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Leprosy care in the era of COVID - 19

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Abstract

Leprosy care services are facing several challenges with the advent of the global COVID-19 pandemic. The impact on case detection has been felt globally, with the annual new cases declining by 37.1% from 2019 to 2020. This trend reflects the disruption in routine health care services and active case finding activities than a true decline in the incidence of leprosy. There are marked differences in the major determinants of the leprosy burden even within countries of South-Asia. Disease modelling has indicated that well over 100% of new cases of leprosy have gone unreported during the pandemic.

Even though the availability of multi drug therapy (MDT) has not suffered significantly, other services like active case finding, post exposure prophylaxis, and reconstructive surgery have been curtailed to a great extent. The use of new technology and social media to reach patients and deliver care have been encouraged.

Co-infections have not shown any significant effect on either leprosy or COVID-19. Even patients who are on immunosuppressants for lepra reactions have not been shown to have a bad outcome in the face of co-infection. Continuation of MDT during active infection with COVID-19 has been recommended as both dapsone and clofazimine have shown anti-coronaviral activity.

Stigma and social discrimination have not been studied in detail. It is postulated that patients affected by leprosy may suffer more social discrimination as both leprosy and COIVD-19 have been associated with stigma. Urgent action is needed to improve case detection in leprosy on a global scale as delay in diagnosis and treatment may lead to further nerve damage and disability.

Key words: COVID-19; Leprosy; Pandemic; World Health Organization.

Introduction

Leprosy is a chronic infection of the skin and the peripheral nerves, affecting persons mostly from a less privileged social background. With the gradual reduction of cases worldwide and the dwindling of expertise, leprosy has been out of the limelight in the international health circles. Leprosy has been included in the list of Neglected Tropical Diseases (NTD) by the World Health Organization (WHO), thus being recognized as a disease affecting marginalized communities needing intensified attention.

With the advent of the COVID-19 pandemic, the entire world has focused attention on the control of this pandemic, with a vast amount of resources being diverted towards COVID-19 related services. This general inequality of distribution of resources, including funding and personnel, may be felt acutely by disease conditions which had been already suffering from lack of resources, expertise and funding. Leprosy, being a NTD affecting less affluent countries and having a chronic subtle clinical course, may feel the brunt of this change in focus.

With this background, it is important to review the available literature to assess the scientific evidence

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regarding the impact of the COVID-19 pandemic on leprosy care.

Impact on case detection of Leprosy

The weekly epidemiological record, published by the World Health Organization (WHO) is the best tool to assess the global burden of leprosy. According to the WHO weekly epidemiological record, the registered prevalence of leprosy at the end of 2020 was 129192, with 127396 new cases being reported.[1] There was a 27.7% reduction in registered prevalence and a 37.1% reduction in new cases as compared with 2019. It has been postulated that this reduction is due to less detection and reporting during the pandemic.[1]Even though data were received from only 127 countries in 2020, as compared with 160 in 2019, all 23 global priority countries had provided data for 2020.[1]

This artificial reduction in cases and data will have an impact on the interpretation of trends in the long term. For example: there was a steady decline in both new cases and child cases during the period 2011-2019. The rate of decline of child cases was higher globally, but the child rates varied considerably among the different WHO regions.[1] These natural trends may be confounded by the artificial decline in the number of cases reported during the pandemic years.

Grade 2 disability (G2D), a valuable indicator of the long term burden of leprosy, showed a 33.5% decline with only 68/121 countries reporting cases with G2D. 4.3% of the new G2D were reported among children.[1]

There was a 31.1% reduction in the number of new cases globally, with India reporting 43.1% fewer cases than in 2019.[1] The treatment completion rates too were sub-optimal. About 6% of multibacillary cases and 3.2% paucibacillary cases were lost for follow up during 2020.[1]

One positive factor is that 15.8% of new cases were detected by contact examination and active case detection activities.[1] This is encouraging, as it indicates the dedication of primary health care personnel even in the face of a global pandemic. However, the proportion of the estimated population that was examined was low, 45.5% among contacts, 42.5% among the general population, and only 2.8% among special populations like prisoners, migrants and refugees.[1]

All countries belonging to the SAARC region are reporting cases with leprosy, while there is a significant variation in case detection among the countries. Even though the SAARC region is considered one geopolitical entity, the eight countries are classified into two different regions by the WHO. An attempt was made to group together the eight countries of the SAARC region and to compare the trends in new case detection, child rate, multi-bacillary (MB) rate, and the grade 2 disability (G2D) rate among these countries. (Table 1) The data were retrieved from the WHO weekly epidemiological record for leprosy 2019 and 2020.[1,2]

Table 1: Reported new case detection in the SAARC region for 2019 and 2020

Country	Total new cases in 2019	Total new cases in 2020	Percentage change in 2020
Afghanistan	31	22	-29.03%
Bangladesh	3638	2897	-20.37%
Bhutan	18	8	-55.55%
India	114451	65147	-43.08%
Maldives	5	1	-80.00%
Nepal	3844	2304	-40.06%
Pakistan	347	225	-35.16%
Sri Lanka	1658	1212	-26.89%
Total	**123 992**	**71 889**	**-42.02%**

Within the SAARC region, there are five countries, namely, Bangladesh, India, Nepal, Pakistan, and Sri Lanka, reporting over 100 new cases of leprosy per year. Among these 5 countries, the new case detection showed a drop ranging from 20.37% (Bangladesh) to 43.08% (India), while the average drop for the whole region was 42.02%.[1,2] The average drop in child rate for the region was 50.77% with Bangladesh showing the lowest drop (17.61%) and Nepal having the highest drop (52.24%).[1,2] (Table 2)This decline in the diagnosis of child cases may have serious implications as children whose treatment is delayed are at higher risk of nerve damage and resultant disability.

Table 2: Reported child rates in the SAARC region for 2019 and 2020

Country	Total child cases in 2019	Total child cases in 2020	Percentage change in 2020
Afghanistan	0	2	+200%
Bangladesh	210	173	-17.61%
Bhutan	0	0	0.00%
India	7859	3753	-52.24%
Maldives	0	0	0.00%
Nepal	293	142	-51.54%
Pakistan	23	14	-39.13%
Sri Lanka	176	130	-26.13%
Total	**8561**	**4214**	**-50.77%**

The drop in MB rate was lower compared to the drop in total new cases. This indicates that relatively more infective cases have been diagnosed. While the average drop in MB cases was 38.42%, Sri Lanka showed only a drop of 20.47% with Bangladesh, India and Pakistan showing a drop close to 40%. The average reduction in detection of cases with grade 2 disability (G2D) was 43.67%. Sri Lanka had only 10.98% drop in G2D at diagnosis. [1,2]

Table 3: Reported G2D rates in the SAARC region for 2019 and 2020

Country	Total cases with G2D 2019	Total cases with G2D in 2020	Percentage change in 2020
Afghanistan	1	0	-100.00%
Bangladesh	252	137	-45,63%
Bhutan	0	0	0.00%
India	2761	1572	-43.06%
Maldives	0	0	0.00%
Nepal	254	101	-60,23%
Pakistan	54	32	-40.74%
Sri Lanka	91	81	-10.98%
Total	**3414**	**1923**	**-43.67%**

Findings similar to the WHO report were seen in Brazil. A study comparing the number of patients with leprosy diagnosed during 2019 and 2020 reported that there was a reduction of 18223 cases (-48.4%) in 2020 compared to 2019.[3] This steep drop is not consistent with the gradual reduction of cases in Brazil seen from 2010 onwards. The average reduction in the number of cases per month was 1518.[3]

In a study on the impact of COVID-19 on the detection of leprosy in a state of Brazil, the investigators compared the findings for the period from January – September in 2019 and 2020. There was a 44.4% reduction of new cases diagnosed in 2020 compared with 2019.[4] During the months after the emergence of the COVID-19 virus in Brazil (April – September 2020), this reduction was 51.1%. A reduction of 24.25% in the number of municipalities reporting cases was also seen.[4] There was a statistically significant inverse correlation between the number of new cases of leprosy and the cumulative number of cases of COVID-19 reported each month.[4] This further highlights the fact that the apparent reduction in the number of cases of leprosy is due to the disruption of service delivery and health seeking behavior rather than a true reduction in cases.

Another disturbing fact is that the percentage of patients whose degree of physical disability was not assessed at diagnosis showed an increase from 16.39% to 22.5% in 2020.[4] This may have been due to the minimal physical contact methods practiced in health care institutions due to the COVID 19 pandemic. However, such omissions at the level of health care institutions may have adverse consequences as patients may develop permanent disability if their neurological impairment goes undetected and untreated at diagnosis.

A population-based and ecological survey of all cases of leprosy reported in Brazil in 2020 confirmed the reduction in reporting of child cases to be 56.82%.[5] Multibacillary cases showed an 8.1% increase.[5] This increase may reflect the tendency to delay seeking treatment for apparently silent tuberculoid leprosy. Some states have shown an almost 100% reduction in new cases in 2020.[5] These findings reflect the seriousness of the decline in public health services for diseases other than COVID-19 during the past two years.

The reduction in case detection in Brazil was studied in more detail by a group of researchers by applying the ARIMA model to predict the under-reporting of new cases in the city of Palamas by studying the leprosy indicators in the city from 2001 to 2020 using the autoregressive integrated moving averages method.[6] The researchers predicted that 177% of new cases of leprosy were not reported in the area under study.[6] This is an eye opener to public health authorities and leprosy control programmes worldwide, highlighting the need for aggressive case finding missions to be undertaken with immediate effect.

Impact on leprosy care services

A cross-sectional online survey among health care professionals from 21 leprosy referral centers, including Bangladesh, India, Nepal and Sri Lanka showed that 80% of leprosy diagnostic services were reduced.[7] The availability of MDT was not affected in all centers but active case finding, delivery of single dose rifampicin, and reconstructive surgery were grossly affected.[7]

Alternative methods of providing care like contacting patients by telephone (71%) and providing written summaries for use in centers other than the original treatment center (62%) have been practiced.[7] All respondents had established special care services for patients, which included establishment of telephone helplines, social media support like WhatsApp, and delivery of special needs.[7] Even though the essential care services remained open, many patients found it difficult to travel to treatment centers due to lockdowns and restrictions in public transport.

Considering the difficulties faced by both clinicians and patients the following steps suggested by Kumar et al. may be considered as alternative methods of providing uninterrupted care.[8] Teledermatology, especially for subsequent visits following diagnosis at a physical consultation, may be used in some situations.[8] With increasing concerns about adverse events due to MDT, regular monitoring of blood investigations is being practiced in most leprosy centers. Continuation of this monitoring activity and ensuring a regular supply of MDT can be achieved by combining accompanied MDT (supplying of several packs of MDT during a clinic visit) and continuing monitoring through WhatsApp communications.

The Indian Association of Dermatologists, Venereologists and Leprologists (IADVL) guidelines on management of leprosy in the context of COVID-19 pandemic suggests employing nonprofit organizations involved in leprosy care and voluntary health workers like ASHA to ensure uninterrupted delivery of MDT.[9] Sri Lanka employed the services of the postal department to deliver MDT and other essential drugs to patients during the long lockdowns. IADVL guidelines also recommend dispensing of MDT to patients approaching any treatment center irrespective of their regular center of follow-up.[9] Another important aspect in leprosy care is monitoring for reactions and nerve damage. IADVL recommends educating patients on the signs and symptoms of reactions and the importance of reporting such symptoms immediately at every available opportunity and to use teledermatology/ WhatsApp services to detect patients needing urgent anti-reactional therapy.[9]

IADVL has updated the guidelines in September 2021 to accommodate the changes due to the Delta variant, introduction of vaccination and the new research evidence.[10] In this guideline, the IADVL recommended to continue the optimal dose of corticosteroids for reactions, while exercising caution during the phase of viraemia and possibly mucormycosis.[10] The guideline recommends using a maximum dosage of 20mg prednisolone daily. It is recommended to use methotrexate and other immunosuppressants judiciously.[10] Elective reconstructive surgery is also recommended under COVID precautions. Vaccination against COVID 19 is strongly encouraged while cautioning patients who are on steroids about the possible sub-optimal uptake.[10]

Leprosy and COVID 19 co-infection

With large numbers of cases of COVID-19 being reported from India and Brazil (major contributors to the global leprosy burden) co-infection with leprosy and COVID-19 is inevitable. A case series from India followed up 6 patients of age 20 to 44 years for a period of 8 weeks after COVID-19 infection. In all patients, the acute COVID-19 infection had no effect on the course of leprosy.[11] One patient developed a type 1 Lepra reaction post-COVID and exacerbation of the preexisting erythema nodosum leprosum (ENL).[11] The cytokine shift due to the COVID infection may have contributed to the late occurrence of reactions in these patients. The authors also noted that those who were on prednisolone for Lepra reactions seemed to have a better outcome with the COVID infection.[11]

A cohort study conducted in Brazil recruited patients with active leprosy, household contacts of patients with leprosy, and controls complaining of skin problems other than leprosy. Patients with active leprosy had a higher risk for COVID-19 infection, but this was considered due to higher exposure to household contacts with COVID-19 infection. The presence of household contact with COVID-19 was the only other significant risk factor.[12] The authors postulated that social factors like poverty, overcrowding, and nonadherence to preventive measures for COVID-19 may have contributed to this increased risk, in addition to the possible immune suppression due to leprosy and medications.[12]

A case report from Brazil described a 43-year-old patient who had taken MDT intermittently due to adverse effects and chronic Chagas disease with cardiomyopathy presenting with symptomatic COVID 19 infection confirmed by RTPCR.[13] She had developed mucocutaneous signs attributable to COVID-19, but there was no aggravation of the features of leprosy. Moreover, her daughter who had received BCG vaccination did not get infected with COVID-19 in spite of being a first level contact.[13]

Safety of leprosy medications in COVID-19 infection

Patients affected by leprosy are on long-term treatment with MDT consisting of rifampicin, dapsone, and clofazimine. In addition to MDT, patients with lepra reactions are likely to be immunosuppressed due to long-term corticosteroids and other anti-inflammatory agents. Fever can be a presenting feature of several potential adverse events due to MDT like dapsone hypersensitivity syndrome, neutropenia/ agranulocytosis, or flu-like syndrome. Fever in a patient on MDT for leprosy should be interpreted with

care. Special attention should be paid to differentiate between drug adverse events and fever due to infections.

Since all components of MDT are potentially heptotoxic, it is justifiable to stop MDT in patients with febrile illnesses like dengue where liver damage may occur. According to the current knowledge, COVID-19 infection is not associated with significant liver damage. In addition, several authors have looked at the actions of both dapsone and clofazimine as potential treatment options for COVID-19 infection. Therefore, it is advisable to continue MDT in patients with leprosy and COVID-19 co-infection.[9,10]

A group of researchers from Korea have done an in-depth study of the molecular and biochemical properties of dapsone and the inflammatory changes occurring in COVID-19 infection to determine the role of dapsone in COVID-19 infection.[14] In this article, published in the prevaccine era, the researchers suggested that dapsone may have a role in preventing the infection or allaying the severity of the inflammatory response. Several actions of dapsone, including anti-inflammatory and anti-neutrophil activity and the role as an inflammasome competitor have been considered in this recommendation.[14] Another important factor pointed out by this team was the absence of respiratory infections (including the 2002 SARS epidemic, 2009 H1N1 epidemic, and the 2013 MERS epidemic) among the long-term inmates of leprosy hospitals in Korea who continue to receive daily doses of dapsone.[14]

Clofazimine has been shown to possess pan-coronaviral inhibitory activity with inhibition of SARS-COV-2 replication in multiple in vitro systems.[15,16] In a hamster model of SARS-COV-2 infection, clofazimine significantly reduced viral load in the lung, reduced faecal viral shedding, and prevented the cytokine storm.[15] Hence, the use of clofazimine as an anti-corona viral agent was recommended.[15,16] In this context, leprosy patients receiving MDT may be at an added advantage if they develop COVID-19 infection.

With the dreaded silent hypoxia which was seen widely with COVID-19 infection, one case report from India highlighted an important differential diagnosis in patients with leprosy.[17] A 24-year-old male was found to have fingertip pulse oximeter readings of 88-90% on room air at day 14 of MDT-MB. With a negative RTPCR for COVID 19, the patient was reassessed and a methaemoglobin assay was 33.3% (biological reference range 0 - 2.0%). A diagnosis of dapsone induced methaemoglobinaemia was made and the patient made a spontaneous recovery 3 days after stopping dapsone.[17] A similar case was managed by the author recently with the methaemoglobin level 10% with oxygen saturation fluctuating around 90–92% (unpublished data). It is important to keep this relatively rare adverse event in mind as timely stoppage of dapsone will be lifesaving in such a situation.

COVID-19 and lepra reactions

During the initial phase of the COVID-19 pandemic, it was postulated that the incidence of lepra reactions would rise with the increasing number of COVID-19 cases.[18] The role of infection as a trigger for reactions and the cytokine storm induced by COVID-19 infection were considered the reasons behind this hypothesis.[18] The same authors also considered the possible immune suppression due to anti-reactional therapies and the risk of severe COVID 19 infection in patients with lepra reactions and COVID 19 coinfection.[18]

A Brazilian study looked at the expression of proinflammatory cytokines in patients with coinfection with leprosy and COVID-19 and compared the results with non-leprosy patients with a history of COVID-19.[19] The expression of TNF-α, IL-1β, IL-8, IL-6, and IL12-B were significantly higher in patients who had contracted COVID-19 compared to leprosy patients without co infection and controls with no leprosy.[19] The same authors did not detect an increase in the occurrence of reactions in patients with co-infection compared to leprosy patients without COVID-19. An important finding from this study was the significant rise in IL-6 expression in the multivariate analysis.[19] With several clinical studies having demonstrated single nucleotide polymorphisms in IL-6 gene to be associated with leprosy reactions and IL-6 being a marker of neuropathic pain, the authors postulate that patients with leprosy and COVID-19 coinfections may be at higher risk for silent neuropathy.[19] Even though this finding has not been proven in clinical studies, it may be advisable to recommend stricter monitoring for nerve damage in leprosy patients who have been infected with COVID-19.

There was a recent case report from Singapore describing the occurrence of type 1 reaction in a patient with multibacillary leprosy (probably borderline lepromatous leprosy) occurring 10 to 15 days after receiving the first dose of Pfizer Biontech vaccine.[20] His leprosy has gone unnoticed until the acute changes of type 1 reaction occurred. The authors postulate that the T -cell-mediated immune upregulation elicited by the vaccine may have triggered the type 1 reaction in this patient.[20]

Further comparisons have been made between ENL reaction and COVID-19 infection as both conditions have shown high neutrophil count and high neutrophil to lymphocyte ratio (NLR).[21] The authors were hopeful that the rapid generation of knowledge concerning COVID 19 would prove to be useful for understanding the role of neutrophils in ENL.[21]

No prospective or retrospective studies on the relationship between COVID-19 and ENL have been published to date. However, there was one case report of severe ENL reaction and COVID-19 coinfection managed with prednisolone and methotrexate with a favourable outcome in both conditions.[22]

Ethics, stigma, and social discrimination in the era of the pandemic

Very few published articles have addressed the issue of social isolation and stigma related to patients affected by leprosy. With the rapid spread of the COVID-19 pandemic, there were incidents of stigmatization of the persons affected. The social distancing measures and widespread lockdowns which were enforced to contain the pandemic have led to many socioeconomic problems, especially to persons belonging to low socioeconomic strata and marginalized populations like those affected by leprosy.

With COVID-19 being considered a priority, many routine health care services were considered non-urgent/ non-essential and were curtailed or stopped temporarily. Even though some countries have tried to organize continued leprosy care services like satellite clinics and distribution of MDT through health volunteers or field health workers, there may have been interruptions to treatment, thus rendering patients at the risk of further disability.[23] The fact that the countries contributing to almost 80% of the leprosy burden were also affected badly by the COVID 19 pandemic highlights the importance of this possibility.[23]

Certain problems common to patients affected by leprosy like cracked extremities may have had a considerable impact on hand washing and sanitizing, making them more at risk to contract the COVID-19 infection.[23]

Several ethical considerations were discussed in an article from Italy describing the history of outbreaks and quarantine measures and their impact on society and the economy. Another point raised by the authors was that the "cure for the pandemic", namely, the measures advocated to curb the spread of the disease like social distancing and lockdowns, should not prove to be more harmful than the disease itself.[24] The impact on the economy, especially those in the South Asian region, has been immense. The resultant restrictions in funding are more likely to be felt by diseases like leprosy and tuberculosis affecting marginalized populations. Currently, there are no published articles on the redistribution of resources or prioritization of health services.

WHO has identified the impact of COVID-19 on the stigma associated with leprosy as an area of research priority in future. There is a need to look at new ways to tackle stigma due to chronic illnesses like leprosy and to explore the possibility of making use of new technologies like social media and conferencing software to support marginalized patient groups. Self-help support groups, peer counseling, and community-based individual care have been identified among the most appropriate interventions to improve the psychological wellbeing of these marginalized groups.[23]

Future challenges and prospects

The major challenge faced by leprosy endemic countries is to improve case detection and find those cases that remained hidden during the pandemic and the resultant disruptions in health care provision.[4-6] Novel methods of spreading the message about leprosy and encouraging patients to present themselves for treatment will need to be devised.[8] Strengthening of health care facilities to cater to the surge of cases that is expected after such a health education campaign will also be a priority.

With the almost universal use of facemasks, there has been a fall in the incidence of respiratory infections. There is a theoretical probability of a break in the transmission of chronic infections spread through the respiratory route such as tuberculosis and leprosy. It would be interesting to monitor the trends in new case detection in the next decade to see whether there will be a true reduction in the disease burden of leprosy.

The use of communication technology for dissemination of knowledge to large groups and the use of telemedicine for the management of patients increased several fold following the social isolation measures enforced to curb the COVID 19 pandemic. These services are now being streamlined with appropriate legislation and guidelines.[25] Such advances in communication may be used for the benefit of patients affected by leprosy in future.

Testing for COVID-19 necessitated the use of PCR technology at an unprecedented scale. It may be worth exploring the possibility of using these machines to improve the diagnostic facilities at leprosy care institutions. Since the PCR facility to test for drug resistance in leprosy is of limited availability, such a step would greatly improve the management of difficult cases of leprosy and possible drug resistance.

Conclusion

The global COVID -19 pandemic has had a significant impact on leprosy worldwide. Urgent steps are needed to find and treat the "missing cases" due to the disruption in general health care services. In addition, psychosocial issues related to both conditions will also play a major role. Concerted efforts by individual countries and organizations involved in leprosy care services will be needed to ensure uninterrupted care to persons affected by leprosy.

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