REVIEW ARTICLE

CHILDHOOD LEPROSY REVISITED

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Abstract

The number of new cases of leprosy reported in India has maintained its level since 2006. Considering the long incubation period of leprosy, the detection of childhood cases is an indication of recent and ongoing transmission of disease in the community. While the introduction of multidrug therapy (MDT) has been effective, it has yet not resulted in the hoped for reduction of childhood cases. The proportion of children with leprosy in India continues to be around 9.04%. Additionally, the diagnosis of multibacillary cases among children as well as cases with grade 2 disability indicate delayed detection due to a lack of recognition of the early signs of leprosy.

The present review flags multiple concerns and examines the current status of the epidemiology, diagnosis, treatment and prevention of childhood leprosy. Besides this, distressing physical consequences as well as its social and domestic repercussions are addressed. The phenomenon of childhood leprosy requires further scientific investigation with a focus on route of transmission, immunological anti - *M. leprae* responses in children and diagnostic aids. Rapid implementation of realistic strategies for prevention and early case detection combined with effective treatment are needed to reduce disease and deformity.

Keywords : Child leprosy, *Mycobacterium leprae*

Introduction

"Child leprosy" is defined as the percentage of children (usually less than 15 years of age) among all new cases of leprosy detected (1) The epidemiological utility of this term lies in its indication to detect recent and ongoing transmission of disease in the community, since the incubation period in children with leprosy would be short.

The common strategies adopted for getting access to children are through contact examination; health surveys in schools; in dermatology/pediatric departments of hospitals; in clinics run by well-established non-governmental organization (NGO); leprosy control programs; and through self-reporting by families at primary health centers. (2,3) Data from long running well conducted field programs serves as a valuable resource for studies on secular trends in the prevalence of child leprosy. (4)

ILEP (International Federations of Anti-Leprosy Associations, London) visualizes that at the beginning of a leprosy-control program the proportion of child leprosy is usually low, subsequently it tends to increase as case detection becomes more efficient through school and house-to-house surveys. A decreasing trend in childhood leprosy may be found in the elimination phase of a well-run and long-established program, with increasing immunity in the population. Newell's critique of the leprosy studies which included aspects relating to self-healing in child leprosy, child infection in leprosy-affected households and the possible contribution of age and genetic susceptibility to exposure from an epidemiological stand-point, which was published in 1966, bears reading even today. (5)

In 2014, 213,899 new cases of leprosy were reported globally. (6) Of these 125,785 (58.8%) new cases were from India. (7) The proportion of children among new cases globally was 8.8%. (6) In India it was 9.04% among which the proportion was higher than 10% in 8 states/ union territories viz., Andhra Pradesh, Maharashtra, Bihar, Meghalaya, Mizoram, Tamil Nadu, Dadar and Nagar Haveli, Andaman and Nicobar Islands. Among these, 2.16% were new childhood cases with grade II disability, indicating delayed detection due to lack of awareness about early signs of leprosy. (7)

It is sufficient to say that the situation is serious enough to merit concern. The many uncertainties about the accuracy and reliability of official statistics notwithstanding, it can be fairly assumed that the widespread employment of multi-drug therapy (MDT) has not yielded the hoped-for reduction in childhood leprosy rates. Even though leprosy is a notifiable disease in India; an important unknown in official statistics is the proportion of children with leprosy treated by private practitioners. Whether there is scope for obtaining factual statistics by incorporating private sector consultant dermatologists in the national program, is controversial. (8,9)

Possible Outcomes of Child Leprosy Infection

As is true for most infectious diseases, an infection in a child caused by Mycobacterium leprae may lead to varying outcomes such as:(a) No overt evidence of infection ever appears, and the child never develops leprosy; (b) early lesions of leprosy may appear, which may remain stationary or disappear entirely on account of an effective immunological response resulting in self-healing; (c) the lesion/s may progress and the child (or in adulthood) may develop advanced leprosy. In the absence of a specific serological marker for susceptibility, or a skin test for infection, prediction of the timeline in a particular case will remain hypothetical. (10)

The phenomenon of self–healing has been reported in earlier studies. Among the classical papers on this subject are those by Lara and colleagues from the Culion Leprosy Sanitarium in the Philippines. (11-13) As early as 1922, Gomez et al reported spontaneous subsidence of papular bacteriologic positive/ bacteriologic negative skin lesions in very young children of women with leprosy. However, the observation period was short – only about nine months, casting doubt on the permanence of the apparent "self-healing". (14) The contribution of Lara and Nolasco to the subject was to assess the durability of spontaneous subsidence of the childhood lesions by extending the period of observation to almost 25 years. In about 75% of sanitarium-born children who showed self-healing lesions, the healing was sustained even throughout stressful events in their adult life, implying that self-healing leprosy in children is frequent and sustained. (13)

Possible Sources of Infection in Childhood Leprosy

A point of agreement among observers across countries and over the decades is that a strong factor in childhood leprosy is the presence at home, among family members or close neighbors of an adult suffering from the bacilliferous form of the disease. (15,16) There is a 4-fold risk of developing leprosy in presence of a neighborhood contact and this risk increases to 9 fold if there is a household contact. (17) Among familial contacts the risk of infection increases from 35% to 65% if the index case is suffering from multibacillary (MB) leprosy as compared to paucibaillary (PB) leprosy. (18) Additionally, it has been shown that a large proportion of PB leprosy cases harbor viable M. leprae. (19) In infants, the most frequent routes of transmission are skin-to-skin contact and through nasal droplets. (20,21) Although bacilli are known to be present in the breast milk of lepromatous mothers, concurrent skin contact between mother and baby is inevitable, thus making contact, inhalation, and ingestion impossible to separate out. (22) There are also reports that leprosy may be transmitted from mothers to fetus via placenta. (23,24)

In 1945, the pioneer leprologist Robert Cochrane, working in south India, reported the first exhaustive study of child leprosy (over 650 children under 14 years of age) in the sub-continent. (25) The observations, conclusions and speculations of modern authors on the subject echo Cochrane in many respects viz., (a) that a knowledge of the epidemiology, pathology and clinical features of childhood leprosy form the basis of understanding the disease; (b) that in an endemic area leprosy largely starts as a childhood disease; (c) that it is a disease of household or "room" contact hence, hence a positive case history is of great epidemiological significance; (d) all children in contact with an infectious case in the household do not necessarily develop the disease; (e) but in those who do, the source of infection can be traced to a lepromatous case in the household or neighborhood; (f) that the age of the child during the period of contact is an important consideration; the younger the age, the more likely the transmission of infection. (26) There appeared to be a direct correlation between the number of skin lesions and a positive history of household contact. Cochrane, like earlier observers, confirmed that self-healing of skin lesions of child leprosy was not at all a rare phenomenon.

The site of the primary lesion was expected to provide clues to the mode and site of entry of the bacillus. Observers have marked that in leprosy-endemic countries, there is a predilection for primary childhood lesions to be situated on uncovered parts of the body. (27) However, Camargo and Bechelli could not confirm the expected high frequency of lesions on the lower limbs in countries where children go barefoot. (28) Abraham et al in their report based on the Gudiatham Taluk field project at Karigiri, India, refined the concept of "exposed areas", by showing that first lesion sites coincided with sites of scars of injuries, abrasions and infected scratches found even in non-leprosy children in the community; hence the site of the first leprosy lesion on an exposed part was not in a strict sense privileged. (27) It would seem that the entry of leprosy bacilli through a defect in the child's skin is a more likely possibility than implied in the bald phrase "skin-to-skin" contact.

Early studies in the search for routes of infection have shown that a large number of bacilli are discharged in mouthwash, nose-blows and from skin by lepromatous patients. (29-31) In the environment, these bacilli remain viable for 9 days or even longer. (32) A possible lead in the search for routes of infection through the environment is reflected in the work of Turankar et al (33) who examined the presence of viable *M. leprae* in the environment. In leprosy-endemic areas of India, 37.5% of 80 soil samples showed the presence of *M. leprae* DNA, whereas 35% tested positive for viable *M. leprae* through the 16s rRNA marker. (34) Samples collected both from the environment and the patients, exhibited the same genotype on the basis of single nucleotide polymorphism indicating the possibility of a common strain being transmitted. (35)

Diagnosis of childhood leprosy

Clinical Diagnosis: The predominant early manifestations among children are a single, few or several hypo-pigmented, less often erythematous, flat skin lesions (macules) on any part of the body, which might later develop into plaques. (36-39) World Health Organization (WHO) has reported the preponderance of single lesions on the upper and lower limbs (84%), followed by the trunk (12.6%) and face (2.1%) among children. However, India did not form part of the populations studied. (28)

Anesthesia is easier to diagnose confidently in older children (12-14 years) especially if the lesion/s are on the limbs or trunk. Anesthesia among facial lesions however would be difficult to detect. The lesions usually fall in the WHO PB category, comprising indeterminate and Ridley-Jopling types TT (tuberculoid) to BB (borderline). Established disease becomes progressively more frequent in the older age groups (11-14 years > 6-10 years > 0-5 years). Although full-fledged BL (borderline lepromatous) or LL (lepromatous) leprosy is known to develop some years after early lesions, their manifestation in infancy is so remarkable in light of the rapid onset of disease pathology so as to merit publication in every case. (40,41)

Other diseases such as pityriasis alba, early vitiligo, birth marks and tenia versicolor also result in similar hypopigmented lesions and should be considered in differential diagnosis of leprosy. (42,43) Inherited peripheral nerve disorders e.g., hereditary sensory and sensory-motor neuropathies of various types, neurofibromatosis, neuropathies associated with developmental defects and acquired neurological conditions viz., iatrogenic injection injuries to the sciatic nerve, and other traumatic neuropathies should also be considered in differential diagnosis. (44)

Histopathological diagnosis: Histopathological examination was found to be useful in proper classification of leprosy. Studies have found that it not only helps in accurately assessing the tissue response at the time of biopsy but also is a better indication of any recent shifts in the patient's position in the spectrum which in turn is helpful for the correct treatment regime. (45,46)

Immunity in children is less effective than in adults due to which the spectrum of leprosy in children is different from that in adults. (47) Granuloma formation is an indication of effective build-up of cell mediated immunity, commonly observed in adult skin and nerve biopsies which is missing in children. (48) Earlier studies have reported low clinico-pathological correlation in childhood leprosy (50-60%) (49) which could be due to improper selection of the site of the biopsy or due to the occurrence of a lepra reaction. (50,51) Paradoxically, recent studies have reported a good histopathological correlation (86-85%). (51,52)

Serological diagnosis: A number of serological markers have been identified and tested. A comprehensive list of unique *M. leprae* markers that may prove to be promising candidates for early diagnosis of leprosy has been identified. (53,54) Of these the PGL-1 (Phenolic glycolipid – 1), 45 kDa antigen, ESAT-6 (early secreted antigenic target protein-6) and CPF-10 (culture filtrate protein) have been tested in India as a combination these has been successful in detecting *M. leprae* in 73% of PB cases. The evaluation of such serological markers across different countries may aid in the identification of few markers that show uniformly significant association across populations. Among these PGL-1 has shown promise in indicating the development of leprosy among contacts in Brazil with 2.7 times higher odds of developing overt disease in school children and household contacts. Its association with PB cases however is uncertain. (55-57) PGL-1 has been widely studied but its diagnostic potential as a single marker in India may be limited due to cross reactivity with Leishmania donovanii.(58) In most cases studied serological markers cannot be used as confirmatory tests for diagnosis, however, their role as a supplementary test has advantages particularly in endemic settings. (56,59)

Molecular markers for M. leprae: *M. leprae* specific genetic markers such as the 16s rRNA, RLEP and TTC repetitive sequences in child cases and contacts have the potential to diagnose early leprosy in childhood lesions. (60,61) with sensitivities of approximately 80% and 30% in MB and PB cases, respectively. (62) Single nucleotide polymorphisms (SNP) markers observed in *M. leprae* also show promise to identify strains among cases as well as environmental sources which may be useful in tracing transmission. (33) However, their use with specific reference to childhood cases needs to be explored.

Components of epidemiology of child leprosy

Cochrane's hypothesis about the immunological vulnerability of children, as compared to adults, to leprosy, has found an echo in the publications of later observers. (63-65) Child susceptibility has been explained as "inexperience" and immaturity of their immune system vis a vis the pathogen. (48)

Age and gender: Amongst children with leprosy, a high prevalence was recorded in children of 5-14 years of age with only 5-6% being less than 5 years of age. (18,38,39) In the late seventies, the prevalence for male (M) and female (F) children was 7 per 1000 and 2.9 per 1000, respectively. (66) It was reasoned that this may be due to greater mobility and increased opportunities for contact in male child. (67,68) This difference has decreased significantly over the past decade. In a survey among school children aged 5-15 years in Orissa, leprosy was detected with a M:F sex ratio of 8:7. (69) In Goa, the ratio was 20:6. (70) Hospital surveys in 2 states of India revealed that more number of boys were being affected than girls. (71-73) On the other hand, in the environment of a leprosy referral hospital in West Bengal, India, the M:F ratio in children up to 15 years of age was almost 1:1. (74) Adding to the uncertainty about sex ratios was the categorical declaration in a WHO monograph on child leprosy that in children there is "no significant difference" (sic) in leprosy prevalence between the sexes. (75)

Infantile Leprosy: This is a special category of childhood leprosy from which much can be learned. Leprosy in children less than one year of age is uncommon, but not unknown. (18,40,76,77) The earliest cited report by Nakajo in 1914, related leprosy to a two and half months old girl. Girdhar et al from Agra reported leprosy in two infants aged 2 and 4 months. (41) In both subjects bacilli were seen in the biopsy of the lesions. Interestingly the negative lepromin test in one infant and the presence of PGL antibodies in the other hinted that both might be prone to full-blown bacilliferous leprosy if left untreated. Leprosy in children as young as 2 months also questions the belief in the long incubation period of the disease.

Genetic basis of susceptibility: In childhood leprosy, studies on twins must play a prominent role in the delineation of hereditary and environment factors. By comparing monozygotic (MZ) and dizygotic (DZ) twins affected with leprosy it is possible to evaluate the role of the human host's immunological response. Such studies have the advantage that differences in environmental factors are minimized. Notable clinical studies on this subject in Indian populations were reported by Mohamed Ali and colleagues in Chingleput in the 1960s. (78,79) This study showed an extraordinarily high concordance rate for co-existence of disease and disease type in MZ twins (89.5%); there were no MZ twins concordant for disease and discordant for disease type. In the case of DZ twins, in 83.3% one twin only had the disease, and 0% were concordant for both disease and disease type. These figures strongly suggested the operation of hereditary factor(s) in the development of leprosy per se, and

of the leprosy type in particular. These findings were confirmed in Chakravartti and Vogel's study (80) where course of the disease as well as the extent of lesions showed striking similarities in MZ twins.

Vogel and Motulsky in 1997 citing this work also pointed out that the difference in leprosy concordance between MZ and DZ twins can be used to determine whether genetic variability plays a role in leprosy; the penetrance (probability of manifestation of the disease) of the gene/s can be estimated; and the conditions of manifestation can be examined. (81) As to environmental risk factors, analysis of MZ pairs discordant for leprosy type suggested that continuous and intensive contact with the infector is most important. On the other hand, since infection is almost ubiquitous in endemic areas, it may be that contracting the disease is also dependent on inherited susceptibility.

The often reported coincidence of child and adult leprosy in households has been viewed as evidence of genetic influences on the former. In contrast, it might equally well reflect differential environmental exposure to the infectious agent. "Households" differ in size and age distribution from "families" and the higher the number of elderly adults, the greater the chance of finding leprosy in them. (82) Thus the phenomenon of family "clustering" of leprosy cases may be due to shared environmental factors, the ease with which transmission can take place within the intimacy of the home, or genetic factors predisposing to or regulating the infection. (83)

Host genetic susceptibility markers: A large number of host genes have been implicated in conferring susceptibility to leprosy. Studies have reported the presence of genetic variants associated with leprosy in numerous regions of the human genome e.g. TLR 1 and TLR 2 cluster, LTA gene, HLA genes, interferon-gamma, Vitamin D receptor, PARK2/ PARKG regions etc. (84-89) However, only a few of these when tested across different populations have revealed a uniformly significant association. The differences may be due to population specific effects which may result in differences in allele frequencies. (90) The role of possible inherited factors in the development of leprosy has indicated an association between HLA haplotype inherited and the type of leprosy developed by the child i.e. tuberculoid or lepromatous. (84)

Immunological Indicators: Chatterji et al's report in 1936 in Bengal on lepromin tests in healthy child contacts of leprosy-affected persons showed the lowest percentage of positive lepromin reactors. This led him to conclude that this was a consequence of massive infection. Additionally, the more elaborate study undertaken by Cochrane himself and colleagues, also used the lepromin reaction to evaluate the effect of degree of contact on leprosy-affected children attending a well-known children's clinic at Saidapet in Chennai. (63) It was found that the group of healthy children in the families of leprosy-affected children gave a smaller percentage of positive reactors than the non-affected group, and the authors tentatively concluded that lepromin negativity was proportional to contact. The finding of a higher percentage of lepromin positivity among the older age children (15-19 years) as compared to younger (0-14 years) could be the reason why children are more susceptible to leprosy than adults.

A useful study in Indonesia found significantly different rates of sero-prevalence of antibodies to (PGL-I) among school children living in high and low endemic regions, respectively. This suggested that the rates reflected the extent of the leprosy problem in the community, which may be used as an index of incidence. (91) Sero-epidemiological correlation of levels of anti-PGL-1 antibodies in house contacts and in schoolchildren in a hyper-endemic area has recently been confirmed in a leprosy hyper-endemic region of Brazil. (92)

Trans-Placental Passage of Mycobacterium leprae and antigens: That whole leprosy bacilli are able to cross the placenta was documented by early workers. (24,93) Duncan et al., cited work showing that passage of the organisms occurred early in pregnancy, which focused attention on the possible development of "immune tolerance" in the young fetus when *M. leprae* antigens reacted with its immature lymphocytes.

Also of possible importance for the immunology of the fetus of a leprosy-affected mother, is transplacental passage of leprosy-related suppressor factors present in maternal plasma. (94) The study by Melsom et al in Ethiopia measured IgA, IgM and IgG anti-M leprae antibodies in cord sera and in sera taken 2 years after birth from 29 babies of mothers with lepromatous leprosy (Group 1) and 16 babies of mothers with tuberculoid leprosy and non-leprosy control mothers (Group 2). The division into these two groups was designed to study the effect of a possible fetal exposure to *M. leprae* compared with infection after birth. (95) High IgM anti-*M. leprae* antibody activity was found in sera from 14 of the 29 babies of mothers with lepromatous leprosy and in four of the 15 babies of tuberculoid leprosy mothers. This indicated that these babies have been infected with *M. leprae* even though six of the eight had no clinical sign(s) of the disease. Clearly the immunological interactions between lepromatous mothers and their unborn and very young children are complex, and leprosy pathogenesis in such children who develop the disease is multi-factorial.

Diet, Nutrition, Environment: There is no direct evidence of a causative, aggravating or ameliorative role for diet in childhood leprosy. However, diet may be an associated variable in the so-called "poverty syndrome". In an epidemiological and socio-economic case control study in south India, leprosy prevalence rates correlated significantly with malnutrition in children 1-4 years of age. Their study in South India produced some counter-intuitive findings, e.g., that neither poverty nor illiteracy nor residence in a rural area per se correlated with leprosy prevalence. (96) Ponninghaus et al. in Malawi, on the other hand, found that extended schooling and housing conditions were

associated with reduced risk of leprosy. (97)

In a more recent case control investigation of the influence of non-genetic factors in a leprosy endemic area of North-East Brazil, it was found that poverty (e.g., food shortage, infrequent changing of bed linen) and culturally determined behavior (bathing in open water sources) were significant associated variables. (98) In an earlier study in the same region, based on ecology, the authors found that population growth and relative economic inequality were associated with higher leprosy rates. (99) These lend credence to the hypothesis that person-to-person transmission may not be the sole determinant of spread of infection.

Preventive Measures:

Contact Surveillance: It is well known that there is a 4-fold risk of developing leprosy in presence of a neighbourhood contact and this risk increases to 9-fold if there is a household contact. (17) Among familial contacts the risk of infection increases from 35% to 65% if the index case is suffering from MB leprosy as compared to PB leprosy. (18) Hence, community education about leprosy along with mandatory household contact and school surveys if implemented nationally would result in the reduction of disease burden. (100) Contact surveillance would however, need to overcome dual challenges of both, the stigma often associated with leprosy as well as rapid attrition of skills needed for critical examination of the skin and nerve lesions of a childhood leprosy patient.

Immunoprophylaxis: Bacillus Calmette-Guerin (BCG), the live attenuated strain of Mycobacterium bovis is widely administered in neonates as part of the anti-tuberculosis program. There is overwhelming evidence that BCG vaccination has a protective effect against leprosy. The level of protection varies greatly with an overall protection of 41% in trial studies and 60% for cohort studies. In most of the studies, BCG vaccination was given to children under 15 years of age. Estimates for subjects over 15 years of age were not available. There was no benefit of revaccination when it is given to school children as compared to adults probably because the protective effect of BCG wanes with time (~30 years). and its efficacy was significantly more for household contacts (66%) when compared to the general population. (53%) All these findings suggest that BCG vaccination of close contacts in addition to treatment of index case may help in preventing leprosy. (100,101) It has also been evaluated in combination with killed *M. leprae* for its protective efficacy. (103) *Mycobacterium indicus pranii* (MIP), previously *Mycobacterium w*, has also been investigated as an immunoprophylactic measure against *M. leprae*. (102) The use of MIP has proven to have a protective effect among contacts. Its efficacy however, wanes after 7-8 years (104) and has not been investigated with particular reference to children.

Chemoprophylaxis: In order to eliminate the disease or reduce the incidence rate to zero, prophylactic treatment of contacts or of total population may be helpful in reducing prevalence. Several studies in the last 50 years have shown significant protective effect with dapsone, acedapsone and rifampicin. (105) Dapsone has been shown to be effective in preventing leprosy in children (106) but it may not be feasible to implement due to its long duration of treatment (twice a week for at least a year). (107) Acedapsone while protective as a chemoprophylactic agent did not have any significant effect on prevalence when children younger than 9 years and older were compared. (108)

On the other hand, effective protection has been reported to be conferred to a large population by a single dose of rifampicin. While this has been evaluated among cases and contacts in general and not specifically in children, the protection was no longer significant beyond 2-3years. (109,110) Furthermore, the protective effect appeared to be lower (24%) for household contacts than in social contacts (70%). This observation arises in view of the fact that 30% of the total incident cases have an index case in the family while nearly 70% come from a population of non-contacts. The combined effect of immunoprophylaxis with BCG and chemoprophylaxis with a single dose of rifampicin is also under assessment. (111,112)

Mass chemoprophylaxis has some merit but can be a challenge in endemic countries with large populations. Beyond cost effectiveness, the issues of adverse effects and irregular intake of drugs by patients should merit serious consideration. Rifampicin remains the nodal drug for the treatment of drug sensitive tuberculosis, a highly prevalent disease in India with elevated levels of drug resistance (113).

Treatment

It has been reported that the implementation of MDT has resulted in a reduction of child cases. In order to further efforts to eliminate leprosy, WHO aims to achieve zero child cases with grade 2 disability by 2020.(114) The introduction of MDT has been largely successful, with a standard 'child pack' being available for children aged 10-14 yrs. For children under the age of 10, doses are administered as - (a) rifampicin: 10 mg/ kg body weight, monthly (b) clofazimine: 1 mg /kg body weight daily and 6 mg/kg body weight, monthly (c) dapsone: 2 mg /kg body weight daily. (115)

However these doses may be excessive for some child cases and the correct doses to be administered need to be evaluated. (116) Available MDT blister packs though convenient are not child friendly. Treatment dropout rates in children range from 10-20% in some programs (39,52), main cause being the child's refusal to cooperate in swallowing tablets. Child friendly treatment options like flavoured syrups are a need of the hour. Given the low priority and high neglect that leprosy commands, today, the development and use of pediatric formulations can only be considered as a wish list for improvement in dosing and compliance.

In cases of hypersensitivity to dapsone, a combination of clofazimine and rifampicin can be administered as an alternative to conventional MDT. In PB cases single dose rifampicin, ofloxacin and

minocycline (ROM) has been used in some parts of the world. However, evidence for safety and efficacy of monthly ROM for children with MB leprosy is lacking. (117) In addition to MDT, used to counter an infection with *M. leprae* certain areas continue to report incidence of reaction, neuritis and grade 2 disabilities as high as 18.6%, 9.4% and 12.8% respectively which need to be addressed. (18,39)

Another aspect that requires attention is the compliance to treatment. Factors such as side effects and hypersensitivity to the drugs as well as a lack of information and education among the parents contribute to non-compliance to treatment in children. (118) A higher proportion of MB cases a delay in diagnosis and indicate a requirement to strengthen health education. Information, education communication (IEC) activities in the community of patients and their parents have improved treatment compliance. (117,119)

Studies have been conducted among adults assessing their response to treatment using clinical, diagnostic measures such as slit skin smears and histopathological analysis as well as predisposition to relapse. Additionally, supplementary information obtained from immune markers such as PGL-1, Antigen 85 and ESAT-6 may be combined to better evaluate the prognosis. (55,56) Such information however, is limited in child cases and needs further evaluation considering the immaturity of their immune system and the predilection of relapse in children.

Conclusion

With the high prevalence recorded for childhood leprosy, the spectre of ongoing transmission of leprosy is alive and well and bodes ill for the achievement of elimination of leprosy in the near future. (6) The issue of prophylaxis for leprosy in children or even in infants assumes significance because of a life-long occurrence of disease relapse and the presentation of deformities which may persist unattended due to lack of facilities and specific skills in the health provider sector. (120) There is a pressing need for training of health providers at the primary level for identifying infant / child suspects beginning with households or families where confirmed leprosy cases are or have been present. The skilling may need to go beyond establishing suspicion to early detection of deformities in which the carer of the child or infant could also be involved. This would be a minimal prerequisite for achieving the goal of zero grade 2 deformity in children by the year 2020. (121) Further efforts would also be needed to motivate the carer to undertake uninterrupted treatment. Here pediatric drug formulations would constitute a useful technology. However, their development in the near future appears as of today, a mere wish list.

The route of transmission of disease continues to remain an enigma. The question of whether transmission occurs from inter-human contact within households or neighborhoods or through environmental bodies like soil, water, forests or intermediate animal hosts remains relatively unexplored and begs dissection. The related question of a child acquiring disease through the portal of genetic susceptibility needs to be tempered with the fact that families and households besides sharing genes also share the environment. Contemporary tools of strain genotyping as well as geospatial mapping should be utilized for determining the weightage of the environmental route of transmission.

The concept of protection against childhood leprosy in a leprosy affected family / household needs to be translated rapidly but the methods need to be investigated and refined. Long term prospective studies need to be undertaken in high burden settings for comparison of efficacies of current candidates for chemo as well as immuno-prophylaxis.

One barrier to the above proposed approach is the still elusive hunt for biomarkers of protection. Indeed, their identities are likely to differ in adults and children, based as they would be on the differing stages of maturity of the immune system. This would also manifest between neonate, infant and child due to the developing ontogeny of the immune system particularly in the first 3 years in the life of the child.

A related fascinating phenomenon is that of self-healing lesions and the mechanisms through which it is achieved. Firstly, does the strain of *M. leprae* establish rapid disease in a child through a short incubation period because of an immature immune response and is there a stage in the child's age where self-healing occurs due to the kick-in of a critical immune component? These difficult prospective studies are likely to provide fascinating insights.

The true burden of childhood leprosy remains unknown and this begs for a prevalence study in India so that the intergenerational burden of disease and deformity can be dealt with realistically. (122) The ominous message of childhood leprosy remains that the disease is alive and well.

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Conflict of Interest

None

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