

Multidrug resistant tuberculosis (MDR-TB) in emerging economies in Sub-Saharan Africa: clinicians' public health concerns

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Abstract: Despite improvement in the control of Tuberculosis globally, the disease remains a major public health problem responsible for high morbidity and mortality. In 2013 alone an estimated 9 million people acquired Tuberculosis, while mortality was at 1.5 million people that year. The emergence of multidrug resistant tuberculosis (MDR-TB) is tending to reverse earlier gains in the Tuberculosis control efforts, especially in resources limited settings in Sub Saharan Africa (SSA). The largest negative impact is expected in high-risk populations in whom the prevalence of pulmonary TB is already high. The challenges in these settings are numerous and are important for the epidemiology of MDR-TB. Alliances of negative forces and social determinants of health such as poverty, low levels of literacy, gender inequality and poorly resourced health systems may play a big role in the spread of MDR-TB. Furthermore, high cost of treatment and lack of health workers are hindrances to proper control of TB. HIV infection and male gender have been cited to be risk factors. Efforts to control this epidemic require control of HIV and more male involvement in the most affected regions. In our perspective we discuss epidemiology of MRD-TB in SSA.

Keywords: Epidemic; HIV/AIDS; multidrug resistant tuberculosis (MDR-TB); public health; Sub Saharan Africa (SSA)

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Introduction

Multidrug resistant tuberculosis (MDR-TB) in Sub Saharan Africa (SSA) is an emerging epidemic adding to the current long-standing pandemics of malaria, TB and HIV in the region. The epidemiology and natural history of MDR-TB have been described in specific settings and levels of HIV prevalence (1-4). However, these data may not be generalizable. The emergence of MDR-TB in SSA in the 21st century poses a new threat to health and development, and will potentially reverse some of the health gains registered on TB control. MDR-TB has disproportionately affected the poorest countries in the sub region (1-8). These same countries are already heavily burdened with malaria, tuberculosis and HIV/AIDS (9-15). A constellation of factors, including poverty, co-existent pandemics such as HIV, lack of public health infrastructure and inadequate health personnel is a lethal alliance for potential further spread of MDR-TB. Exacerbating the matter is the reality that countries in this sub region are struggling to scale up diagnosis and appropriate treatment for MDR-TB (10,14).

History of TB drug resistance

The history of TB drug resistance dates back to 1950s when resistance to streptomycin was recognized (16,17). By the 1970s the availability of safer and efficacious medications against the disease remained a re-assurance to public health. Recently, however, reported resistance to multiple antituberculosis drugs especially isoniazid and rifampicin have posed a new threat amidst lack of alternative drugs for first-line treatment (18,19).

MDR-TB and poverty: cause or effect

Poor health infrastructure and systems in SSA are

illustrative of the challenges that many developing countries face (20,21). Poverty remains an ill in the sub-continent in which many countries are emerging as post conflict economies. These situations have made many of these countries inadequately prepared for epidemics. When coupled with low levels of literacy, gender inequity and high burden of TB in the region; poverty exacerbates the spread of MDR-TB. Poor infrastructure including inferior road networks, rudimentary curative clinical services and inadequate public health responses to the new epidemic are all indicative of prevalent background poverty. Inadequate diagnostic and human resource capacity in the health systems remain hindrances to initial and sustainable interventions for the control of MDR-TB.

MDR-TB and HIV link

One cannot think of an emerging disease burden in Africa without thinking of HIV/AIDS. The sub-continent currently has two thirds of the global burden of HIV/AIDS (22), a scenario which is likely to fuel the impact of a pandemic MDR-TB. Already, evidence indicates that patients with HIV are more likely to develop MDR-TB (1,3,7). A paucity of data on interactions between antivirals for HIV/AIDS and antibiotic treatment for MDR-TB among African populations remains a challenge, making the already MDR-TB vulnerable HIV/AIDS patients at risk of potential drug interactions (6,23). The efficacy of BCG vaccine for TB in SSA has recently come into question and requires urgent re-evaluation.

Transmission

The majority of current infections are primary MDR-TB. There is potential that some cases are secondary MDR-TB. Case definitions of primary and secondary MDR-TB are difficult to make, but are required so as to improve identification of contact, at risk, probable and confirmed case categories. In addition, proper case definitions will enable appropriate case management and prevention efforts. Mapping of the epidemic across the region remains a public health challenge. Case recognition and confirmation are inadequate, and no accurate estimates of resources needed to tackle the problem have been made. The most socially and economically vulnerable populations especially children, women, elderly and inmates in prisons, remain at greater risk. However, the relative risk for MDR-TB among different populations, age strata, health status and

geographical locations remains poorly described (2,5). The risk of transmission of MDR-TB infections may be similar to risk models described for other airborne infectious diseases. Evidence from some data on MDR-TB indicates that the risk of transmission of MDR-TB is dependent on poorly diagnosed and/or incorrectly treated TB in a patient (5), poor anti-TB drug adherence and inadequate dosing (1), background prevalence and the type of resistance (primary or possible secondarily acquired resistance) (5). Other risk facts include underlying HIV status of either the primary TB case or the exposed contact (1). It is also plausible that the frequency of contact with infectious aerosol is a risk factor. The early picture of MDR-TB in the SSA region is that of marked heterogeneity. This may be due to poor diagnostics, low index of suspicion by clinicians or background distribution of other predisposing factors. Like many previous epidemics, there is a potential of MDR-TB to diffuse widely in the community over a period of time. The duration and the lifespan of the epidemic will be dependent on availability of effective interventions and control measures.

Approaches to management of MDR-TB

There are few models of effective treatment of MDR-TB in areas with a high prevalence of HIV (3,7). The high costs for treatment of MDR-TB are prohibitive for poorer countries (24). Moreover, the region is also faced with a lack of research into effective and culturally acceptable strategies for prevention and treatment of this condition. Resources for such research have also not been adequately channeled into this culturally diverse region (25). Furthermore, the region has lost a large portion of its trained health personnel to wealthier countries, who have recruited them to manage their own shortfalls (26-31). These healthcare workers will be desperately needed as the MDR-TB epidemic diffuses through the subcontinent's vulnerable population already burdened with the four poverty related ills of malaria, tuberculosis, malnutrition and HIV/AIDS.

The recommended quinolone based therapy for MDR-TB includes antibiotics already widely used for other conditions. The long duration of MDR-TB regimen (32) may compromise patient compliance, which may be a risk for extensively drug-resistant TB (1). There are no effective national or regional guidelines in most parts of SSA restricting the available antibiotics for MDR-TB for exclusive use for this condition only (33). Lessons from HIV/AIDS treatment programmes may offer some insight

to potential management approaches, but first they need to be proven. The shortage of trained health workers for HIV treatment programmes was circumvented by allowing lower cadre health workers to diagnose HIV and prescribe antiretroviral therapy (34). These packages may not be easily replicated in treatment of MDR-TB because of the current complex diagnostic and treatment protocols involved. At the moment, specialized treatment centres with adequate capacity are recommended to handle MDR-TB. Another contrast is that in HIV/AIDS treatment, outpatient and home care have cut down on long in-hospital stays (35).

The front line clinicians in SSA have a huge challenge recognizing, diagnosing and successfully treating MDR-TB, resulting in delays in patient care.

Summary

Multidrug resistant TB has posed a public health problem with potential to reverse some of the health gains in the control of TB in the SSA. Joint national, regional and continental efforts are required to control this epidemic. Whereas the history of TB drug resistance has been on for about 5 decades that of MDR-TB is only in the recent times. However, this may be a precursor of an era of XDR-TB. Efforts to control this epidemic require control of HIV and more male involvement in the most affected regions.

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References

- Cox HS, McDermid C, Azevedo V, et al. Epidemic levels of drug resistant tuberculosis (MDR and XDR-TB) in a high HIV prevalence setting in Khayelitsha, South Africa. PLoS One 2010;5:e13901.
- 2. Cooke GS, Beaton RK, Lessells RJ, et al. International spread of MDR TB from Tugela Ferry, South Africa. Emerg Infect Dis 2011;17:2035-7.
- 3. Seung KJ, Omatayo DB, Keshavjee S, et al. Early outcomes of MDR-TB treatment in a high HIV-prevalence setting in Southern Africa. PLoS One 2009;4:e7186.
- 4. Padayatchi N, Friedland G. Decentralised management of drug-resistant tuberculosis (MDR- and XDR-TB) in South Africa: an alternative model of care. Int J Tuberc Lung Dis 2008;12:978-80.
- 5. Menon S. Preventing nosocomial MDR TB transmission in sub Saharan Africa: where are we at? Glob J Health Sci 2013;5:200-10.
- Brust JC, Shah NS, van der Merwe TL, et al. Adverse events in an integrated home-based treatment program for MDR-TB and HIV in KwaZulu-Natal, South Africa. J Acquir Immune Defic Syndr 2013;62:436-40.
- 7. Brust JC, Shah NS, Scott M, et al. Integrated, home-based treatment for MDR-TB and HIV in rural South Africa: an alternate model of care. Int J Tuberc Lung Dis 2012;16:998-1004.
- 8. Loveday M, Wallengren K, Voce A, et al. Comparing early treatment outcomes of MDR-TB in decentralised and centralised settings in KwaZulu-Natal, South Africa. Int J Tuberc Lung Dis 2012;16:209-15.
- Tshikuka Mulumba JG, Atua Matindii B, Kilauzi AL, et al. Severity of outcomes associated to types of HIV coinfection with TB and malaria in a setting where the three pandemics overlap. J Community Health 2012;37:1234-8.

- Goldberg DE, Siliciano RF, Jacobs WR Jr. Outwitting evolution: fighting drug-resistant TB, malaria, and HIV. Cell 2012;148:1271-83.
- 11. Hedt BL, Laufer MK, Cohen T. Drug resistance surveillance in resource-poor settings: current methods and considerations for TB, HIV, and malaria. Am J Trop Med Hyg 2011;84:192-9.
- Kerouedan D. The Global Fund to fight HIV/AIDS, TB and Malaria 5-y: evaluation policy issues. Bull Soc Pathol Exot 2010;103:119-22.
- Kerouedan D. The Global Fund to fight HIV/AIDS, TB and malaria policy issues. Med Trop (Mars) 2010;70:19-27.
- Fontela PS, Pant Pai N, Schiller I, et al. Quality and reporting of diagnostic accuracy studies in TB, HIV and malaria: evaluation using QUADAS and STARD standards. PLoS One 2009;4:e7753.
- Birx D, de Souza M, Nkengasong JN. Laboratory challenges in the scaling up of HIV, TB, and malaria programs: The interaction of health and laboratory systems, clinical research, and service delivery. Am J Clin Pathol 2009;131:849-51.
- Dissmann E. Clinical and bacterial resistance during treatment of tuberculosis with streptomycin, PAS, TB 1 and INH. Tuberkulosearzt 1953;7:205-14.
- 17. Pothmann FJ, Fehr KO. Resistance of the tubercle bacillus to streptomycin and to streptomycin in combination with TB I in tuberculous meningitis. Beitr Klin Tuberk Spezif Tuberkuloseforsch 1950;103:422-30.
- Sormani MP. Modeling the distribution of new MRI cortical lesions in multiple sclerosis longitudinal studies by Sormani MP, Calabrese M, Signori A, Giorgio A, Gallo P, De Stefano N [PLoS One 2011;6(10):e26712. Epub 2011 October 20]. Mult Scler Relat Disord 2012;1:108.
- 19. Kimerling ME, Kluge H, Vezhnina N, et al. Inadequacy of the current WHO re-treatment regimen in a central Siberian prison: treatment failure and MDR-TB. Int J Tuberc Lung Dis 1999;3:451-3.
- Cluver L, Boyes M, Orkin M, et al. Poverty, AIDS and child health: identifying highest-risk children in South Africa. S Afr Med J 2013;103:910-5.
- 21. Muula AS. My Africa. Poverty, health, disease, and medical

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- journalism. Croat Med J 2009;50:598-9.
- 22. Ramjee G, Daniels B. Women and HIV in Sub-Saharan Africa. AIDS Res Ther 2013;10:30.
- 23. Van der Walt M, Lancaster J, Odendaal R, et al. Serious treatment related adverse drug reactions amongst anti-retroviral naïve MDR-TB patients. PLoS One 2013;8:e58817.
- 24. Ollé-Goig JE. Drugs for MDR-TB in Uganda. Int J Tuberc Lung Dis 2004;8:271.
- 25. Sherr K, Requejo JH, Basinga P. Implementation research to catalyze advances in health systems strengthening in sub-Saharan Africa: the African Health Initiative. BMC Health Serv Res 2013;13 Suppl 2:S1.
- Kasper J, Bajunirwe F. Brain drain in sub-Saharan Africa: contributing factors, potential remedies and the role of academic medical centres. Arch Dis Child 2012;97:973-9.
- 27. van Rensburg T. Realities of medicine in South Africa lie behind its brain drain. BMJ 2012;344:e201.
- 28. Oberoi SS, Lin V. Brain drain of doctors from southern Africa: brain gain for Australia. Aust Health Rev 2006;30:25-33.
- 29. Rodnick JE. Africa: some thoughts on the medical brain drain. Fam Med 2006;38:62-3.
- Sangosanya GO. Health in Africa: medical brain drain is a consequence of bad policy. BMJ 2005;331:905.
- 31. Makasa E. Africa's medical brain drain: why I want to stay in Africa. BMJ 2005;331:780;discussion 780-1.
- 32. Mirsaeidi SM, Tabarsi P, Khoshnood K, et al. Treatment of multiple drug-resistant tuberculosis (MDR-TB) in Iran. Int J Infect Dis 2005;9:317-22.
- 33. Tang S, Tan S, Yao L, et al. Risk factors for poor treatment outcomes in patients with MDR-TB and XDR-TB in China: retrospective multi-center investigation. PLoS One 2013;8:e82943.
- 34. Adams-Chapman I, Stoll BJ. Neonatal infection and long-term neurodevelopmental outcome in the preterm infant. Curr Opin Infect Dis 2006;19:290-7.
- 35. Bharty S, Prakash B, Saraf S, et al. Initiation of MDR TB treatment: is hospitalization worth? Indian J Tuberc 2014;61:57-64.