### **Review Article**

## How endemic countries can accelerate lymphatic filariasis elimination? An analytical review to identify strategic and programmatic interventions

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### ABSTRACT

Lymphatic filariasis (LF) is endemic in 81 countries in the world, and a number of these countries have targeted for LF elimination. This review of literature and analysis was conducted to identify additional and sustainable strategies to accelerate LF elimination from endemic countries. This review noted that adverse events due to mass drug administration (MDA) of diethyl carbamazine (DEC) tablets, poor knowledge and information about LF amongst health workers & communication are the major barriers in LF elimination. The new approaches to increase compliance with DEC tablets (including exploring the possibility for DEC fortification of salt), targeted education programmes for physicians and health workers, and IEC material and inter personal communication of physicians and health workers, ensure quality of trainings on MDA, strengthen IEC delivery mechanisms, implement internal and external monitoring of MDA activities, sufficient funding in timely manner, and to improve political and programmatic leadership. It is also time that lessons from other elimination programmes are utilized to accelerate targeted LF elimination from the endemic countries.

Key words Elimination; India; lymphatic filariasis; mass drug administration; neglected tropical disease

### Background

Lymphatic filariasis (LF) is endemic in 81 countries of the world and is the second leading cause of permanent disability and meets the criteria for being a potentially eradicable disease<sup>1–3</sup>. The World Health Organization (WHO) estimates that 1.1 billion people live in high risk areas, 120 million of these people are already infected with LF, and 76 million people have suffered from damaged lymphatic and renal systems<sup>3,4</sup>. Southeast Asia Region contributes to almost 2/3<sup>rd</sup> of global cases with India having a total of 590 million people at risk of LF, and 10% of them already suffering from LF<sup>5</sup>. Mass drug administration (MDA) with diethyl carbamazine (DEC) tablets has been proven as the most feasible strategy for LF elimination (recently, a few countries have started using DEC and albendazole tablets in MDA)<sup>6,7</sup>. MDA has been implemented in 51 of the 71 eligible countries<sup>4</sup>. It is recommended that a coverage rate of 70 to 80% continuously for 5-6 yr be achieved during the annual MDA campaign to reduce transmission at very low level<sup>3,4</sup>. However, MDA activities have achieved limited success, even after recommended coverage is achieved. The most common reason cited for partial success in MDA has been the poor compliance with DEC tablet consumption, due to adverse drug reactions<sup>8,9</sup>. Therefore, search for additional and synergistic approaches to achieve LF elimination is an urgent felt need<sup>10,11</sup>. This review analyzes the bottlenecks in achieving high coverage with MDA, and identifies sustainable additional strategies to guide the world towards accelerated LF elimination.

### **Data synthesis**

The published information was collected from major bibliographic databases for biomedical journals, i.e. PubMed, EMBASE, Scopus, Google Scholar, Ovid, & WHO Database. Hand search of the articles and full text of the cross references on lymphatic filariasis and mass drug administration (MDA) was conducted. Personal communication, either by phone or e-mails, was made with researchers and experts on LF in India and other countries. The main focus was on community-based studies, and findings from endemic countries. Articles on use of health education material and inter personal communication were analyzed to assess their effectiveness to increase the compliance for MDA. This systematic search generated a number of articles, which were further shortlisted for inclusion in the review. Full texts of all relevant articles and the information received from experts were read and analyzed and available evidences and main findings were summarized. The suggestions to improve performance are based upon the literature review and analysis and also on the programmatic insight and carefully considered judgement of the authors, one of whom (CL) has extensively been involved in the activities related to LF elimination.

### **Existing challenges in LF elimination**

### Improve coverage and compliance with DEC

MDA has been or is being done in 51 countries for achieving LF elimination; however, the success has been inconsistent<sup>4</sup>. Studies have noted that in spite of high coverage, compliance is poor<sup>12–16</sup>. The major reason for poor results with MDA is the low compliance, which is desirable but difficult to achieve<sup>12</sup>.

A possible approach to address the issue of poor compliance with MDA has been seen in salt fortification. It was reported that salt fortification with DEC have been significantly reduced the prevalence and density of microfilariae<sup>1,17</sup>. There is evidence from Brazil, China, Tanzania, India, and Japan to suggest significant reduction in LF by way of salt fortification with DEC<sup>17-21</sup>. These studies point out that DEC fortified salt might have both micro-filaricidal and adulticidal properties with long-lasting beneficial effects<sup>22</sup>. Furthermore, the children <2 yr of age, and pregnant women are excluded from MDA and salt fortification addresses these challenges<sup>23-24</sup>. Salt fortification has shown similar results in one or two years than what we expect at the end of 4-6 yr of MDA, with minimal adverse effects<sup>10,11,25,26</sup>. Nevertheless, it is to be noted that continuous surveillance and other interventions are critically important with both MDA and salt fortification strategies<sup>27–29</sup>. There are examples from countries like Fiji, Samoa, and French Polynesia, where prevalence was initially reduced significantly<sup>27-29</sup> but increased subsequently when other interventions were ignored<sup>30</sup>.

# Continuous medical education for physicians and health workers

Physicians and health workers have been reported to have limited knowledge about MDA, while a clear understanding of rationale of the MDA programme and positive attitude among physicians increases the compliance<sup>31</sup>. A study from Orissa, India reported that only 34% of the physicians at Primary Health Centre (PHC) and 6.7% of

the private physicians believed that elimination of LF could be possible through MDA programme. The physicians in private sector have poor understanding of MDA than those in government sector and a greater proportion of them did not believe in effectiveness of MDA strategies. Many physicians still believe that 21 days treatment is needed for LF, which they had learned in medical schools in earlier times<sup>16</sup>.

Educational programmes have been demonstrated to have significantly improved knowledge of the physicians and drug distributors<sup>32</sup>, a point in favour of an orientation during Continued Medical Education (CME) programmes. A study in Puducherry, India found that health workers achieved relatively higher coverage and compliance than non-health staff working as drug distributors. It was noted that the health workers had better knowledge, which helped them in passing the correct information to the beneficiaries and improving compliance<sup>33</sup>. Two main problems reported in MDA training programmes were lack of quality assessment, and long time lag between trainings and actual field activities<sup>34</sup>, both of which can severely affect the quality of activities. The CME efforts targeted at health workers can help in improving the coverage and compliance as some of the knowledge into the practice of the health worker can make significant difference.

### IEC material and educational programmes

Studies have reported a statistically significant noncompliance in individuals, who were unaware of the risk of getting LF and benefits of MDA<sup>35,36</sup>. A few other studies have noted that only 3% of local inhabitants knew about MDA activities, and those who were aware, could perceive benefits, and were more likely to comply<sup>13,34</sup>. A study from India reported that approximately 50% of the IEC budget was allocated to newspaper advertisements, in a predominantly rural setting, where people had limited access to print media<sup>34</sup>. It was found that 'fear of adverse reactions', 'lack of perceived benefits', and 'inconsistent implementation of MDA programmes' are the chief barriers to achieve compliance  $^{34,37}$ . The studies have reported School Health Education (SHE) as a cost-effective public health strategy to improve compliance<sup>38</sup>. A study conducted in endemic districts of India where school teachers were educated about MDA activities, who in turn delivered messages to the school students noted that these children had shared this information with their families<sup>39</sup>. Even after 5 months, the results were statistically significant, which indicate sustainable effects of SHE<sup>40,41</sup>. The misconceptions, myths and rumours of or a true adverse event following MDA, may create distrust amongst the community and health professionals involved with LF elimination

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strategies, which is possible to be reduced by effective community educational programme and interpersonal communication<sup>42</sup>.

### **Operational challenges and solutions**

The commonest problem with MDA reported is inadequately managed adverse drug reactions, which leads to poor compliance<sup>34,42–44</sup>. This is especially important as the adverse reactions are more frequent in people with higher microfilariae load, who need DEC tablets most. The reason is that adverse reactions occur due to release of cytokines to counter the effects of filarial antigen, released from dying microfilariae derived molecule<sup>45</sup>. Salt fortification addresses the issue of adverse drug reactions and resulting poor compliance. Nonetheless, better management of adverse events following MDA should be emphasized to ensure higher compliance.

Salt fortification with DEC has few other programmatic and operational benefits: first, the excluded groups of pregnant women and children <2 yr of age are also covered in salt fortification (this group is not given DEC tablets and work as a 'reservoir host' of filariasis, which may result in rapid reversion of filaria, when coverage and compliance is poor). Second, MDA is done in the day time, when a majority of the targeted beneficiaries (working age groups and school going children) are not available at home<sup>34</sup>, which also contribute to poor coverage and compliance. Switching of MDA activities to the night schedule may not be accepted by the drug distributors and community for variety of socio-cultural and geographic reasons. This difficulty can be overcome by DEC fortified salt. Third, DEC salt fortification procedure is simple<sup>21</sup>, almost similar to Iodine fortification<sup>16</sup> that can be done even at village-level, and is logistically and economically feasible even in the rural and remotely located areas. Simplicity of procedure and production at villagelevel can significantly reduce the cost, making it a sustainable public health programme, if implemented properly. Nonetheless, salt fortification has its own challenges, similar to that faced in Iodine fortification of salt<sup>46</sup>. Therefore, a decision on salt fortification also requires careful deliberation and should derive lessons from Iodine fortification programmes in the respective countries. Furthermore, though DEC and Iodine can be fortified together in salt without affecting their efficacy and any additional adverse event<sup>39,47</sup>, many legal and ethical issues are inherent as DEC is not a routine nutrient like Iodine and there are issues of informed consent and governmental liabilities. It also needs approval from the government's ethical committee to deliver drug directly to food. Salt fortification can also lead to complacency in programme people and may have rebound in the LF cases, if sustained attention to other complimentary activities is not paid.

Physicians at the Primary Health Centre (PHC) level are the primary responsible group for the implementation of MDA and often doctors in rural areas have great influence on the community. The influence of doctors on the community members should be used in public health programmes as a tool to increase community acceptance. Lack of perceived benefits of MDA<sup>15,48,49</sup>, and fear of adverse reactions affects compliance. The IEC material and educational programs either are not available or are poorly planned<sup>34</sup>, and a lack of focus on educational programmes may cause poor compliance<sup>35</sup>. IEC material should not be limited only to the description of facts but it should be interactive and appealing to the local community. Folk media for example, drum beating, would be an excellent strategy in the rural community because of their inherent acceptance. Messages on television, radio and newspapers work, if strategically planned and the use of slides in local cinema halls can work as an effective strategy to provide information to the poor and rich people simultaneously<sup>50</sup>. The poor understanding of MDA strategies among health professionals<sup>14,31</sup> need to be immediately addressed by targeted CME<sup>51</sup>.

There are other areas of attention in LF elimination. Urban areas facilitate vector transmission more often than rural areas<sup>52</sup>. Therefore, comprehensive strategies should be developed for urban and crowded areas to increase compliance otherwise these areas will serve as a persistent source of filarial infection. Similarly, case management is a forgotten part and people and health systems should be enabled for LF case management. The presence of LF in any community is an opportunity to understand health system performance. Accessibility of health services should be carefully evaluated in the endemic areas as LF is a disease of the poor. It is because of the limited accessibility to the health services, that many poor people receive treatment for drug adverse reaction from private practitioners, at out of pocket expenditure. Therefore, identification of community members who can record and communicate messages to the PHCs can substantially improve the accessibility and can reduce the treatment cost for poor and high risk populations. There are practical experiences of effective management of adverse events in mass campaigns following measles vaccination in India and other countries too. In the mass measles campaigns in India, proper training of the medical officers in Adverse Events Following Immunization (AEFI) case management, providing them treatment kits, and generating awareness, which helped in effective AEFI case management and successfully running the campaign. The measles campaigns were conducted as school and community-based campaigns and adverse event management was successful in both the settings.

The best practices on LF elimination from different parts of the world should be incorporated in the training programmes, because these provide 'visible examples' and help motivate work-force. A survey was conducted in an endemic area of Japan and blood films from every community member were collected, following which subjects were administered with DEC for 12 days. They were subsequently followed up to understand the relationships between the levels of microfilariae and adverse effects of drug administration<sup>53</sup>. This study could show the relationship between drug adverse reactions to the load of microfilariae. Thereafter, findings from this study were used to generate awareness among people by extensive community education about the MDA programme and vector control activities. This experience also suggested that people from other similar programmes, i.e. malaria control programme can share knowledge and experiences; and can provide technical assistance to contribute to interdisciplinary competencies to improve MDA programme performance<sup>53</sup>. Experiences from within and outside the country on community-based elimination programmes, i.e. Yaws and Polio, should be shared with people involved in LF elimination and lessons derived for improving programme performance<sup>54,55</sup>.

The authors also suggest a few additional points, which are not fully covered in this review. Any opportunity for advocacy with community leaders and other stakeholders should be optimally utilized. Vector control measures have proven very effective in disease control<sup>56,57</sup> and programmatic attention should also be on selective vector control for LF, on night clinics, and case management aspects. The quality of trainings prior to implementation of MDA activities should be improved. Regular evaluation of programme performance and intensive external monitoring of MDA activities are other cross cutting areas, which need strengthening. The broad suggestions to improve programme performance are given in Box 1.

### Conclusions

The effective strategies to improve compliance with DEC tablet ingestion (and exploring the possibility for salt fortification with DEC), targeted continuous medical education programmes for physicians and health workers, and IEC material to improve the knowledge of the community, need immediate re-enforcement in the endemic areas. Additionally, there is a renewed and immediate felt

### Box 1: Programmatic interventions suggested for accelerated LF elimination in endemic countries

- Conduct operational research on the feasibility of salt fortification with DEC and use those lessons for programmatic modifications
- Evolve sustainable and institutional mechanism for continuous medical education of physicians and other health workers about LF, disease, elimination, and MDA activities
- Develop IEC and inter-personal communication strategies to generate awareness amongst community members about LF and MDA
- Ensure the quality of the trainings conducted just prior to the MDA activities, these trainings may be externally monitored
- Intensive monitoring of MDA activities by external monitors and observers, with priority being assigned to the high focus areas
- Ensure sufficient and sustainable funds available at various levels in a timely manner
- Enhance political leadership, with regular review of the programme performance at various levels
- Derive and share lessons from successful implementation of other disease elimination and eradication programmes

need to conduct operational research, evolve sustainable and institutional mechanisms for physicians and health workers education on LF elimination and MDA, strengthen IEC delivery mechanisms, implement internal and external monitoring of the programme implementation, ensure quality of trainings on MDA, make sufficient funds available in timely manner, and to improve political and programmatic leadership. The lessons from other finished and ongoing elimination programs can also be put to use for improving LF elimination programme. The best practices from endemic countries should be used to accelerate LF elimination. It is time that available programmatic knowledge is optimally utilized for global elimination of LF, as soon as possible.

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