform India. National Health Policy, goals to be achieved. <https://data.gov.in/keywords/national-health-policy>
8. Ministry of Health and Family Welfare, Department of Health and Family Welfare. Rare Diseases. <https://www.mohfw.gov.in/diseasealerts/rare-diseases>
9. Sundar SA, Rai M, Chakravorty J. Single – dose indigenous liposomal amphotericin B in the treatment of Indian visceral leishmaniasis: A phase 2 study. *Amj Trop Med Hyg*.2015; 92: 512 – 7. <https://pubmed.ncbi.nlm.nih.gov/25510715/>
10. <https://doi.org/10.4269/ajtmh.14-0259> Drugs for neglected diseases initiative. New VL treatment in Asia.

- www.dndi.org/diseases-projects/portfolio/new-vl-treatments-asia
11. WHO. Visceral leishmaniasis rapid diagnostic test performance. 2011.
<https://www.who.int/tdr/publications/documents/vl-rdt-evaluation.pdf>
 12. Bandhopadhyay S, Chatterjee M, Pal S. purification ,characterization of O-acetylated Sialoglycoconjugates-specific IgM, and development of an enzyme-linked immunosorbent assay for diagnosis and follow-up of Indian visceral leishmaniasis patients. *Diagn Microbiol Infect Dis*;50:15-24.
<https://pubmed.ncbi.nlm.nih.gov/15380274/#:~:text=doi%3A%2010.1016/j.diagmicrobio.2004.04.014>
 13. GHIT Fund accelerates promising efforts to find new treatments, vaccines and diagnostics. *Eureka Alert*.2017.

http://www.eurekaalert.org/pub_releases/2017-10/b-gfa103117.php

14. Avishek K, Kaushal H, Gannavaram S, Dey R, Angamuthu S, Ramesh V et al. Gene deleted live attenuated *Leishmania* vaccine candidates against visceral leishmaniasis elicit pro-inflammatory cytokines response in human PBMCs. *Sci Rep*.2016;6:33059. <https://doi.org/10.1038/srep33059>
15. TDR, The Special Program for Research and Training in Tropical Diseases. Vaccine development: Leishmaniasis.
www.who.int/tdr/research/progress/9900/vaccine_dev_leish/en
16. Mologen AG, Press Release: Presentation of DNA vaccine against leishmaniasis at IMED 2014.
www.mologen.com/en/investor-relations-press/news/press-releases/2014/detail-view/article/mologen-praesentier-dna-impfstoff-gegen-leishmaniose-auf-der-imed-2014.html
17. Pan X, Pike A, Joshi D, Bian G, McFadden MJ, Lu P et al. The bacterium *Wolbachia* exploits host innate immunity to establish a symbiotic relationship with the dengue vector mosquito *Aedes aegypti*. *ISMEJ*.2018;12:277-88.

DOI: [10.1038/ismej.2017.174](https://doi.org/10.1038/ismej.2017.174)

18. Slatko BE, Taylor MJ, Foster JM. The *Wolbachia* endosymbiont as an anti-filarial nematode target. *Symbiosis*.2010;51:55-65.
doi: [10.1007/s13199-010-0067-1](https://doi.org/10.1007/s13199-010-0067-1)
19. Thomas Z, Saha GK, Gopakumar KM. Can India lead the way in neglected diseases innovation? *BMJ*.2019;364
doi: <https://doi.org/10.1136/bmj.k5396>
20. World Health Organization. Research and development to meet health needs in developing countries: strengthening global financing and coordination.2012.
<https://www.who.int/phi/CEWG-Report-5-april-2012.pdf>
21. Mitra AK, Mawson AR. Neglected tropical diseases:Epidemiology and Global Burden. *Trop Med Infect Dis*.2017;2:36
doi: [10.3390/tropicalmed2030036](https://doi.org/10.3390/tropicalmed2030036)