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Invited Commentary

Leprosy: The challenges ahead for India

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ABSTRACT

In India and rest of the world, there has been a tremendous decline in the number of leprosy patients over the last four decades. However, one of the major challenges faced by India is the continued occurrence of new leprosy cases, evidenced by almost a static new case detection rate (NCDR) over the last decade. The article discusses the challenges faced by the country and the solutions available for achieving the target of 'Zero Leprosy'.

Keywords: Leprosy, India, Challenges, Zero leprosy'

In India and rest of the world, there has been a tremendous decline in the number of leprosy patients over the past four decades. However, one of the major challenges faced by India is the continued occurrence of new leprosy cases, evidenced by almost a static new case detection rate (NCDR) over the past decade. One of the important factors for it could be the hurried declaration that India had reached the leprosy "elimination" target in 2005, which led to a false sense of security, loss of focus, and to erosion of expertise among program planners and health-care professionals. According to the report of the National Sample Survey and situational analysis done in 2015 by National Leprosy Eradication Programme (NLEP), India, the major issues to be addressed by the program were delay in case detection, hidden case loads, low awareness regarding leprosy in the community, and the lack of quality monitoring.[1] These effects can be evidenced by the World Health Organization (WHO) weekly epidemiological report of 2020, which mentions that out of 202,189 new cases reported globally, 114,451 (57%) are contributed by India.[2] In addition, in India, there are more than 3 million people with leprosy deformities needing attention and care.

Let us look at this issue in further detail. The post-elimination annual NCDR was far higher than what is expected in certain states and blocks compared to the national average. It is very high in a few states such as Chhattisgarh (16.2/100,000 population), Bihar, Jharkhand, and Odisha.[3] High NCDR appears to be due to continued transmission of the disease, evidenced by >50% multibacillary cases and more than 9% child leprosy rate in new cases detected in 11 states/union territories (UTs) of India. These trends indicate that despite the successful implementation of multidrug therapy (MDT), the transmission of leprosy in India is still a matter of concern.[4] After 40 years of strategies based almost entirely on early diagnosis and treatment with MDT, it is clear that there is a need to find additional tools to interrupt transmission, while continuing the efforts for vigorous new case finding. Some of the challenges faced and the measures required, to galvanize the elimination of leprosy in India are outlined below.

EFFORTS TOWARDS EARLY AND ACTIVE CASE DETECTION

Finding new leprosy cases early is the accepted cornerstone of leprosy control strategy. However, early diagnosis of leprosy is easier said than done as it needs active surveys picking up hidden cases from a large population of India which is a logistical and administrative challenge. NLEP which works under the umbrella of National Health Mission (NHM), India, was conducting leprosy case detection campaigns (LCDC) in selected blocks of high prevalence from 2015 to 2019.[5] However, from the year 2020, NLEP has abandoned this "campaign" mode approach and is carrying out "*active case detection and regular surveillance*" nationwide around the year for the detection of hidden leprosy cases. Once detected, the contacts of patients will also be screened for leprosy. The screening rounds will be one or two per year in each area, depending on whether the areas are low or high endemic for leprosy.[6]

It will not be out of place to look at the additional initiatives taken up by NHM, India, from 2020 to make leprosy case detection a more comprehensive and inclusive strategy. To accomplish this, the mobile health teams of *Rashtriya Bal Swasthya Karyakram* who conduct nationwide health program for school-going children are now trained to recognize leprosy, and the counselors of *Rashtriya Kishor Swasthya Karyakram* who take care of adolescents are now being given special training to detect child leprosy. In addition, screening for leprosy is included in the protocols of the *National Urban Health Mission* which serves the health-care needs of the urban population with focus on urban poor, migrants, and industrial workers. Moreover, in the community-based assessment charts (C-bac) of *Health and Wellness Centres* of Ayushman Bharat, leprosy has been added which will facilitate screening of village populations (*Rekha Shukla, Jnt. Sec. NLEP, Health and Family Welfare, Govt. of India: Excerpts of plenary talk, Indian Association of Leprologists* [*IAL*] *Conf., April 2021*). These are welcome initiatives from NLEP and the Government of India to strengthen the early new case detection, needed for speeding up the eradication of leprosy from India.

FOCUS ON INTERRUPTION OF TRANSMISSION

The new mantra of leprosy control globally is to focus on "interruption of transmission," rather than "elimination of leprosy." Naturally, the countries with the highest leprosy burden would be the ones to be targeted, with India at top of the list. It has been observed that household contacts of leprosy patient have 3.5 times more likelihood of having leprosy and social contacts are 2.5–3 times more likely to have leprosy than the general population.[7] A randomized control study has shown that chemoprophylaxis with single-dose rifampicin (SDR) has 57% overall risk reduction in preventing the development of leprosy for contacts during the first 2 years after its administration.[8] Based on the observations of such studies and recommendation of the WHO, the post-exposure chemoprophylaxis (PEP) with SDR for contacts (adults and children above 2 years) has been recommended for both household and social contacts of leprosy patients in India. SDR is considered a highly cost-effective intervention towards leprosy control in the Indian context. India introduced SDR-PEP after satisfactory results of its feasibility study conducted in the Union Territory of Dadra and Nagar Haveli. Operational guidelines were developed in 2019. Expert group of Indian Council of Medical Research (ICMR) recommended implementation of chemoprophylaxis in programmatic mode in 163 districts identified for conducting LCDC. Identified contacts of all new cases detected were administered SDR from 2018 to 2020. A total of 1.3 million contacts were identified and 65% of them were given SDR-PEP.[9]

It was observed that SDR-PEP implementation provided a unique opportunity to comprehend the entire leprosy program at a field level and make improvements.[9] The acceptability and perception of PEP need to be looked through sociocultural and psychological aspects of the index patient for implementation of this intervention. The screening of neighborhood/social contacts is more complex as patients are hesitant to expose their disease status outside their family. A blanket approach of providing PEP to whole targeted population in a high endemic segment/zone could be an option, as such methods were shown to be less stigmatizing with better outcomes in some countries with small populations such as Micronesia and Kiribati.[10,11] As SDR-PEP implementation is still at an early stage in India, lot more planning may be needed for successful nationwide implementation of this strategy. It is also time that SDR-PEP be recommended and implemented by all the stakeholders in India; by national leprosy institutes, non-governmental organizations, and leprosy associations such as IAL and Indian Association of Dermatologists, Venereologists and Leprologists (IADVL), as it is an approved preventive strategy for leprosy both by ICMR and Govt. of India so that the fruits of this intervention would have a wider reach and benefit.

AVAILABILITY OF DIAGNOSTIC TESTS APPLICABLE IN FIELD SITUATIONS

For leprosy, the diagnosis is mainly based on clinical symptoms and supported by skin smears (SS) for the detection of acid-fast bacilli (AFB). However, SS often fail to detect AFB when the concentration of bacilli is below 10^4 bacilli/ml and hence not reliable in patients with low bacillary load. Skin biopsy for histopathology, though very useful in leprosy diagnosis, is not feasible in most field

settings and for all clinical types of leprosy. The development, standardization, and application of reliable diagnostic tests for the early detection of leprosy are a global priority.

Several *Mycobacterium leprae* specific antigens have been identified in leprosy, especially after the genome sequencing. Testing for the both IgG and IgM antibodies against these antigens has been developed and also tested.[12] Prominent among them is the phenolic glycolipids-I (PGL-1) antibody detection. However, this test has a limitation that PGL-1 cross reacts with other mycobacteria such as *Mycobacterium avium* and *Mycobacterium paratuberculosis*. Second, although it is positive in most multibacillary (MB) cases, its positivity in paucibacillary (PB) cases is about 40%–60%. Moreover, it can also be detected in contacts of leprosy patients who do not manifest disease. Serological tests using antigens other than PGL-I are being developed and studied in different regions of the world. Some of them are known by their acronyms such as leprosy IDRI diagnostic-1 (LID-1) and conjugate of natural disaccharide and human albumen linked by Octyl (NDO). The combination of NDO-LID has shown great potential because of its high specificity and sensitivity to detect leprosy before the appearance of any clinical signs. These tests while being used widely in South American countries are yet to be introduced in India for field use.

Polymerase chain reaction (PCR) has been found to be an effective detection tool over the past two decades for the identification of *M. leprae* in various clinical specimens. PCR is a simple and sensitive diagnostic tool to detect the presence of *M. leprae* and sometimes their viability in the given sample. It is based on specific sequence amplification of *M. leprae* genome and DNA or RNA fragments identification. *M. leprae* specific PCRs were developed using genes *hsp65*, *18kDa*, *36kDa*, *16SrRNA*, *sodA,* and *M. leprae* specific repetitive sequences (RLEP) among others.[4] Recently, real-time PCR technology has been found to have improved detection rate, increased sensitivity and specificity and appears to be a robust tool for identification and quantification of mycobacteria in difficult to diagnose clinical situations.[13] These target fragments can be identified by PCR in SS, in tissues sections and body fluiids, and were found to be more sensitive than the serological assays. RLEP-PCR was found to be the most sensitive and specific of all the gene targets. The existing evidence suggests that PCR on a skin biopsy is the ideal diagnostic test. Nevertheless, PCR on SS seems to be most applicable for its practical value and ease at primary health-care settings, as a potential point-of-care test.[14] As of now, PCR testing for leprosy is being made use of for research purposes in India and is yet to be recommended for a wider use by the NLEP.

Translational research focusing on laboratory tests for the early diagnosis of leprosy is a priority. Overall, despite the efforts to develop a user-friendly and reliable test for early detection of leprosy in patients and their contacts, the ideal diagnostic test is yet to be uncovered. There is a need for improving the sensitivity of PCR and specificity of serological tests. Most of them fail to detect high percentage of PB leprosy with cardinal signs. Another major concern is their positive results in significant numbers of contacts not showing any clinical signs of leprosy.[4] It is hoped that in the next few years, we will be able to discover a reliable diagnostic point-of-care test which can support the early diagnosis of leprosy in the field.

CHALLENGES IN THERAPY OF LEPROSY

The WHO-MDT for leprosy has been a success story in India, as the prevalence and incidence of leprosy have decreased significantly since its introduction. However, if we aspire to eradicate leprosy and strive towards "*Zero leprosy*," we need curative therapy rather than therapies that are best suited for control of leprosy or that arrest the progression of the disease. While there have been significant changes in all aspects of leprosy program over the past four decades, the same MDT regimen, consisting of three drugs, dapsone, clofazimine, and rifampicin, continues to be used from 1982 onwards, from the year of its inception. It should be pertinent to note that the WHO MDT drug combinations introduced in 1981 were based on consensus recommendation of experts and were not a result of field trials. Over the past 40 years, other drugs such as minocycline, ofloxacin, clarithromycin, moxifloxacin, rifapentine, and diarylquinoline were found to have very good antileprosy effects. A couple of them were in fact recommended as part of 'rifampicin, ofloxacin and minocycline (ROM) therapy' for single skin lesion leprosy way back in 1998 but it fell out of favor of the WHO within the next 5 years.[15]

While there were attempts to shorten the WHO MB therapy for leprosy to 6 months from 2003 onwards, fortunately research studies and a recent guidelines of the WHO on treatment noted that such shortening of duration has a potential to increase the risk of relapse and has no evidence of equivalent outcomes to support it.[16,17]

At present, the combinations of newer drugs, other than those included in the WHO MDT, are recommended in the program, only in case of confirmed rifampicin resistance or for those who cannot take rifampicin because of side effects or intercurrent diseases.[18] These effective second-line drugs still are not recommended/or included in the WHO MDT schedules being provided to other leprosy patients, neither by the WHO nor by NLEP.

The WHO MDT was first recommended in 1982 to eliminate leprosy as a public health problem, when the global leprosy burden was 14 million. The same regimen, with a shortened duration for MB leprosy, is still being followed, when the global leprosy prevalence is 0.2 million. With the reduction in numbers, the profile of leprosy has changed significantly

in India, with a steep increase in MB leprosy percentage. To make this explicit, in the year 2005, there were 73,149 MB cases (45%) out of 161,457 new cases in the country, while in 2019, there were 62,119 MB cases (54%) out of 114,451 new cases detected.[2,19] It is being observed that significant percentage of these MB patients presents with high bacteriological index (BI > 3+) and hence is the single most important reservoir of *M. leprae* and a cause for transmission in the community. It is imperative that this high BI group should not be undertreated, which happens many times with the present 1-year MDT-MB of fixed duration. This is because relapses are largely confined to borderline lepromatous or lepromatous leprosy patients with a high initial BI and occur long after the discontinuation of therapy.[20] It is important also to repurpose a wider range of effective antimicrobials against these forms of leprosy. Proper management of these patients is crucial for the success of our dream of a leprosy-free world.[21]

The present global WHO strategy for 2021–2030 mentions that it plans to implement integrated, *country-owned zero leprosy roadmaps* for all endemic countries.[22] This provides an opportunity for countries like India to choose strategies and remedies best required for it. An ideal approach towards patients with a high initial BI would be a prolonged MDT-MB for 2–3 years or up to smear negativity, as similar approach is being successfully implemented in many countries including England and Japan for decades.[23,24] In addition, NLEP may also consider the use of daily rifampicin as a part of MDT which is being practiced successfully in the United States of America health program.[25,26] To further strengthen the program, immunotherapy with *Mycobacterium indicus pranii (MiP)* vaccine should also be taken up for nationwide implementation, as NLEP has already introduced the *MiP* vaccine in a project mode in India in 2016.[5] India should also consider *rational* use of newer potent bactericidal drugs such as clarithromycin, minocycline, ofloxacin, and moxifloxacin, both for PEP and as modified MDT in special settings.

All these interventions have to go hand in hand with improved commitment from all stakeholders involved in leprosy for achieving the target of *zero leprosy* in India. The coronavirus disease 2019 (COVID-19) pandemic has impacted all health programs and leprosy is no exception. The reallocation of staff and resources to limit the pandemic and the travel restrictions imposed, have definitely affected the leprosy program. Nonetheless, efforts are on to reorient leprosy program including drug delivery to patients and overcome these temporary hardships to reach the desired goal of leprosy free India.

Declaration of patient consent

Not required as there are no patients in this article.

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Conflicts of interest

There are no conflicts of interest.

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