Letter in Response to Previous Publication

Redesigning multi-drug therapy: Hasty or judicious?

Dear Editor,

We read with interest the study by Singh I *et al* (2023),[1] "Efficacy of fixed duration multidrug therapy for the treatment of multibacillary leprosy: A prospective observational study from Northern India", which strongly suggests redesigning the treatment regimen for highly bacillated cases given positivity of viable lepra bacilli evidenced by histopathology and two-step real-time polymerase chain reaction in-spite of completing currently recommended WHO MDT regimen. The study also showed active granuloma with foamy macrophages having a substantial load of *acid-fast bacilli* (AFB) in haematoxylin and eosin (H&E) stained image at the time of recruitment as well as at the time of release from treatment primarily having slit skin smear positivity of ≥4+.

Redesigning alternate regimens for highly bacillated cases despite having a highly potent and effective standard MDT regimen raises concerns since, the efficacy of WHO-MDT has been repeatedly tested from time to time which proves worthy. It is also imperative to know whether antimicrobial resistance (AMR) testing was done for all the viable bacilli-positive cases after therapy and whether second-line treatment was considered. As per WHO, the relapse rate is very low (0.1% per year for PB and 0.66% per year for MB) on average. Additionally, the lower frequency of side effects has made it highly acceptable to patients.[2]

A previous study by Hamlet C and Nair P (2023) showed that 18.1% of patients required substitution of standard multi-drug therapy (MDT) with alternate drugs or required alternative treatment regimens; however, about two-thirds of patients who received modified treatment were for adverse drug reactions.[3]

About 10 cases in the study were non-responders to standard MBMDT. The authors also suggested that the lack of response could be due to drug default by patients, persistent bacilli, or drug resistance.

Even after the standard MDT regimen is completed, live bacilli warrant surveillance for antimicrobial resistance (AMR). According to the declaration by the National Strategic Plan and Roadmap for Leprosy 2023–2027, nationwide robust surveillance for anti-microbial resistance (AMR) must be set up, and all relapse cases should be adequately treated as per the NLEP guidelines. The Guidelines Development Group (GDG) by WHO recommends that leprosy patients with rifampicin resistance have to be treated using at least two of the following second-line drugs, i.e. clarithromycin, minocycline or a quinolone (Ofloxacin, levofloxacin or moxifloxacin) plus clofazimine daily for 6 months, followed by clofazimine plus one of the second-line drugs daily for an additional 18 months. For rifampicin plus ofloxacin resistance, quinolones should be avoided, and the recommended treatment is clarithromycin, minocycline and clofazimine for 6 months, followed by clarithromycin or minocycline plus clofazimine for an additional 18 months.[4]

A study by Girdhar B. K. *et al.* (2000) favours treatment duration of patients with high bacillary load may be continued till smear negativity.[5]

A study by Williams D. L. *et al.* (2012) suggests alternative drugs in resistant cases and favours standard WHO MDT regimens to reduce the development of drug resistance.[6]

In the above studies and following standard guidelines, it is evident that viable smear-positive cases must be meticulously tested for antimicrobial resistance (AMR) to identify drug resistance and must be treated as per the standard protocol. So, we conclude that before consequential redesigning of the presently available multidrug treatment (MDT) regimen, strict attention may be given to testing antimicrobial resistance in all cases showing viable bacilli after completion of standard MDT.

Critical analysis of the manuscript

It is noted that the reporting of acid-fast bacilli in the H&E image is inaccurate. No AFB were appreciable in Fig. 1 as AFB visualisation mostly requires a special staining procedure (Ziehl Neelsen staining & Wade Fite staining). Hence, the assertion of showing isolated acid-fast bacilli in the H&E stain is not correct.

How to cite this article: Sagar HK, Pawar HS. Redesigning multi-drug therapy: Hasty or judicious? Indian J Dermatol Venereol Leprol 2023;89:871-2.

Received: August, 2023 **Accepted:** September, 2023 **Published:** October, 2023

DOI: 10.25259/IJDVL_897_2023

Declaration of patient consent
Patient consent is not required as there are no patients in this study.

Financial support and sponsorship
Nil.

Conflict of interest
There is no conflict of interest.

Use of Artificial Intelligence (AI)-Assisted Technology for manuscript preparation
The authors confirm that there was no use of Artificial Intelligence (AI)-Assisted Technology for assisting in the writing or editing of the manuscript, and no images were manipulated using the AI.

Harish Kumar Sagar, Harpreet Singh Pawar[1]

Clinical Division, [1]ICMR-National JALMA Institute For Leprosy And Other Mycobacterial Diseases, Tajganj, Agra, India

***Corresponding author:**
Dr. Harish Kumar Sagar, M.D, Scientist D
Clinical Division, ICMR-National JALMA Institute For Leprosy And Other Mycobacterial Diseases, Tajganj, Agra, India.
drharishkumarsagar@gmail.com

References

1. Singh I, Ahuja M, Lavania M, Pathak VK, Turankar RP, Singh V, Sengupta U, Das L, Kumar A, Saini GB. Efficacy of fixed duration multidrug therapy for the treatment of multibacillary leprosy: A prospective observational study from Northern India. Indian J Dermatol, Venereology and Leprology 2023 Mar 20;89:226–32.
2. Kar HK, Gupta R. Treatment of leprosy. Clin Dermatol 2015;33:55–65.
3. Hamlet C, Nair PS. Scenarios warranting modified treatment regimens in leprosy: A 5-year retrospective study from a tertiary care center. J. Skin Sex. Transmitted Dis 2023;1–5.
4. World Health Organization. Guidelines for the diagnosis, treatment and prevention of leprosy 2018.
5. Girdhar BK, Girdhar AN, Kumar AN. Relapses in multibacillary leprosy patients: effect of length of therapy. Lepr Rev 2000;71:144–53.
6. Williams DL, Gillis TP. Drug-resistant leprosy: monitoring and current status. Lepr Rev 2012;83:269–81.

Authors' reply

Sir,

This is with reference to the letter to the Editor published as 'Redesigning multi-drug therapy: Hasty or judicious?'[1] based on our article 'Efficacy of fixed duration multidrug therapy for the treatment of multibacillary leprosy: A prospective observational study from Northern India'.[2] We would like to thank our readers for taking an interest in our article. The valuable readers have commented regarding the antimicrobial resistance (AMR) testing for all the viable bacilli positive cases after completion of the treatment and if the second-line treatment was taken into consideration or not. In our study, all the cases were tested for the presence of viable load of bacilli after the completion of therapy. However, AMR was done at the time of recruitment only. If the patient was found resistant to any of the drugs of MDT, the regimen was shifted to alternate regimen as recommended by the WHO. We have already published one comparative study on the resistant cases with both MDT vs. WHO-recommended alternate regimen. We tested the load of bacilli in 175 new cases before and after the therapies. In our previous study, we administered a group of rifampicin-resistant relapse cases with an ALT regimen and compared their BI with another rifampicin-resistant group administered the WHO-MB-MDT regimen. We observed in this study that there was a significant reduction in the BI during the treatment of rifampicin-resistant cases with the ALT regimen ($P = 0.0009$). We showed that alternate regimen is showing good response in bacillary clearance in comparison to MDT.[2] The readers have also commented on the accuracy of the reporting of acid-fast bacilli in H&E image. No AFB was appreciable in Figure 1 as AFB visualisation mostly requires special staining procedure (Ziehl Neelsen staining & Wade Fite staining), so the assertion of showing isolated acid-fast bacilli in H&E stain is not correct. In our study,[1] we have done H&E staining to find out whether the granuloma is still active after 12 months of treatment. Hence, the figure legend to Figure 1 mentioning 'Arrows showing foamy macrophages with acid fast bacilli and active granuloma in panel B' is wrong. This error is inadvertent and we sincerely appreciate the readers' feedback on this. We agree that the legend should now read as 'Arrows showing foamy macrophages and active granuloma'.

How to cite this article: Singh I, Ahuja M, Lavania M, Pathak VK, Authors' reply. Indian J Dermatol Venereol Leprol 2023;89:872-3.

Received: October, 2023 **Accepted:** October, 2023 **Published:** October, 2023

DOI: 10.25259/IJDVL_1056_2023